

Department: UAMS Institutional Review Board
Policy Number: 1.7
Section: Principles and Authority
Effective Date: February 8, 2005
Revision Date: March 29, 2007; January 24, 2011

SUBJECT: Executive Committee

I. Purpose

The purpose of this policy and procedure is to describe the role and responsibility of the IRB Executive Committee (EC).

II. Policy

The EC will be maintained as an active resource to identify new IRB policies and procedures necessary to ensure the efficient operation of the IRB, to review and amend current policies and procedures as needed and to ensure compliance with the standards of human subject protections as set forth in the Belmont Report and federal, state and institutional rules and regulation.

EC Composition: The EC will consist of the Vice Chancellor for Research, the Chair(s) of IRB, the Director of the IRB and the Research Compliance Officer or designee. As needed, IRB reviewers, research staff or representatives from other offices or institutions, such as the Research Support Center, Arkansas Children's Hospital Research Institute or the General Counsel's office will be invited as needed.

III. Procedure

1. Required Meeting: Each year, the EC will conduct a meeting to review the resources allocated to the human research protection program to ensure that the necessary protections are in place for thorough and timely review and oversight. This will include at a minimum a review of:

- a. The financial allocations for IRB operations, including staffing, office equipment and space;
- b. The number of IRBs in operation;
- c. The volume and types of research reviewed;
- d. The associated workloads of the IRB Reviewers, Chairs and Staff Members; and
- e. The performance of the IRB Reviewers and any training or replacement recommendations.

2. Additional Meetings: The EC will meet, as needed, to address policy concerns, updates, or new regulations and to review, revise and/or draft policies and procedures. Recommendations for agenda items may originate from the IRB Committees, Administrators, Research Personnel or other Institutional Committee.

Department: UAMS Institutional Review Board
Policy Number: 1.1
Section: Principles and Authority
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 5, 2004;
February 8, 2005; January 24, 2011

SUBJECT: Principles Governing the Committee

All human subject research conducted by the University of Arkansas for Medical Sciences (UAMS), its staff, employees, faculty, students and any institution or individual using the UAMS IRB, is guided by the ethical principles set forth in the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (the "Belmont Report") .

The three basic principles relevant to the protection of human subjects in biomedical and behavioral research as set forth in the Belmont Report are:

Respect for Persons: recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy;

Beneficence: obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm; and

Justice: fairness in the distribution of research benefits and burdens.

The IRB operates under a Federalwide Assurance (FWA) in which it agrees to uphold the ethical principles of the Belmont Report and to apply 45 CFR 46 and its Subparts to all human subject research, regardless of funding source. In addition, the IRB operates according to state and institutional regulations.

In order for the IRB to meet its ethical principles for review and remain free from undue influence, it is critical that the confidentiality of all IRB proceedings be maintained.

Access to the IRB database, protocols provided for review or consultation, and attendance at IRB meetings will potentially provide information concerning research ideas, confidential information of companies, pre-marketing data and many other kinds of confidential and sensitive personal and business materials.

Access to this information is for IRB decision making purposes only, and use of such information for any other purpose would be a violation of the confidentiality agreement previously signed and the legal and ethical principles by which the University of Arkansas is bound.

All discussions, meetings, documents and decisions of the IRB must be kept confidential.

The IRB Director or Vice Chancellor for Research should be notified of any individual (i.e. colleague, media representative) attempting to obtain information about specific IRB proceedings. Media representatives must also be directed to the UAMS Office of Communications and Marketing.

Department: UAMS Institutional Review Board
Policy Number: 1.2
Section: Principles and Authority
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 5, 2004; February 8, 2005;
January 24, 2011

SUBJECT: Authority of the Committee

As outlined in the UAMS Human Research Protections Program Plan, the IRB has the authority to:

1. Approve, disapprove, or require modifications of all Human Research activities;
2. Require progress reports from the investigators and oversee the conduct of the studies;
3. Suspend or terminate approval of an ongoing study;
4. Reopen terminated/closed protocols;
5. Observe or have a third party observe the consent process and the research

In order to approve Human Research, the IRB shall determine that all of requirements outlined in IRB Policy 7.1 are satisfied.

In its review of Human Research, the IRB has jurisdiction over all aspects of the research including, but not limited to:

Methods of identifying potential subjects

Methods proposed for contacting potential subjects

Materials to recruit subjects and proposed compensation

Pilot studies

Proposals to use or provide stored blood, tissues, or confidential data

Surveys and questionnaires

The informed consent process and forms

Surveys, questionnaires, and any other research-related materials that will be seen by the subject

The protocol and summary of the research

Evaluation of risks and benefits to subjects

Unanticipated problems involving risk to subjects

Proposed changes to the research

Continuing reviews

Use of investigational drugs and devices in emergencies

Humanitarian use of drugs and devices

Eligibility for exemption or expedited review

No Human Research project may begin until IRB approval has been received. Human Research approved by the IRB may be subject to further review by other institutional committees or officials. The institution where the research will be conducted retains the right to disapprove any research covered by these policies. However, an institution may not approve any research that the UAMS IRB has disapproved or declined.

Department: UAMS Institutional Review Board
Policy Number: 1.4
Section: Principles and Authority
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 5, 2004; February 25, 2005; March 5, 2008; January 24, 2011

SUBJECT: Studies Requiring Review and Human Research Determinations

I. Purpose

The purpose of this policy and procedure is to explain the types of projects for which the IRB has review oversight responsibilities and how to obtain a determination as to whether a project is Human Research.

II. Definitions

A. ARIA: Abbreviation for Automated Research Information Administrator. Electronic IRB submission system.

B. Clinical Investigation: Any experiment that involves a test article and one or more human subjects AND that is subject to the Food and Drug Administration (FDA) regulations by one of the following:

- 1) Meets the requirements for prior submission to the FDA under section 505(i) of the Federal Drug, Food and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice; or
- 2) Meets the requirements for prior submission to the FDA under 520(g) of the Federal Drug, Food and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; or
- 3) Any activity the results of which are intended to be submitted or inspected by the FDA to support applications for research or marketing permits for products.

C. Human Subject (subject and participant used interchangeably):

- 1) An individual who is or becomes a participant in research either as a recipient of a test article, as a control, or an individual on whose specimen an investigational device is used; or
- 2) A living individual about whom an investigator (whether professional or student) conducting research obtains:
 - a. Data, of any kind, through intervention or interaction with the individual; OR
 - b. Identifiable private information even in the absence of intervention or interaction.

For the purposes of this definition:

- **Intervention** means physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject's environment that are performed for research purposes.
- **Interaction** means communication or interpersonal contact between Investigator and subject or participant.
- **Private Information** means information about behavior that occurs in a context in which an individual can reasonable 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 Information** means information that is individually identifiable (identity of subject is or may readily be ascertained or associated with the information).

D. Human Research: Any activity that meets the definition of:

- 1) Research AND involves Human Subjects; OR
- 2) Clinical Investigation.

E. Non-Human Research: An activity that does not meet the definitions of Human Research as per this policy.

- F. Research:** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Systematic: Activities must be systematic to be considered research. Activities that involve predetermined methods for answering a specific question, testing hypotheses or theories are systematic and might include interviews, program evaluations, and observational studies. Activities that are not normally systematic are training activities where an individual is trained to perform a certain technique or task or to teach proficiency in using a certain method.

Generalizable Knowledge: Activities must contribute to generalizable knowledge or have an intent to extend beyond an internal use or department. Many thesis, dissertation or preceptorship projects are intended to extend beyond the graduate's department and therefore are considered research. Activities that are typically not generalizable are course evaluations that cannot be generalized to others and quality assurance type activities that are only intended to improve the performance of a unit, division, or department.

- G. Test Article:** Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product or any other article subject to FDA regulations.

III. Policy

- A. Human Research:** All activities where UAMS employees, students and agents are clearly engaged in Human Research must submit a new protocol application to the IRB through ARIA. UAMS follows OHRP Guidance on "Engagement of Institutions in Research". This applies to all Human Research, regardless of whether the activity is exempt, expedited or requires full board review. No Human Research study may be initiated prior to IRB approval.
- B. Determinations:** Activities, in which it is unclear as to whether it is Human Research, must be submitted to the IRB for determination according to the procedures described below. In questionable cases, the IRB retains the authority to make the final determination whether an activity meets the definition of Human Research.
- C. Decedents/Cadavers:** A research project involving cadavers or data/specimens collected solely from decedents is not Human Research, provided the research does not involve the use of a Test Article. The research may, however, still be subject to HIPAA requirements. If conducting this type of research, contact the IRB, which also serves as the Privacy Board, for more information on decedent research.
- D. Case Reports:** For the purpose of this policy, a case report is defined as the collection and/or presentation of existing clinical information from three or fewer patients to illustrate an interesting or unique situation. Activities meeting this definition are not considered Human Research by the UAMS IRB and do not require IRB Review or Approval. The use and disclosure of patient information in this manner is still subject to HIPAA requirements.
- E. Non-Human Research:** Projects which are clearly Non-Human Research are not required to submit a Determination Form to the IRB. Investigators may choose to submit a determination if they wish. Some third parties such as journals, commercial tissue suppliers and funding agencies ask for documentation of institutional acknowledgment of even Non-Human Research projects.

The IRB has the expertise and experience in the application of the regulatory definitions. Investigators are encouraged to proceed with caution when making their own determinations of when something is clearly Non-Human Research. If the IRB reviews a project previously determined by an Investigator to be Non-Human Research and disagrees with the Investigator's determination, the IRB decision will be the authoritative decision and IRB Policy 12.6 will be followed.

IV. Procedure for Human Research Determination

- A.** Submit completed Determination Request Form to irb@uams.edu. The IRB Director or Designee will determine whether the activity is Human Research and provide a Determination Letter.
- 1. Human Research:** If the activity is determined to be Human Research, a new protocol application will need to be submitted in ARIA.
 - 2. Non-Human Research:** If the activity is not Human Research, no further IRB review is needed unless the scope of the activity changes. If the intent or scope of the activity changes, contact the IRB for an additional determination.

Department: UAMS Institutional Review Board
Policy Number: 1.5
Section: Principles and Authority
Effective Date: August 12, 2004
Revision Date: February 8, 2005; January 24, 2011

SUBJECT: IRB Independence from Undue Influence

I. Policy

Individual IRB Reviewers, whether employed by the institution or affiliate or community reviewers, have both the obligation and right to report any undue pressure upon them to make decisions at the convened IRB meetings that would favor an individual investigator or the institution over the welfare and safety of the research subject. The IRB is supported by other individuals (i.e. IRB Director and staff, compliance personnel, research administrators) who also have an obligation to report under this policy. These individuals may be pressured to provide guidance, take certain actions or to ignore certain events that would favor an investigator or the institution over the welfare and safety of the research subject.

II. Procedure for Reporting of Undue Influence

Concerns may be reported, in person or in writing, to the IRB Chair, IRB Director, Vice Chancellor for Research, Legal Counsel, Deans, or Department Chairs. Individuals may also report concerns anonymously basis by calling the Compliance Hotline at (888) 511-3969.

III. Response to Reports of Undue Influence

Regardless of the reporting option chosen, the Vice Chancellor for Research at UAMS will be informed and will be responsible for the official investigation of the reported undue pressure. In a timely manner, the Vice Chancellor for Research at UAMS will inform the person making the report (if the reporter did not wish to remain anonymous) of the investigation findings and actions taken.

IV. Examples of Undue Influence that Must be Reported

The IRB member is an Assistant Professor in an academic department and is due for consideration of promotion and tenure. A full Professor on the same department's Promotion and Tenure Committee has a grant that has received a favorable score for funding. The IRB has found problems with the proposed protocol and consent resulting in what the full Professor considers needless delays. The full Professor asks the IRB member to disclose proceedings of the convened IRB meeting at which his protocol was discussed and voted on. In particular, the full Professor asks for names of IRB Committee members who reviewed and/or spoke up against his protocol or voted unfavorably so he can contact them to express his displeasure and perhaps to bring his concerns with them to the Dean. Because the IRB member knows that all convened meeting proceedings are confidential, he must refuse the full Professor's request and report the incident.

A Departmental Chairman requests a visit with an IRB member who is a senior faculty member in their department. The Chairman expresses concern that the IRB committee has been making too many unfavorable decisions regarding protocols from that department. The IRB member is asked to divulge information concerning how the convened IRB Committee makes decisions and how the process could be made more favorable to the department's applications. Specific protocols are not discussed but the Chairman clearly is seeking to influence decisions made by the IRB. The IRB member, knowing that all IRB proceedings are confidential, should refer the Chairman to the IRB Director for more information about IRB operations.

The Office of Research Compliance identifies a study for routine audit. The study involves a product developed by a start-up company in which the Institution has an interest. The compliance office contacts the study team to schedule the audit. The next day, the Research Compliance Officer is contacted by an individual in upper administration involved in the budget process. The administrator mentions that he's just been notified the study is up for an audit and how the timing is unfortunate since great strides are being made with the product. The compliance officer explains that this is just a routine audit and that if everything is in order there should be no impact on the study. The administrator ends the conversation by reminding the compliance officer that the budget for the research compliance office is up for review soon and it would be a shame if the recent budget cuts had to be applied to the compliance office. The audit should continue as planned and the Research Compliance Officer should notify the Vice Chancellor for Research.

Department: UAMS Institutional Review Board
Policy Number: 2.1
Section: Relationships
Effective Date: July 31, 2002
Revision Date: August 23, 2004

SUBJECT: To the Administration

The University of Arkansas for Medical Sciences (UAMS) IRB is appointed by the Vice Chancellor for Academic Affairs and Sponsored Research at UAMS. Selection of members is representative of the academic units of the campus: College of Medicine, College of Nursing, College of Pharmacy, College of Health Related Professions, College of Public Health, the Office of Educational Development; and lay members from the community and other affiliated and non-affiliated institutions.

Administratively, the IRB support staff reports to the Associate Director of the Office of Research and Sponsored Programs (ORSP). ORSP is under the direction of the Vice Chancellor for Academic Affairs and Sponsored Research at UAMS.”

Research that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of UAMS. However, those officials may not approve the research if it has not been approved by an IRB according to appropriate federal regulations.

Department: UAMS Institutional Review Board
Policy Number: 2.2
Section: Relationships
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 5, 2004; February 8, 2005; January 24, 2011

SUBJECT: To Other University or Affiliated Committees/Departments

I. Purpose

The purpose of this policy and procedure is to explain how the IRB coordinates its review with other committees from UAMS or affiliated institutional committees or departments.

Policy: The UAMS IRBs function independently of (but coordinates its activities with) other committees and departments at UAMS. The IRBs will work in conjunction with other university or institutional committees; however, it will review research projects independently to ensure that human subjects will be adequately protected.

1. As appropriate to the type of research proposed and therefore the other committee approvals required, the IRB will grant its approval as follows:

1.1 Institutional Biosafety Committee: Human Research involving the direct and deliberate transfer of biologically derived products listed below into human subjects must receive approval from the appropriate Biosafety Committee before final IRB approval may be granted:

- 1.1.1 Experimentation using BL2 or BL3 infectious microorganisms.
- 1.1.2 Experimentation using carcinogenic (known or suspected) or highly toxic compounds.
- 1.1.3 Recombinant DNA, if BL2 or BL3 organisms are involved or if genetic modification might increase pathogenicity, transmissibility, host range or antibiotic resistance of a pathogen. The transfer of toxin genes lethal for vertebrates at an LD₅₀ of <100 ng/kg.
- 1.1.4 Modification of the germline genes of animals (transgenic).
- 1.1.5 Human gene therapy even if the recombinant DNA is produced elsewhere.

The IRB may grant final approval pending approval of the Institution's Biosafety Committee. The IRB Chair or experienced IRB member designated by the Chair will review the approval of the Institution's Biosafety Committee. If the approval raises issues or questions that are directly relevant to the determinations required by the IRB, or request more than minor changes to the research approved by the IRB, the information or changes will be placed on the agenda of a convened IRB meeting for review. Otherwise, the IRB Chair or experienced IRB member designated by the Chair may grant final approval under expedited procedures.

1.2 Radiation Safety Committee: Human Research involving exposing human subjects to radiation through x-rays or radionuclides for which the subject would otherwise not have been exposed except for the research must receive approval from the appropriate Radiation Safety committee before final IRB approval may be granted. The IRB may grant final approval pending approval of the radiation safety committee. The IRB Chair or experienced IRB member designated by the Chair will review the approval of the Radiation Safety Committee. If the approval raises issues or questions that are directly relevant to the determinations required by the IRB, or request more than minor changes to the research approved by the IRB, the information or changes will be placed on the agenda of a convened IRB meeting for review. Otherwise, the IRB Chair or experienced IRB member designated by the Chair may grant final approval under expedited procedures.

1.3. Conflicts of Interest Committee: Research involving any actual or perceived conflicts of interest as *per* institutional policies must receive approval from the Conflict of Interest Committee. The IRB will not review research with a declared financial interest until the Conflicts of Interest Committee has completed its evaluation and a management plan is in place. The written determination of the Conflicts

of Interest Committee, and the reasons for those determinations, will be provided to all IRB members for review at a convened meeting. ORSP maintains all the annual disclosures of conflicts of interest and the proposed management plan. The IRB shall have access to conflict disclosures in order to determine if the conflict of interest affects the IRB approval criteria. The IRB has the final authority to determine whether the conflict and the management plan as written allow the research to be approved. While the COIC may provide suggested language to be used to disclose the conflict in the consent form, the IRB retains the authority to require changes to the suggested language.

1.4 Pharmacy Approval. Pharmacy approval from the involved institution's pharmacy will be required prior to granting final IRB approval. The IRB may grant final approval pending approval of the institution's pharmacy. The IRB Chair or experienced IRB member designated by the Chair will review the approval of the institution's pharmacy. If the approval raises issues or questions that are directly relevant to the determinations required by the IRB, or request more than minor changes to the research approved by the IRB, the information or changes will be placed on the agenda of a convened IRB meeting for review. Otherwise, the IRB Chair or experienced IRB member designated by the Chair may grant final approval under expedited procedures.

1.5 Other Committees. Research projects may be subject to review and approval of other committees where the research is being conducted or for certain types of research (Examples: GCRC, PRMC, grants and contracts office). Approval from such other committees will not be required prior to IRB final approval, however, the research should not begin until those approvals are obtained.

2. Investigators will, as applicable:

- 2.1** Seek approval from other committees as required by the IRB or institutional requirements prior to commencing the research project.
- 2.2** Ensure that all recommendations and requirements are incorporated and submitted to and approved by the IRB before implementation.

Department: UAMS Human Research Advisory Committee
Policy Number: 2.3
Section: Relationships
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; March 5, 2004; November 18, 2002

SUBJECT: To Other Institutions

Purpose: The purpose of this policy and procedure is to describe the relationship that the UAMS IRBs have to other Institutions.

Definitions:

IRB Authorization Agreement: Formal, written agreement documenting the roles and responsibilities of Institution providing the IRB and Institution relying on the IRB.

IRB of Record: IRB listed as an approved reviewing body for Institution's research.

Performance Site: Location where human participant research is being conducted either under the direction of or in direct collaboration with PI utilizing UAMS IRB.

Policy: In order to avoid duplication of effort in research projects with performance sites, UAMS may enter into IRB Authorization Agreements with other institutions to review research for the site, or to have research reviewed for UAMS. Each institution remains responsible for safeguarding the rights and welfare of human subjects and for complying with the terms of the Federalwide Assurance. UAMS will only rely on other IRBs that are operated by AAHRPP accredited organizations.

References: IRB Policies 1.3 and 2.7

UAMS serves as the IRB of Record for all of the research conducted at:

University of Arkansas for Medical Sciences (UAMS)
Arkansas Children's Hospital (ACH)
Arkansas Children's Hospital Research Institute (ACHRI)
Central Arkansas Veteran's Healthcare System (CAVHS)

UAMS serves as the IRB of Record for certain research at:

Arkansas Department of Health (ADH) – All research involving ADH employees conducted at or in conjunction with UAMS, ACH, ACHRI or CAVHS

National Center for Toxicological Research (NCTR) – All research involving NCTR employees conducted at or in conjunction with UAMS, ACH, ACHRI or CAVHS, provided that the FDA IRB retains initial review requirements.

University of Arkansas at Little Rock (UALR) – All research involving UALR students or employees conducted on the UAMS, ACH, ACHRI or CAVHS campus.

Procedure:

1. Investigator will:

- 1.1 Identify All Performance Sites in ARIA Application for New Submission or in ARIA Modification if needing to add a new Performance Site after Initiation.
- 1.2 For any Performance Site that has its own FWA and IRB:

- 1.2.1 Provide FWA# and IRB approval from that Performance Site before initiation of research at that site. OR
- 1.2.2 If Performance Site is AAHRPP accredited and wishes to assume IRB responsibilities for any individual subject to the UAMS IRB oversight or name the UAMS IRB as its IRB of record for a limited study, contact the IRB Director for assistance, preferably prior to ARIA submission, to see if allowable and to arrange IRB authorization agreement.
- 1.3 For any Performance Site that has a FWA but no IRB: Contact the IRB Director for assistance. UAMS will serve as the IRB of record under an IRB authorization agreement for many local organizations working with UAMS investigators.
- 1.4 For any Performance Site that does not have a FWA or an IRB: Each site engaged in research must operate under appropriate assurances. Contact the IRB Director in order to assist the Site with obtaining a FWA and putting in place an IRB Authorization agreement if allowable.

2. IRB Director or Designee will:

- 2.1 For all Performance Sites:
 - 2.1.1 Check the OHRP website for approved assurances to see if Performance Site has a current FWA and IRB of Record.
 - 2.1.2 Review the planned research and roles of the investigator, in conjunction with IRB Chair or Office of Research Compliance as necessary, to determine if it would be most expedient, as applicable, to:
 - 2.1.2.1 Rely on the other Site's IRB for specific research project and enter into an IRB Authorization Agreement delegating IRB review responsibilities for specific study to other Site, provided other Site's IRB is operated by an AAHRPP accredited organization;
 - 2.1.2.2 Enter into a Dual oversight agreement with Site;
 - 2.1.2.3 Assist Site in obtaining their own FWA through OHRP; and/or
 - 2.1.2.4 Enter into an IRB Authorization where UAMS becomes Site's IRB of record for specific study.
 - 2.1.3 Relay decision either way to Investigator.
 - 2.1.4 Follow-up as needed.

Department: UAMS Institutional Review Board
Policy Number: 2.4
Section: Relationships
Effective Date: July 31, 2002
Revision Date: March 5, 2004; January 24, 2011

SUBJECT: To the UAMS Office of Research Compliance

The UAMS Office of Research Compliance (ORC) coordinates UAMS' comprehensive research compliance program. The ORC demonstrates UAMS' commitment to human subject protection through oversight and education promoting the responsible conduct of research. The ORC also investigates allegations of noncompliance and advises the IRB on regulatory issues. ORC reports to the Vice Chancellor for Institutional Compliance (VCIC) and works cooperatively with, but is independent of, the UAMS IRB.

The research compliance program applies to all research approved by the UAMS IRB and conducted by its faculty, staff, students, residents and other affiliated agents, including volunteer faculty who utilize university resources or personnel. ORC will coordinate compliance efforts on behalf of the UAMS administration at Arkansas Children's Hospital Research Institute and other institutions using the UAMS IRB.

Audits of research studies and IRB Operations will be conducted by ORC auditing staff as described in ORC policy. The IRB or IRB director may request ORC audits or other auditing activities. All audit proceedings, audit reports, memoranda or other data are confidential. ORC audit reports will normally be provided to the IRB for its review. The IRB may request ORC involvement in audit-related remediation activities.

Subject complaints regarding research participation may be forwarded to the ORC when ORC participation in investigating the complaints is required.

The ORC also may serve as a liaison between the IRB and federal regulatory agencies.

Department: UAMS Institutional Review Board
Policy Number: 2.5
Section: Relationships
Effective Date: July 31, 2002
Revision Date: March 5, 2004

SUBJECT: To the Office of Research and Sponsored Programs

The UAMS Office of Research and Sponsored Programs (ORSP) serves as the central coordination point for all research and sponsored programs. This office works directly with principal investigators to insure that the management of funds from granting agencies are made available with minimum loss of time and effort. ORSP is responsible for protecting UAMS interests through the review of sponsored project proposals, contract and grant award review and negotiation, administration of funds, and policy and procedure initiation and implementation. In addition, ORSP offers educational opportunities for researchers and other health care support staff. ORSP works with the IRB by referring principal investigators to the IRB submission process when grants involving human subject research are received. In addition, continuation grant awards are dependent upon continuing review approvals issued by the IRB for research protocols originating from grants. ORSP is an independent department within the Academic Affairs Division and reports directly to the VCAA.

Department: UAMS Institutional Review Board
Policy Number: 2.6
Section: Relationships
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 5, 2004; February 8, 2005; April 5, 2007; March 5, 2008; January 24, 2011

SUBJECT: Reporting to Appropriate Federal Oversight Bodies, Institutional Officials and Research Sponsors

DHHS and FDA regulations require reporting in three situations:

1. Unanticipated problems involving risks to subjects or others, defined in IRB Policy 10.2
2. Serious or continuing non-compliance, defined in IRB Policy 12.6
3. Suspensions or terminations of IRB approval, defined in IRB policy 7.9

When a determination is made that requires reporting under this policy, the IRB Director, or designee, will draft the report for review and signature by the Vice Chancellor for Research. The report will be completed within 15 days of the initial IRB action.

The Office of Research Compliance, General Counsel or affiliated institutions, such as Arkansas Children's Hospital Research Institute, will be consulted as needed.

The report will include:

- a) A description of the event
- b) Classification assigned by the IRB
- c) Actions taken by the IRB and the reasons for these actions
- d) Any administrative actions taken
- e) Any corrective action plans or plans for continued investigations
- f) Outcomes and sanctions

All reports will be sent to OHRP. Copies of the report will also be sent to:

- a) FDA, if the research is regulated by FDA
- b) Other governmental agencies when the research is overseen by those agencies and they require reporting separate from that of OHRP
- c) Sponsors or funding agencies, as appropriate
- d) Affiliated institutions involved in the research
- e) ARIA Protocol file
- f) Other institutional officials or committees at UAMS as appropriate

Department: UAMS Institutional Review Board
Policy Number: 2.8
Section: Relationships
Effective Date: July 31, 2002
Revision Date: July 23, 2004; January 24, 2011; March 11, 2011

SUBJECT: International Research

All transnational Human Research submitted to the UAMS IRB shall be reviewed according to the policies and procedures that are applied to Human Research conducted domestically. These policies will apply throughout the project, including initial and continuing review and any modifications.

This will specifically include ensuring that the researchers and staff who will be conducting research in other countries are qualified to conduct research in that country and well versed in the local laws and cultural context of that country, that any post-approval monitoring plans address the issues related to the transnational nature of the research project, and that procedures are in place to appropriately address any subject complaints, non-compliance or unanticipated problems involving risks to subjects or others.

The IRB may invite consultants under IRB Policy 3.9 to provide or evaluate information regarding the legal and cultural issues that may arise in international research.

Department: UAMS Institutional Review Board
Policy Number: 3.1
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: March 5, 2004; June 1, 2005; January 24, 2011;
March 11, 2011

SUBJECT: Qualifications of Committees

Diversity. Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

Each IRB shall include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. Each IRB shall include at least one member who represents the perspective of research subjects. Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues, which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB. The IRB Committee membership must be sufficiently qualified through the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel.

Number of Members. Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

Composition. The roster of IRB members identifies each member by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant. Changes in IRB membership shall be reported to the Office for Human Research Protections (OHRP).

Composition of the membership of the IRB Committees must be adequate in light of the anticipated scope of the UAMS research activities, and the types of subject populations likely to be involved. The IRB Committee must also be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

Member's Primary Interest. Each IRB Committee must include at least one member whose primary interests are in a scientific area, one member whose primary interests are in a nonscientific area, one member who represents the perspective of research subjects and one member who is not affiliated with the UAMS (*i.e.* not a family member or spouse of an employee, not an alumnus).

Although the regulations do not specifically require the presence of a member representing the perspective of research subjects or a member not otherwise affiliated with the institution to constitute a quorum, UAMS

considers the presence of such members an important element. Therefore, members representing the perspective of the subject and non-affiliated members should attend at least 10 of 12 meetings per year for each Committee assignment.

The intent of the requirement for diversity of disciplines was to include members who had little or no scientific or medical training or experience. Therefore, nurses, pharmacists and other biomedical health professionals should not be regarded to have "primary concerns in the nonscientific area". In the past, lawyers, clergy and ethicists have been cited as examples of persons whose primary concerns would be in non-scientific areas. Some members have training in both scientific and non-scientific disciplines, such as a J.D., R.N. While such members are of great value to an IRB, other members who are unambiguously non-scientific should be appointed to satisfy the non-scientist requirement.

Child Representative. A IRB Committee considering a protocol involving children as subjects should (A) assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities and (B) consider inclusion of one or more individuals who are knowledgeable about and experienced in working with children. To fulfill this requirement, the IRB Committee may invite nonvoting individuals to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members.

Prisoner Representative. Federal Regulations require that the IRB Committee membership be modified if it is to review research involving prisoners. Therefore, if any IRB Committee will review research involving prisoners, at least one member of the IRB Committee shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.

If a prisoner representative is selected to serve on the IRB Committee, the person must have a close working knowledge of prison conditions and the life of a prisoner. Suitable individuals could include present or former prisoners; prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or any individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience.

In situations where a protocol is reviewed by more than one board, only one board needs to satisfy the requirement that at least one member of the board be a prisoner, or a prisoner representative.

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.

Department: UAMS Institutional Review Board
Policy Number: 3.2
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: March 5, 2004; June 1, 2005; January 24, 2011

SUBJECT: Quorum

Except when an expedited or exempt review procedure is used, the IRB Committee may take official actions regarding proposed research only at convened meetings in which a majority of the voting members of the IRB Committee are present, including at least one member whose primary interests are in nonscientific areas.

The Chair counts toward quorum and must vote on every action.

Approval of research is by a majority of those members present at the meeting.

Prior to Calling a Meeting to Order in ARIA: The IRB Administrator running the meeting will check for the following before informing the Chair that the meeting can be called to order:

Minimum number of reviewers required for the specific committee is present;

At least one individual experienced in working with children is present

A non-scientist representative is present;

And note any alternates present and the primary member for whom they are substituting.

If any item on the agenda includes prisoners, pregnant women, mentally disabled or economically or educationally disadvantaged persons, the IRB Administrator in conjunction with the staff person taking minutes, will document that at least one member present is knowledgeable or experienced in working with this type of participant. If no reviewer with the appropriate background is present, the item will be deferred until a later meeting.

Failure of Quorum During Meeting. Should the quorum fail during a meeting (e.g., loss of a majority through abstention of members with conflicting interests or early departures, or absence of a nonscientist member), the IRB may not take further actions or votes unless the quorum can be restored.

Department: UAMS Institutional Review Board
Policy Number: 3.3
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: March 5, 2004; June 1, 2005; January 24, 2011

SUBJECT: IRB Reviewer and Consultant Conflict of Interest

I. Purpose

To ensure the IRB obligation to protect the rights and welfare of subjects is not compromised by competing interests.

II. Definitions

A. Conflict: Exists when a Reviewer, or Immediate Family, has a Financial or Non-Financial Interest in the research or entity sponsoring the research.

B. Financial Interests: Exists when the Reviewer or Immediate family has one of the following in the research study or the entity sponsoring the research.

1. Ownership interest, stock options, or other financial interest related to the research unless it meets two tests:
 - a. The interest is publicly traded on a stock exchange.
 - b. No arrangement has been entered into where the value of the ownership interests will be affected by the outcome of the research.
2. Compensation (received or anticipated) where the value may be affected by the outcome of the study.
3. Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
4. Board or executive relationship related to the research, regardless of compensation.

C. Immediate Family: Reviewer's spouse, minor children, and other persons living in the same household or financially dependent on the Reviewer.

D. Reviewer: For purposes of this policy includes appointed IRB Reviewers and Consultants asked to assist the IRB.

E. Non-Financial Interest: Exists when a Reviewer is involved in the design, conduct and reporting of the research study. This includes but is not limited to roles such as investigator, coordinator, or data manager. Also exists when a Reviewer has (or had) interactions with the study team which would make it difficult to review his/her study with a non-biased eye.

III. Policy

A. No Reviewer may participate in the review of any study in which the Reviewer or Immediate Family has a Conflict, except to provide information regarding the study as requested. This applies to all IRB review functions, including new, expedited, review of unanticipated problems and noncompliance.

B. No individual may serve as a Reviewer if that person is employed to raise funds or obtain grants for research at UAMS, ACH/ACHRI or other affiliated institutions.

IV. Procedure for IRB Reviewers

A. Upon receipt of agenda, review assigned studies as well as the other studies on the agenda. Reviewer should notify the IRB if there are any studies in which he or she has a Conflict.

B. If a Conflict is discovered during the meeting, the Reviewer shall inform the Chair of the Conflict. The Reviewer will be asked to leave the room during the discussion and vote during the study in which there is a Conflict.

V. Procedure for IRB

A. Continuing Conflicts. The IRB Chair and IRB Staff shall determine which issues and situations constitute a continuing Conflict for any particular Reviewer. This information will be taken into account when assigning reviewers; however, it is still the Reviewer's responsibility to disclose all Conflicts.

B. Individual Study Conflicts

1. For any study in which the originally assigned reviewer indicates a conflict, the IRB will reassign the study review to a different reviewer.
2. IRB Chair or Staff will ask the Reviewer to leave the room during the discussion and vote on the study in which there is a Conflict. Upon the request of the Committee, the Reviewer may be asked to provide additional information relating to the study. Reviewers who are out of the room due to a conflict will not count towards quorum.
3. The minutes will note that the Reviewer was out of the room due to a conflict in accordance with IRB Policy 6.3.

Department: UAMS Institutional Review Board
Policy Number: 3.4
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: March 5, 2004; March 29, 2007; January 24, 2011

SUBJECT: IRB Chair

Appointment. Each IRB Chair must demonstrate knowledge about human rights and ethical issues and regulations relevant to the use of human subjects in research and applications thereof, and must have previous experience as an IRB reviewer. The Vice Chancellor for Research appoints Chairs based on the above mentioned criteria.

Duties.

The duties of the Chair include, but are not limited to the following activities:

1. Reviewing protocols submitted for exempt or expedited review;
2. Assigning studies to IRB reviewers;
3. Determining the IRB committee agenda;
4. Convening and conducting IRB meetings;
5. Summarizing IRB review recommendations to be sent to investigators;
6. Reviewing and signing letters generated from committee actions;
7. Reviewing minor modifications and responses to minor contingencies;
8. Providing guidance to investigators;
9. Reviewing SAE and safety reports and determining when reports need full committee review.

The Vice Chancellor for Research will evaluate the Chair on an annual basis. Failure to perform duties in an appropriate way may lead to dismissal of Chair.

Department: UAMS Institutional Review Board
Policy Number: 3.5
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: March 12, 2004; January 24, 2011

SUBJECT: IRB Vice-Chair

Appointment. The Vice Chancellor for Research may appoint Vice-Chairs as necessary to provide support to the IRB Chairs. Each IRB Vice-Chair must demonstrate knowledge about human rights and ethical issues and regulations relevant to the use of human subjects in research and applications thereof, and must have previous experience as an IRB reviewer.

Duties. The Vice-Chair assumes the duties of an IRB Chair when the Chair is not available to conduct a meeting or has to recuse due to a conflict of interest.

Evaluation. The Vice Chancellor for Research will evaluate the Vice-Chairs on an annual basis. Failure to perform duties in an appropriate way may lead to dismissal of a Vice-Chair.

Department: UAMS Institutional Review Board
Policy Number: 3.6
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: January 25, 2005; June 1, 2005; January 24, 2011

SUBJECT: IRB Reviewers

I. Purpose: To outline the appointment process and provide an overview of the duties of IRB Reviewers

II. Process

A. Reviewer Recruitment

1. Individuals who wish to serve as an IRB Reviewer may submit a CV to the Vice Chancellor for Research, IRB Director, a Chair or other Reviewer.
2. The Vice Chancellor for Research will ask Deans, Division Chiefs and Department heads to identify reviewers from their respective departments.
3. The IRB may seek reviewers from the community in a variety of ways and methods, such as personal relationships, recruitment from local civic clubs or professional organizations.

B. Appointment

The Vice Chancellor for Research extends invitations to serve on the IRB in writing. Reviewer appointments will occur as needed, based upon the volume and nature of the IRB workload. The term of the appointment is open-ended.

III. Overview of Duties

IRB Reviewers play an important role in the UAMS human research protection program. The primary mission of an IRB Reviewer is to evaluate human subject protection issues. An IRB reviewer's duties include reviewing new and ongoing studies in accordance with the regulatory criteria for approval. Prior to review assignments, Reviewers must meet the educational requirements as outlined in IRB Policy 3.8. Reviewers are provided with checklists outlining the basic regulatory criteria and the criteria for review of research involving vulnerable populations, INDs/IDEs, and HIPAA. Reviewers are expected to consistently use these checklists.

IRB meetings require access to an online electronic system. UAMS laptops are assigned to each reviewer, unless the reviewer prefers to use his/her own laptop. Reviewers must complete their reviews prior to the meeting. A completed review is one in which any contingencies or comments have been entered into ARIA before the meeting time. Reviewers should allow plenty of time to contact the study staff or other reviewers for information or guidance as well as unexpected obstacles such as technical issues with ARIA or internet connections.

Reviewers are expected to bring their laptop to each meeting in order to participate in the review process. The contingencies, comments and motions will be projected during the meeting. Reviewers are responsible for ensuring that contingencies and motions captured on the screen are an accurate reflection of the committee decisions.

Reviewer performance will be assessed as per IRB Policy 1.7.

Department: UAMS Institutional Review Board
Policy Number: 3.7
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: March 12, 2004

SUBJECT: Alternate Members

The IRB, at its discretion, may recruit alternate members to substitute for certain regular members of the IRB.

Appointment

The procedure for appointment of an alternate member is the same as that of a regular voting IRB member. An alternate member must be formally appointed and listed on the membership roster as an alternate. To ensure maintaining an appropriate quorum, the alternate's qualifications should be comparable to those of the primary member to be replaced.

Voting

Alternate members will have voting rights, when requested to attend for purposes of establishing quorum. Alternate members will be included in determining or establishing quorum at IRB meetings, but not when they are present without invitation.

Review Materials

When an alternate substitutes for a primary member, the alternate should have received and reviewed the same material the primary member would have received.

Meeting Minutes

Meeting minutes must document when an alternate member is attending by invitation.

Department: UAMS Institutional Review Board
Policy Number: 3.8
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 12, 2004; February 8, 2005; March 29, 2005; March 29, 2007; January 24, 2011

SUBJECT: IRB Reviewer Training Requirements

I. Policy

All IRB Reviewers must complete initial orientation and the web-based Human Subject Protection training courses appropriate to IRB Reviewers at <http://www.citiprogram.org>. Reviewers must also participate in continuing education which can take many forms.

II. IRB Reviewer Orientation Training

All new Committee members are required to complete an initial orientation before being allowed to serve on the IRB Committee, which includes the following:

1. IRB Overview, Regulatory Criteria and HIPAA
2. How to Review a Protocol
3. How to use the Reviewer Checklists
4. Code of Conduct for IRB Membership
5. Introduction to ARIA
6. What to expect in an IRB Meeting
7. IRB Contacts, Process for Agenda Assignments
8. Resources (includes IRB Policies, The Nuremberg Code, Declaration of Helsinki, Belmont Report, select CFR sections)

New IRB Reviewers will be added to the rosters as voting members after attending and observing at least one IRB meeting. Assignment of initial study reviews will be in conjunction with a Chair or other reviewer acting as a mentor.

III. Continuing Education

1. Ongoing education is incorporated into scheduled IRB Committee meetings as pertinent topics are circulated or policies or procedures change.
2. "IRB TIPS" are short educational messages that will be sent to all committee members on a variety of topics as required.
3. IRB Reviewers are required to participate in at least one continuing education opportunity each year. Reviewers are encouraged to attend as many human research protections courses as possible. Regular training sessions are offered at UAMS and ACH.

IV. Assessment

IRB Reviewers should regularly assess their understanding of the regulatory and policy issues encountered during the meetings. As necessary, Reviewers should seek out additional training by contacting the IRB Director for resources.

Reviewer performance will be assessed as per IRB Policy 1.7.

Department: UAMS Institutional Review Board
Policy Number: 3.9
Section: Committee Membership
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 12, 2004; February 8, 2005; January 24, 2011

SUBJECT: Consultants

Policy: The IRB may invite individuals who have special scientific, scholarly or cultural expertise to serve as consultants to assist the IRB in its review process. Individuals may be from within UAMS but are not required to be. The identities of the individual consultants will be kept confidential to the extent allowed by federal regulations.

Procedure:

1. IRB Members may:
 - 1.1 Request the Chair identify a consultant if they are assigned a review that is out of their area of scientific or scholarly expertise.
 - 1.2 Obtain consultations by directly contacting a colleague, provided they are cognizant of potential or real conflicts of interest and confidentiality issues.
 - 1.2.1. If Member contacts a colleague directly, s/he will provide a written summary of the consultation in the comments section of ARIA, noting the qualifications of the consultant.
2. The IRB Chair will
 - 2.1 Evaluate submitted research for the need for consultation.
 - 2.2 If a consultant is needed, the chair will identify and contact an appropriate consultant.
 - 2.3 Provide the consultant with a copy of the IRB Conflict of Interest Policy, or verbally explain the Policy to the consultant, and determine whether the consultant has a conflicting interest. If the consultant has a conflicting interest, identify a replacement consultant.
 - 2.4 Provide the IRB with written summary of the consultant's determinations.
3. The Consultant will:
 - 3.1 Have access to all documents submitted to the IRB relevant to the specific project under review
 - 3.2 Immediately notify the Chair if upon review discovers s/he has a conflict, so that the Chair may identify a new consultant.
 - 3.3 Provide a written summary of their review and recommendations.
 - 3.4 Attend IRB meeting, if requested, to participate in the deliberations and make recommendations on the project.
 - 3.5 Not be included in determining or establishing quorum at the meetings and will not have the authority to vote.

Department: UAMS Institutional Review Board
Policy Number: 4.1
Section: Committee Operations
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; March 12, 2004; November 18, 2002

SUBJECT: Number of Committees

Policy:

The number and composition of IRB Committees at UAMS may vary at times to support the volume and type of human research to be reviewed in a thorough and timely manner. Composition of the individual committees will in general be along the discipline lines of biomedical and behavioral and social sciences. Committees with a different focus may be added if warranted to meet the needs of the research program.

Procedure:

1. The Behavioral and Social Science IRB will review human participant research studies that primarily focus on the *examination of human behavior* related to interpersonal interaction, observation, group or individual behavior relating to interventions or experiences. Methods include but are not exclusive to open-ended questions or interviews, or surveys inquiring about individual or group knowledge, attitudes, perceptions, experiences or behavioral activities. These studies may test educational, motivational and/or behavioral intervention effectiveness.

2. The Biomedical IRBs will review human participant research studies that *examine clinical outcomes* from the administration of drugs, supplements, medicines, surgical and other clinical procedures and diagnostics, medical devices, treatment regimens, and clinically applied interventions affecting the progression, symptom management, diagnosis or prevention of disease. Methods include the administration of these techniques, substances, and procedures to measure endpoints and outcome effectiveness.

Department: UAMS Institutional Review Board
Policy Number: 4.2
Section: Committee Operations
Effective Date: July 31, 2002
Revision Date: March 12, 2004

SUBJECT: Sub-committees

A sub-committee may be formed at the request of the chairperson to address policy issues or to investigate issues related to specific studies or investigations that require more information than can be obtained in written communications.

Department: UAMS Institutional Review Board
Policy Number: 4.3
Section: Committee Operations
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; March 12, 2004; November 18, 2002

SUBJECT: Meeting Schedule

Information concerning meeting schedules for the various IRB Committees can be found on the IRB website at <http://www.uams.edu/irb/irb.asp>. Additional meetings can be called by the IRB Chair which may not be posted on the web site. Such meetings deal with special issues and would be made known to all concerned parties through written or oral communications.

Department: UAMS Institutional Review Board
Policy Number: 4.4
Section: Committee Operations
Effective Date: July 31, 2002
Revision Date: November 18, 2002; March 12, 2004; February 8, 2005; January 24, 2011

SUBJECT: Assignment of Reviewers

For all items that must be reviewed by the convened IRB, at least two reviewers will be assigned to review the following:

1. New studies undergoing initial review
2. Previously tabled items
3. Study modifications that do not meet the expedited review criteria; these items will be listed on the agenda as Updates by Two Reviewers.
4. Committee requested major revisions,

All other items will have at least one assigned reviewer.

Reviewers with non-scientific backgrounds may be assigned to review under any category of review.

The IRB office maintains reviewers' CVs with information regarding their expertise. The IRB staff, in conjunction with the Chair, assigns protocols to ensure that at least one reviewer assigned has the relevant scientific or scholarly expertise appropriate to the study.

If no reviewer on the assigned Committee has the necessary expertise to perform an appropriate in-depth review, review may assigned to a different Committee or consultation will be sought in accordance with IRB Policy 3.9.

Department: UAMS Institutional Review Board
Policy Number: 4.6
Section: Committee Operations
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; March 12, 2004; November 18, 2002

SUBJECT: Duties of IRB Staff

1. Study Specific

1.1 Review materials for completeness before review by the IRB:

- a. Full protocol
- b. Informed consent form
- c. Appropriate completion of Original Submission Form
- d. Any relevant merit reviews or grant applications
- e. Investigator's brochure
- f. Advertisements or subject information
- g. Subject surveys or questionnaires
- h. Appropriate documentation of required investigator training certificates
- i. Indemnity letter from sponsor, if appropriate
- j. HIPAA Authorization, if appropriate
- j. Data Safety Monitoring Plan
- k. Appropriate completion of Continuing Review Forms
- l. Appropriate completion of Modification Forms

1.2 Verify receipt of current consent form and/or protocols for study revisions and adverse event reports.

1.3 Contact researcher for additional materials or submission changes when appropriate.

2. Meeting specific

2.1 Coordinate the location and snacks for meeting.

2.2 Verify attendance at meetings to assure quorum, both prior to and during the meeting.

2.3 Prepare and disseminate agenda prior to the meetings.

2.4 Provide members with appropriate background and summary information on policies, rules, and regulations pertaining to issues relevant to protocol review.

2.5 Assist the Chair in taking notes at the IRB meeting.

2.6 Prepare correspondence for signature by the Chair.

2.7 Follow up as needed on all items marked as Pending, such as IND/IDE #s or other committee approvals.

3. General Duties

3.1 Ensure accuracy of data in database.

3.2 Disseminate and collect annual IRB questionnaires on COI and Affiliation.

3.3 Provide assistance to members and research staff with questions regarding regulations, policies, and ARIA and IRB procedures.

Department: UAMS Institutional Review Board
Policy Number: 4.7
Section: Committee/Staff Operations
Effective Date: February 8, 2005
Revision Dates: NA

SUBJECT: Participant Phone Calls

Purpose:

The purpose of this policy and procedure is to describe how IRB staff should respond to participant phone calls.

Policy:

Current, prospective, or past research participants can call and discuss any problems, concerns, or questions regarding research conducted at UAMS. All calls should be treated as confidential. Each IRB staff member is expected to know general information regarding the rights of research participants and be able to answer general questions.

Materials:

Participant Contact Form

References

None

Procedure:

1. IRB Staff Members will:
 - 1.1. Document each phone call received from a participant with the Participant Contact Form ("Form"). Note on the Form the date, who called, the facts presented to them, information provided, open questions, and actions promised.
 - 1.2. Request the participant's contact information in case there is a need to call them back after seeking assistance.
 - 1.3. Answer the participant's questions when possible.
 - 1.4. Forward the Form to the Director for assistance if unable to answer participant's questions.
 - 1.5. For concerns, complaints, research-related injuries, inform the participant that the Director or IRB Chair will contact them, and immediately forward the Form to the Director or IRB Chair.
 - 1.6. If the participant cannot reach the study team, use the ARIA database or UAMS e-phone book to locate contact information, and attempt to connect the study

team and participant. Staff members will not forward the participant to a phone number unless the study team has been directly contacted and they expect the call.

1.6.1. If staff member is able to connect the study team and the participant, Staff member will ask the team to notify them upon resolution.

1.6.2. If staff member cannot connect the study team and participant and the request is not urgent, arrangements will be made to contact the study team at another time and follow-up with the participant. Otherwise, the staff member will immediately notify the Director/designee.

1.7. Track unresolved issues and follow up as needed with the Study Team to obtain a resolution.

1.8. Indicate on the Form when a clear resolution has been reached.

1.9. Once resolved, submit Forms to the Director/designee for review.

2. Director/Designee will:

2.1. Review Forms.

2.2. Document on the form any additional communications or actions noting who was present, facts presented to him/her, information provided, and actions promised.

2.3. Notify the UA System General Counsel's Office of research related injuries, and other concerns and complaints on a case-by-case basis.

2.4. If the situation involves serious risks to participants, consider asking for a directed audit, with ongoing reporting to the IRB.

2.5. Track unresolved issues and follow up as needed to obtain a resolution.

2.6. File Forms.

3. IRB Chair will:

3.1. Review Forms provided by IRB staff

3.2. Document on the form any additional communications or actions noting who was present, facts presented to him/her, information provided, and actions promised.

3.3. Track unresolved issues and follow up as needed to obtain a resolution.

3.4. Once resolved submit Forms to the Director/designee for review and filing.

Department: UAMS Institutional Review Board
Policy Number: 5.1
Section: Records
Effective Date: July 31, 2002
Revision Date: November 18, 2002; August 25, 2004; February 8, 2005; January 24, 2011; March 11, 2011

SUBJECT: IRB Records

I. Purpose

The purpose of this policy is to describe the maintenance of IRB records

II. Policy

The IRB shall retain all documents submitted to it or created by it in accordance with federal, state and local law, and any applicable sponsor or organizational requirements. This includes items sent for exempt, expedited or convened IRB review. In order to maintain the confidentiality of such records, access to records, whether paper or electronic, is restricted to authorized personnel. Each study will be assigned a unique IRB study number and maintained in a separate file.

III. Process

A. The IRB Staff will:

1. Maintain the following records:

- a. A current list of IRB membership and qualifications.
- b. Agenda and minutes of meetings, including information regarding member attendance, discussions held, decisions made, and voting results.
- c. All materials submitted to the IRB for review. These materials include, but are not limited to: IRB applications, protocols, submitted and final consent forms, investigator brochures, recruitment materials, reports of Unanticipated Problems Involving Risk to Subjects or Others, audits, new findings, serious adverse event and death reports, reports of injuries or complaints, proposed amendments, progress reports, data and safety monitoring reports, correspondence between the committee and the investigators, and, where applicable, correspondence from sponsoring agencies.

2. At reasonable times and in a reasonable manner, provide access to ARIA or paper records for inspection and copying by authorized personnel. Authorized personnel shall specifically include OHRP and the FDA. Institutions which rely on UAMS as their primary IRB of record, to include but not be limited to ACH and ACHRI, shall also be provided access. Access should be limited to site specific records or records in which their employees are involved. For entities not specifically mentioned here, the IRB Director or Chair should be contacted prior to providing access.

B. All records submitted after the implementation of ARIA, or scanned into ARIA upon closure, are retained electronically in the system indefinitely. There are currently no plans to purge ARIA of any study records. However, if electronic storage should become an issue, all IRB records will be retained in accordance with federal, state and local law, and any applicable sponsor or organizational requirements. For protocols cancelled without subject enrollment, this shall include retaining IRB records for at least three years after cancellation.

Department: UAMS Institutional Review Board
Policy Number: 5.2
Section: Records
Effective Date: July 31, 2002
Revision Date: April 9, 2004

SUBJECT: Database

The IRB support staff and committee members have access to the Automated Research Information Administration (ARIA) database that contains information on all protocols, including the protocol number, protocol title, Principal Investigator, Sub-investigators, IRB approval date, and protocol expiration date. The IRB Database is a key element in coordinating human subjects research. The IRB Manager relies on this database to generate letters and reports, and to ensure that the PI is conducting an approved study, and using an updated, appropriate and approved consent form.

Department: UAMS Institutional Review Board
Policy Number: 6.1
Section: Documentation
Effective Date: July 31, 2002
Revision Date: May 7, 2004; February 8, 2005; January 24, 2011

SUBJECT: Agenda

I. Purpose

The purpose of this policy and procedure is to describe how the IRB Agenda for each meeting is set.

II. Policy

The IRB Office shall generate an agenda for each meeting. For each protocol item under review, all relevant documentation will be listed as pending in ARIA. The agenda will also include any minutes from a prior meeting which are to be voted on. Minutes are accessible for review in ARIA.

The agenda shall include the Type of Review, IRB Record number, full title of protocol, assigned reviewer and any documents associated with the submission.

III. Procedure

A. The IRB Office will:

1. Place Items on the appropriate agenda in ARIA based upon date of submission.
2. Lock the Agenda at the close of the day (4:30 p.m.) on the submission deadline date.
3. Distribute the Agenda and Agenda Key via email notice to the IRB Members at least one week prior to the meeting.

B. The IRB Members will:

1. Immediately notify the IRB office and Chair if they are unable to attend a scheduled meeting.
2. Notify the IRB if upon review of their assigned studies realize they have a conflict of interest.

C. The IRB Chair or Designee will:

1. Review the Agenda for accuracy and completeness prior to distribution to the Members.
2. Reassign protocols submitted by the deadline to a later committee meeting if there is an undue volume of submissions, ensuring that no protocol will be reassigned if that reassignment alone might cause expiration of the study approval.
3. Under extenuating circumstances, add any item submitted after the published deadline when deemed to be appropriate.

Department: UAMS Institutional Review Board
Policy Number: 6.3
Section: Documentation
Effective Date: July 31, 2002
Revision Date: February 1, 2005; June 1, 2005; January 24, 2011;
March 11, 2011

SUBJECT: Meeting Minutes

I. Policy

The IRB office will prepare minutes for each convened IRB meeting.

II. Process

A. Attendance. The minutes of all IRB Committee meetings must be in sufficient detail to show attendance at the meetings, including:

1. When there is a consultant or guest attending.
2. Whether an alternate is voting.
3. When a member leaves the room.
4. The continued existence of a quorum.
5. Initial and continued presence of a majority of members, including at least one nonscientist member.
6. Presence of non-voting members.

B. Actions. For each item reviewed, the minutes must document the following:

1. The IRB protocol number, title, and assigned reviewers.
2. Actions taken by the IRB Committee
 - a. The vote on these actions including the number of members voting for, against, and abstaining. The abstaining member's name will be listed to verify non-conflict.
 - b. The name of any member who leaves the meeting due to a conflict of interest.
 - c. Discussion and resolution of controverted issues.
 - d. Document approval versions.
 - e. Revisions required and the basis for any revisions required, or for declining or tabling a study.
 - f. Accrual goal, for new protocols only.
 - g. For new submissions and continuing reviews, a determination on the length of time between continuing reviews (approval period).
 - h. For new protocols, the level of risk assigned to the study. For Continuing Reviews, whether based on the information presented, there has been any change in the risk.
3. When a new protocol is approved, the IRB records should reflect that the IRB Committee determined that all approval criteria as outlined in IRB Policy 7.1 were met.
4. For Continuing Reviews, it should be noted that the study still meets each of the approval criteria or if information presented impacts any of the approval criteria, changes required in order to grant approval.

C. Specific Findings. When specific findings on the part of the IRB Committee are required, these findings should be fully documented in the minutes and should include protocol-specific information justifying each IRB finding.

1. If a waiver or alteration of informed consent was approved, documentation that the requirements as outlined in IRB Policy 15.3 were met.
2. For device studies, a determination of Significant Risk or Non-Significant Risk and the basis thereof as outlined in IRB Policy 18.2.
3. In studies to be suspended or terminated, when treatment may continue for safety reasons as outlined in IRB Policy 7.9.
4. In studies involving prisoners, or those likely to become incarcerated, the seven findings and category of research as outlined by IRB Policy 17.9, as well as the presence of the Prisoner Representative.
5. In studies involving children or wards, the specific requirements and determinations made as outlined in IRB Policy 17.1.

6. In studies involving pregnant women, fetuses, or *In Vitro* Fertilization, the specific requirements and determinations as outlined in IRB Policy 17.8.
7. In studies involving the cognitively impaired, the specific requirements as outlined in IRB Policy 17.2.
8. For any study in which a DHHS approved sample informed consent document has been provided, any substantive modifications or deletions required.

D. Distribution and Finalization of Minutes. Minutes from the prior meeting of a particular committee are distributed with the next agenda for that committee. Any corrections/comments to the minutes are noted in the minutes of the next meeting. Once approved by the convened IRB, the minutes may not be modified. A copy of the final minutes is filed and posted on the ARIA website and accessible to IRB Reviewers and compliance personnel. The minutes shall be retained in ARIA indefinitely.

Department: UAMS Institutional Review Board
Policy Number: 6.4
Section: Documentation
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; May 7, 2004

SUBJECT: Membership Roster

A list of IRB members is maintained with OHRP, in the IRB office and placed on its website. Members are identified by name; gender; earned degrees or applicable licenses; primary scientific/non-scientific specialty area; representative capacity; and any employment or other relationship between each member, or their immediate family and the institution or its affiliates.

Department: UAMS Institutional Review Board
Policy Number: 7.1
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: May 7, 2004; February 8, 2005; January 24, 2011

SUBJECT: Criteria for IRB Approval of Research

Policy

In order to approve research, the IRB must determine that all of the regulatory criteria set forth below are met. This applies to reviews by the convened IRB or the expedited review process. These criteria must be used to approve research for initial review, continuing review and review of modifications.

A basic checklist, encompassing these criteria, is provided to all reviewers with each agenda. Additionally, all new IRB Reviewers receive training on these criteria during initial orientation and are provided with a set of detailed checklists to use in their reviews.

Approval Criteria

1. Risks to subjects are minimized:

- a. By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
- b. By using procedures already being performed on the subjects for diagnostic or treatment purposes, whenever appropriate.

2. Risks to subjects are reasonable in relation to:

- a. **Anticipated benefits, if any; and**
- b. **The importance of the knowledge that may reasonably be expected to result.**

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

3. Selection of subjects is equitable.

In making this assessment the IRB should take into account the purposes of the research, the setting in which the research will be conducted, the selection criteria, the recruitment procedures and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, cognitively impaired or economically or educationally disadvantaged persons.

4. To the extent required, informed consent will be sought as described in IRB Policy 15.1.

5. To the extent required, informed consent will be documented as described in IRB Policy 15.1.

6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects. See IRB Policy 7.8.

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

The name of the HIPAA rule aside, privacy concerns people and confidentiality concerns data. In evaluating privacy interests, the IRB should consider how the Investigator will access information from or about participants.

8. When appropriate, additional safeguards have been included in the study to protect the rights and welfare of subjects vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled, or economically or educationally disadvantaged persons. See Section 17 of the IRB Policies.

Department: UAMS Institutional Review Board
Policy Number: 7.2
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: May 7, 2004; February 8, 2005; January 24, 2011

SUBJECT: Principal Investigator Qualifications

Principal Investigator Requirements:

1. Training

1.1 In order to best protect those participating in research, Principal Investigators (PI) should have the necessary training and background to conduct studies in accordance with the protocol, organizational policies and procedures, applicable regulations, such as those concerning IRB review, informed consent requirements, reporting requirements, maintenance of records, retention of records, and supervision of research conduct.

1.2 Research specific training courses as required by UAMS Administrative Guide Policy 16.1.06.

2. Resources

2.1 Before undertaking a project, the PI must verify that has the time, equipment and necessary staff in terms of numbers and/or qualification in order to conduct the research in a way that will protect participants.

3. No Unmanageable Conflict of Interest

3.1 All PIs must reveal on their application to the IRB whether they or any other person responsible for the design, conduct, or reporting of the research has an economic interest in, or acts as an officer or a director of any outside entity whose financial interests would reasonably appear to be affected by, the research.

NOTE: The IRB will not review research with a declared financial interest until the Conflict of Interest Committee has completed its evaluation and management plan. See IRB Policy 2.2.

4. Additional Requirements for Student Conducted Research.

4.1 All activities that meet the definition of Human Research as outlined by IRB Policy 1.4 whether conducted by students or others must be reviewed by the IRB. Fellows and Resident physicians are considered students.

NOTE: Oversight by Faculty/Advisor is required. All students applying as PI on a study for IRB review must list their faculty advisor as a co-investigator or responsible staff member.

Department: UAMS Institutional Review Board
Policy Number: 7.3
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: May 7, 2004; February 8, 2005; June 1, 2005;
January 24, 2011

SUBJECT: Exempt Categories of Research

I. Purpose

The purpose of this policy and procedure is to set out the criteria for studies classified as Exempt under the Federal Regulations

II. Policy

UAMS requires all Human Research, including studies meeting one of the Exempt categories, to be submitted for review and approval by the IRB. No Investigator or Department shall have the authority to make this decision other than the IRB.

Exemption determinations may be made by an IRB Chair; Experienced IRB Reviewer as defined in IRB Policy 7.5; or the IRB Director or Assistant Director, collectively referred to as "Reviewer" in this policy.

Exemption determinations may not be made by an individual with a Conflict, as defined in IRB Policy 3.8.

All research, including that in the Exempt categories, must meet the ethical principles outlined in the Belmont Report. The Reviewer may require additional protections to meet these principles, including, but not limited to, a level of informed consent appropriate to the research or additional confidentiality or privacy measures.

Studies receiving an Exempt classification will be required to submit a one page Study Update every three years in order to keep the study open. The IRB shall be made aware of any changes in the study scope or design prior to implementation of the changes to insure that the study continues to meet the Exempt Criteria.

No research involving, or potentially involving, prisoners, as participants may be classified under the Exempt Categories listed below.

III. Exempt Categories

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

NOTE: This category may be applied to research involving children.

NOTE: This category may not be applied to FDA regulated research.

2. Research involving the use of **educational tests** (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

- Information obtained 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 human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

NOTE: The section of this category pertaining to standardized educational tests may be applied to research involving children. This category may also apply to research with children when the investigator observes public behavior but does not participate in that behavior or activity. This section is not applicable to survey or interview research involving children.

NOTE: This category may not be applied to FDA regulated research.

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

- a. The human subjects are elected or appointed public officials or candidates for public office or
- b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

NOTE: This category may not be applied to FDA regulated research.

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.

- a. To qualify for this exemption the data, documents, records, or specimens must be in existence before the project begins. Investigator must describe where the information exists.
- b. Under this exemption, an investigator (with proper institutional authorization) may inspect identifiable records, but may only record information in a nonidentifiable manner. Investigator must describe how information will be obtained, what data elements will be recorded, and whether any links to identifiers will be recorded.

NOTE: Inclusion of fetal tissue in the pathological specimens category of exempt research is prohibited and requires additional IRB review.

NOTE: This category may not be applied to FDA regulated research.

5. Research and demonstration projects which are conducted by or subject to the approval of federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:

- a. Public benefit or service programs; this exemption is for federally supported projects and is most appropriately invoked with authorization or concurrence by the funding agency. The following criteria must be satisfied to invoke the exemption for research and demonstration projects examining "public benefit or service programs."
 - i. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act)
 - ii. The research or demonstration project must be conducted pursuant to specific federal statutory authority.
 - iii. There must be no statutory requirement that an Institutional Review Board review the project.
 - iv. The project must not involve significant physical invasions or intrusions upon the privacy of participants.
- b. Procedures for obtaining benefits or services under those programs;
- c. Possible changes in or alternatives to those programs or procedures;
- d. Possible changes in methods or levels of payment for benefits or services under those programs.
- e. Before invoking this exemption, the IRB will obtain concurrence of the funding agency that this exemption can be applied.

NOTE: This category may not be applied to FDA regulated research.

6. Taste and food quality evaluation and consumer acceptance studies if:

- a. wholesome foods without additives are consumed or
- b. if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

NOTE: This category may be applied to children.

NOTE: This category may be applied to FDA regulated research.

IV. Procedure

A. The Investigator will:

1. Submit a protocol and application through ARIA, including all surveys, questionnaires or other instruments to be used.
2. Provide any additionally requested information.
3. Submit any proposed or anticipated changes to the IRB, through ARIA Modifications, prior to implementation.
4. Submit an Exempt Study Update Form through ARIA every three years to keep study open.

B. The Reviewer will:

1. Review requests for exemption using the Reviewer's Checklist for Exempt Determinations.
2. Request additional information or modifications in order to ensure the study is conducted ethically.
3. Document in the Approval Letter which Exempt Category the study is approved under or notify Investigator that the study will need to be reviewed by either Expedited or Full procedures.
4. Place on Agenda under Exempt Studies Approved by the Chair/Designee.

Department: UAMS Institutional Review Board
Policy Number: 7.4
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: May 7, 2004; February 8, 2005; June 1, 2005; March 5, 2008; January 24, 2011

SUBJECT: Review by Convened IRB

I. Policy

The convened IRB will review research that does not qualify for expedited or exempt review. The Chair will ensure that the reviewers have expertise in the areas under review for a particular meeting, or invite outside individuals with the appropriate expertise in accordance with IRB policy 3.9.

Each agenda item under review by the convened IRB will be individually presented and discussed. The IRB approval criteria outlined in IRB Policy 7.1 will be used for all reviews of research, including initial and continuing review and modifications to previously reviewed studies. In order for the item to be approved, it must receive the approval of a majority of those members present at the meeting.

All actions taken by the IRB will be reported to the study team in writing. This includes motions to approve, disapprove, table, or require major or minor contingencies. Should a study be tabled or disapproved, the IRB's letter will include the reasons for the decision. All study personnel listed in ARIA will have access to the IRB letter. However, only the Investigator and Study Contact will receive email notification that a new letter has arrived.

II. Reviewer Obligations and Process

A. Agenda and Access to Studies under Review

At least one week prior to each Committee meeting, the Agenda, Agenda Key, Approval Criteria Checklist and Minutes from the Committee's last meeting will be sent to the reviewers. All reviewers have access to the complete study submission in ARIA. Refer to the agenda category or office notes section of the agenda to identify the specific items to be acted upon under this Agenda.

B. Reviewer Obligations Prior to Meeting

1. Assigned Reviewers. Reviewers will be assigned in accordance with IRB Policy 4.4. The review and presentation to the convened IRB should address each of the approval criteria outlined in IRB Policy 7.1, plus any additional approval requirements specific to the type of research or agenda category. Contingencies should be added to ARIA prior to the meeting.

a. New Studies. For each new study assigned, the reviewer should conduct an in-depth review of the entire submission, including all associated documents.

b. Continuing Reviews. For continuing reviews, the review should encompass the protocol, current consent form, previously approved modifications and any other reporting that may reflect a possible change in the risk/benefit ratio in conjunction with the Continuing Review Form.

c. Updates by Two Reviewers. For modifications that could not be expedited, the review should encompass the Modification Form and associated documents.

d. Major Revisions. For responses to major contingencies, the reviewer will need to access the previous IRB letter and confirm that the submitted response meets each of the contingencies.

e. All Other Agenda Items. Other assigned items may include audit reports, reports of non-compliance or reports of unanticipated problems involving risk to subjects or

others. Reviews of these items should be in conjunction with IRB Policies 10.2, 12.5 and 12.6 as applicable.

2. Other Reviewers. Committee reviewers who are not assigned a specific protocol should be able to participate in the discussion and vote on each protocol. All reviewers have access to the entire study file. At a minimum, the following documents should be reviewed:

a. New Studies: Original submission form, proposed consent document and recruitment materials.

b. Continuing Reviews: Original submission form (or most recent modification form), currently approved and any newly proposed consent documents and the continuing review form.

c. Updates by Two Reviewers. Modification Form outlining what changes are requested and the documents associated.

C. Reviewer Obligations during Meeting for:

1. All Agenda Items

a. Determine whether the research, proposed modification, or contingency response meets the regulatory criteria for approval. Every reviewer has an obligation to raise issues encountered during review/discussion.

b. IRB Policy 9.1 identifies the range of IRB motions that are allowed.

c. If any review reveals significant new findings that may relate to a subject's willingness to continue participation, the IRB must determine the process to provide that information to the subjects.

d. No IRB reviewer should vote to approve a protocol unless they feel comfortable the rights and welfare of the subjects are protected to the fullest extent and that they understand the motion, including any contingencies, that is being put forward.

2. New Studies. For studies undergoing Initial Review, the IRB must also determine:

a. Which protocols need review more often than annually (the approval period); and

b. The risk category as defined in IRB Policy 16.1.

3. Continuing Reviews – Based upon information presented, the IRB must also determine whether:

a. The current consent form(s) is still accurate and complete;

b. Continuing review should occur at an interval less than one year; and

c. To seek verification from sources other than the study team that no material changes have occurred since previous review.

The following are examples of studies that may more frequent review or verification from other sources:

- i. Involvement of vulnerable populations
- ii. The involvement of recombinant DNA or other types of gene transfer protocols
- iii. Classified research
- iv. Phase 1 studies

- v. Disproportionate number or severity of SAEs
- vi. Findings of serious or continuing non-compliance or previous suspension of the researcher
- vii. Recommendations from other intra-institutional committees
- viii. The information provided is internally inconsistent and the inconsistency cannot be resolved through discussion with the investigator.

Department: UAMS Institutional Review Board
Policy Number: 7.5
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: May 7, 2004; June 1, 2005; March 13, 2008; July 28, 2008; January 24, 2011

SUBJECT: Expedited Review

I. Policy

A limited class of research may be reviewed by the expedited procedure rather than the convened IRB. The requirements to review and approve research using the expedited procedure are identical to those used by the convened IRB. All regulatory approval criteria, outlined in IRB Policy 7.1, must be met and all submission forms and requirements are the same. Additionally, the standard requirements for informed consent (or its waiver, alteration, or exception) apply and the protocols must still be reviewed at least once per year.

The expedited review may be conducted by an IRB Chair or Experienced IRB Reviewer as defined below. The reviewer may exercise all of the authorities of the convened IRB except that the reviewer may not decline the research. The reviewer may choose to refer the study to the convened IRB as warranted. The use of "IRB" throughout these policies may mean IRB, IRB Chair or Experienced IRB Reviewer as appropriate to the action under review.

All items reviewed by the expedited procedure will be reported on the agenda prepared for the convened IRB. The convened IRB will have access to the complete study file for all studies reviewed by the expedited procedure.

II. Definitions

A. Experienced IRB Reviewer: In order to serve as an Experienced IRB Reviewer and conduct reviews using the expedited procedure, the following criteria must be met:

1. Served on an IRB for a minimum of one year.
2. Demonstrate a consistent and comprehensive pattern of reviewing assigned protocols as an IRB Reviewer.
3. Willing to devote the appropriate amount of time to conduct the expedited reviews. This may be in addition to assignments for review with the convened IRB.
4. Willing to undergo training in principles of reviewing, documenting and approving items submitted under the expedited process.
5. Actual experience with conducting human subject research.
6. Recommendation by Chair and approval by the Executive Committee.

B. Minor Modifications. In order to be considered a minor modification, the proposed change may not add more than minimal risk to the subjects or substantially change the aims or design of the study. If procedures are added, the procedures must fall into one of the first 7 expedited categories below.

III. Expedited Review Procedure

A. All Reviews under the Expedited Review Procedure

1. Reviews under the expedited review procedure must be conducted with the same depth and attention to detail as the reviews conducted by the convened IRB. This includes reviewing the same information Assigned Reviewers are expected to review per IRB Policy 7.4.
2. Reviewers should consider the need for additional expertise under IRB Policy 3.9.
3. The criteria for approval of research, as outlined in IRB Policy 7.1, must be used for all expedited reviews.

4. If during the review it is discovered that the reviewer has a conflict, the IRB staff should be notified so that the review may be assigned to another reviewer.

5. If the research involves prisoners, consult IRB Policy 17.9 for the limited circumstances in which the expedited review procedures may be used. If the study does not meet the criteria for expedited review of research involving prisoners, ask the IRB Staff to place the study on the agenda for the next meeting in which the Prisoner Representative can attend.

6. Any action taken should be documented in a letter to the PI through ARIA. The following actions may be taken:

- a. Approve
- b. Require modifications
- c. Send to the convened IRB

B. Review Categories

1. Clinical studies of drugs and medical devices only when the conditions below are met.

a. Research on drugs for which an investigational new drug application is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.); or

b. Research on medical devices for which (i) an investigational device exemption application is not required; or (ii) the medical device is cleared or approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or

b. From other adults and children, when 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 are considered. 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. Children are defined in the federal regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted". In Arkansas, this age is 18 years old.

3. Prospective collection of biological specimens for research purposes by noninvasive means, for example:

- a. Hair and nail clippings in a nondisfiguring manner;
- b. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;
- c. Permanent teeth if routine patient care indicates a need for extraction;
- d. Excreta and external secretions (including sweat);
- e. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
- f. Placenta removed at delivery;
- g. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
- h. Supra and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques;

- i. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
- j. Sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

- a. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
- b. Weighing or testing sensory acuity;
- c. Magnetic resonance imaging;
- d. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
- e. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
- f. Collection of data from voice, video, digital, or image recordings made for research purposes.

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

NOTE: Some research in this category may be exempt from the requirement that it obtain IRB approval (See IRB Policy 7.3). (This listing refers only to research that is not exempt.

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

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

NOTE: Some research in this category may be exempt from the requirement that it obtain IRB approval (See IRB policy 7.3). (This listing refers only to research that is not exempt.

8. Continuing review of research previously approved by the convened IRB as follows:

- a. where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- b. where no subjects have been enrolled and no additional risks have been identified; or
- c. where the remaining research activities are limited to data analysis.

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

C. Initial Review. For the initial review of research to qualify for review by the expedited procedure, the reviewer must determine that the research:

1. Presents no more than minimal risk to human subjects;

Minimal Risk means that 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. Does not involve the identification of the subjects and/or responses which 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;

3. Is not classified; and

4. Falls into one or more of the Regulatory Categories that allow review using the expedited procedure. Note that inclusion on the list does not automatically make the research minimal risk. It merely means that the activity is eligible for review provided the circumstances of the specific proposal involve no more than minimal risk to the subjects.

Document the category of approval and approval period in ARIA and in the approval letter to the Investigator.

D. Continuing Review. For continuing review of research to qualify for review by the expedited procedure, the Reviewer must determine:

1. The research falls into one or more regulatory categories that allow continuing review using the expedited procedure.
2. The current or proposed consent document is accurate and complete.
3. If any review reveals significant new findings that may relate to a subject's willingness to continue participation, the IRB must determine the process to provide that information to the subjects.
4. Whether verification from sources other than the Investigator is needed to ensure that no material changes have occurred since previous review by the IRB. See IRB Policy 7.4 for examples of studies that may warrant outside verification.
5. Whether the research requires review more often than annually.

Document the category of approval and approval period in ARIA and the approval letter to the Investigator.

E. Modifications to previously approved research. Modifications to previously approved research may only be reviewed by the expedited procedure when the change is a Minor Modification. The reviewer must determine that the proposed modification represents a Minor Modification.

F. Responses to Minor Revisions Required. Responses to Minor Revisions Required may be reviewed by the expedited procedure. IRB Policy 9.1 defines Minor Revisions.

Department: UAMS Institutional Review Board
Policy Number: 7.6
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: February 5, 2005; June 1, 2005; March 8, 2008; July 28, 2008; January 24, 2011; March 11, 2011

SUBJECT: Continuing Review

I. Background

Periodic review of all human research activities is necessary to determine (1) whether the risk/benefit ratio has changed, (2) whether there are unanticipated problems involving risks to subjects, and (3) whether any new information regarding the risks and benefits should be provided to subjects.

II. Policy

The IRB must conduct substantive and meaningful continuing review of research at intervals appropriate to the degree of risk. The IRB must decide the frequency of continuing review for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects. The IRB must review each study at least once per year and can require more frequent reviews. All non-exempt research protocols must be periodically reviewed, not less than one time per year, in accordance with this policy.

Studies deemed as Exempt must complete an Annual Update form. See Policy 7.3.

III. Information for Investigators and Continuing Review Submission Process

A. Reminders: As a service, ARIA automatically emails the Principal Investigator and Primary Contact listed in ARIA continuing review expiration notices at approximately 8 and 12 weeks prior to the project's continuing review expiration date with a suggested return deadline. However, Investigators should not rely solely on the ARIA emails. Investigators retain responsibility for submitting and receiving continuing review approval on time. Sufficient time should be allowed for processing the report and IRB approval prior to the project's expiration.

B. Expiration Date and Calculation. The expiration date is the last date on which study activities may occur. The expiration date may change from year to year. Each time the convened IRB conducts continuing review, the study calendar is reset to the date of that meeting.

Several scenarios for determining the date of continuing review apply for protocols reviewed by the convened IRB. To determine the date by which continuing review must occur, focus on the date of the convened meeting at which IRB approval occurs. (These examples presume the IRB has determined that it will conduct continuing review no sooner than within 1 year).

Scenario 1: The IRB reviews and approves a protocol without any conditions at a convened meeting on October 1, 2010. Continuing review must occur within 1 year of the date of the meeting, so the expiration date is September 30, 2011.

Scenario 2: The IRB reviews a protocol at a convened meeting on October 1, 2010, and approves the protocol contingent on specific minor conditions the IRB chair or his/her designee can verify. On October 31, 2010, the IRB chair or designee confirms that the required minor changes were made. Continuing review must occur within 1 year of the date of the convened IRB meeting at which the IRB reviewed and approved the protocol. Since changes did not require review by the convened IRB, the expiration date is September 30, 2011.

Scenario 3: The IRB reviews a study at a convened meeting on October 1, 2010, which requires major revisions or is tabled. The study is reviewed at subsequent convened meetings on October 15 and October 29, 2010. At the October 29, 2010 meeting, the IRB completes its review and approves the study. Continuing review must occur within 1 year of the date of the last convened meeting at which the IRB reviewed and approved the protocol, so the expiration date is October 28, 2011.

C. Consequences of Study Expirations: Failure to submit a timely continuing review will result in expiration of the protocol. If the IRB has not reviewed and approved a research study by the continuing review expiration date, all research activities must stop. No new subjects may be recruited or enrolled.

Interventions and interactions with current subjects must stop. If the Investigator believes there are current subjects whose safety might be at risk by stopping all procedures, the Investigator must contact the IRB immediately upon expiration notice. Interventions and interactions with current subjects may only then occur if the IRB finds an over-riding safety concern or ethical issue involved that makes it in the best interests of individual subjects to continue participating in the research interventions or interactions. Only an IRB Chair may authorize this continued interaction. Investigators may not make this decision. No other research activities may be authorized by the IRB Chair.

If continuing review expires on a drug/device study, the involved Pharmacy contact will be notified.

Generally, study expirations do not need to be reported to regulatory agencies. However, a pattern of study expirations may indicate non-compliance and will be reviewed and classified as per IRB Policies 12.5 and 12.6.

D. Submission Requirements for Continuing Review Form: For all studies undergoing review by the convened IRB or expedited review process, the Investigator must provide the following:

1. A completed Continuing Review Form in ARIA. This form requires the number of subjects accrued, withdrawn and reasons for withdrawal. See IRB Policy 14.5 for accrual and enrollment definitions. The form also requires a summary of activity since the last IRB review. Activities to be summarized include:
 - a. Adverse events and adverse outcomes experienced by subjects;
 - b. Unanticipated problems involving risks to participants/others;
 - c. Complaints about the research and resolution thereof
 - d. Relevant recent literature
 - e. Interim findings
 - f. Relevant multi-center trial reports
 - g. Current risk-benefit assessment based on study results to date
2. Informed Consent Document Verification – ARIA automatically loads the currently approved consent document, if applicable, into the CR form. The Investigator **MUST** verify that the document listed as the current approved form is correct.

IV. IRB Review Process

A. Convened IRB. For all studies requiring review by the convened IRB, the processes outlined in IRB Policy 7.4 will be followed.

B. Expedited Review. Studies which qualify for expedited continuing review will be handled according to IRB Policy 7.5.

Department: UAMS Institutional Review Board
Policy Number: 7.8
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: August 18, 2004; February 8, 2005;
January 24, 2011

SUBJECT: Data and Safety Monitoring Plans

I. Policy

A criterion for approval of research is that when appropriate, the research makes adequate provisions for monitoring the data to ensure the safety of subjects. The IRB must evaluate whether submitted research satisfies this criterion.

Research that is submitted as, or determined to be, greater than minimal risk must provide a plan for monitoring the data to ensure the safety of the subjects. The plan should be tailored to fit the expected risk level, complexity, phase and size of the particular study

Research determined to be minimal risk does not require provisions for data and safety monitoring to protect subjects.

II. Definitions

A. Data and Safety Monitoring Plan (DSMP): A DSMP describes how the Investigator plans to oversee the research subject's safety and welfare.

B. Data and Safety Monitoring Board (DSMB): A DSMB is an independent committee set up to monitor data throughout the study to determine if continuation of the study is appropriate scientifically and ethically.

C. Data and Safety Monitor (DSM): An individual assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. The individual should have relevant medical, ethical and scientific, and monitoring expertise.

III. DSMP CONTENT AND SUBMISSION PROCESS

A. Investigators submitting research that is greater than minimal risk must submit a Data Safety Monitoring Plan to the IRB with initial submission. This may be a separate document in the submission or incorporated into the protocol. The content of each plan will vary based on the complexity and risk level of the study and should be tailored accordingly. All DSMPs must contain at a minimum:

1. The specific data that will be monitored. This should always include safety and efficacy data and any associated events.

Depending on the complexity of the research, the plan may also need to include such things as assessments of data quality, timeliness, participant recruitment, accrual and retention, procedures for analysis and interpretation of the data, how adverse events will be characterized, whether certain events or endpoints trigger other safety measures to be implemented.

2. Identification of the Monitor. This may be a person or group.

In some studies, it will be appropriate for the Investigator, or other member of the study team, to serve as monitor. In other studies, the monitor may need to be independent of the Investigator or Sponsor.

3. The frequency of the monitoring. Identify if the monitoring will occur at specific time points, such as quarterly or every six months, or if it is based on milestones, such as after every 5 subjects or if a certain event occurs.
4. Procedures for communication from the monitor to the IRB. This should address that the IRB will be promptly provided with information from the monitor.

This may be the normal processes for communicating with the IRB if the Monitor is part of the study team or it may require that the Investigator provide the IRB with monitoring reports from an outside Monitor.

IV. IRB REVIEW

A. In order to meet the criteria for approval, the convened IRB must ensure that all research which is greater than minimal risk submits a DSMP with adequate provisions for monitoring the data to ensure the safety of subjects. The adequacy of a plan will vary from study to study. For studies determined to be greater than minimal risk, reviewers should:

1. Verify that the study submission includes a DSMP. The DSMP may be an ARIA generated document based on the submission form, incorporated into the protocol or a separate document in the submission.
2. Determine if the provisions outlined in the DSMP are adequate based on nature of the study.

Factors to consider include but are not limited to whether the appropriate data is being monitored, whether the monitoring is frequent enough, whether the monitor needs to be independent, whether a DSMB is needed or if there is one whether it is independent enough.

Research that may indicate the need for a DSMB is listed below. Being on the list does not require a DSMB but is one factor to take into account in determining the adequacy of submitted DSMP.

- a. Study involves highly toxic therapies or dangerous procedures.
 - b. Study expects high rates of morbidity or mortality.
 - c. It would be ethically important for the study to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet fully addressed.
 - d. Study involves a large study population or is conducted at multiple sites.
3. If no DSMP is found or if the protections in the submitted DSMP are inadequate, the study may not be approved. Contingencies for failure to submit a DSMP must be classified as major revisions required.

Department: UAMS Institutional Review Board
Policy Number: 7.9
Section: Procedures for Study Review
Effective Date: July 31, 2002
Revision Date: May 20, 2004; February 8, 2005; January 24, 2011

SUBJECT: Suspension or Termination of Approval for Cause

I. POLICY

The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB Policies or has been associated with unexpected serious harm to subjects.

On an urgent basis, the Chair or Experienced IRB Reviewer may also suspend studies if a report under IRB Policy 10.2 indicates subjects or others are at immediate risk of harm. The suspension will be reported to the IRB in accordance with IRB Policy 10.2

The Vice Chancellor for Research may suspend or terminate approval of research studies or privileges of individual investigators. The Vice Chancellor will notify the IRB of these decisions.

II. DEFINITIONS

A. Suspension for Cause: An action taken by the IRB to temporarily stop some or all research procedures until the outlined requirements are met.

NOTE: When continuing review of a research project does not occur prior to the end of the approval period, the IRB approval expires automatically. While research activities must stop in most cases, this is not considered a suspension or termination of IRB approval.

B. Termination for Cause: An action taken by the IRB to permanently stop some or all research procedures.

An example of suspensions or terminations for cause might include: inappropriate involvement of human subjects in research, serious or continuing noncompliance with federal regulations or IRB policies, new information regarding increased risk to human subjects, etc.

III. PROCESS

A. Notification to PI. If a study is suspended or terminated for cause, the notification letter to the Investigator will include reasons for the IRB's action.

B. Consideration for Subjects Currently Enrolled. If the study has currently enrolled subjects, the IRB will consider:

1. What actions are needed to protect those subjects;
2. The procedures for withdrawal of those subjects must take into account their rights and welfare. This may include such actions as making arrangements for care off study, transferring to another Investigator or continuing the research under independent monitoring.
3. Whether current subjects should be informed of the suspension or termination and the process for informing those subjects.

C. Investigator Reporting Obligations. Even if a study is suspended or terminated, Investigators must continue to meet the reporting requirements as required by IRB Policy 10.2

D. IRB Reporting Obligations. All suspensions or terminations for cause will be reported in accordance with IRB Policy 2.6.

Department: UAMS Institutional Review Board
Policy Number: 7.10
Section: Procedures for Study Review
Effective Date: May 13, 2004
Revision Date:

SUBJECT: Cooperative Protocol Research Program (CPRP) Protocols

Review of Cooperative Protocol Research Program (CPRP) Protocols. Continuing IRB review is required as long as individually identifiable follow-up data are collected on subjects enrolled in DHHS-supported Cooperative Protocol Research Program (CPRP) protocols. This remains the case even after a protocol has been closed at all sites and protocol-related treatment has been completed for all subjects.

CPRP protocols are those projects, which involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort (45 CFR 46.114). Such arrangements must be approved by the UAMS IRB, its Chair or designee.

Department: UAMS Institutional Review Board
Policy Number: 8.1
Section: Change in Protocol
Effective Date: July 31, 2002
Revision Date: February 1, 2005; June 1, 2005; March 5, 2008;
January 24, 2011

SUBJECT: Modifications to previously approved research

I. POLICY

The UAMS IRB must review and approve all proposed modifications to approved research prior to implementation. The term “approved research” encompasses all study documents, processes and procedures.

All modifications will be reviewed to determine that the research satisfies all of the regulatory approval criteria outlined in IRB Policy 7.1. When modifications affect one or more of the approval criteria, also called Major Modifications, the modification must be reviewed by the convened IRB. Minor Modifications may be reviewed by the expedited review process.

II. PROCESS

A. Investigator Process:

1. Modifications must be submitted through the ARIA Modification Form. Each modification will include:

a. A summary describing the changes; the reason for the change; Investigator’s opinion as to impact of change on study and on subjects; and whether changes are needed to the consent form.

If the modification constitutes a change that might affect a subject's willingness to continue in the study, the Investigator must submit a plan for informing all currently enrolled subjects. The plan should address timing (e.g. immediately, next visit) and method (e.g. mailed notification, re-consent) and should be tailored to the nature of the research and the new information.

Investigator may submit a PI letter to the IRB to supplement the brief overview requested at the beginning of the Modification Form.

b. Revisions to the appropriate sections of the submission form.

c. All modified documents, including but not limited to consent forms, protocols, recruitment materials, and Form 1572s. If a sponsor or a granting agency has requested the modification, a copy of the communication from the sponsor should be submitted.

NOTE: All documents to be modified must be submitted with the proposed modifications tracked. The IRB reserves the right to defer review if the changes are not highlighted or tracked on the document to be revised. If a document is received from a sponsor where tracking changes is not possible, then an outline of the protocol changes may be substituted.

If the change affects the consent form, both a tracked version and a clean version must be submitted.

d. If the modification is to change study personnel, information must be provided to show who specifically is being added to the study and their role and qualifications. In order to add an individual as study personnel, that person must have an ARIA account and current CITI training. If the personnel change or addition impacts the information in the consent form, tracked and clean versions of the consent form should also be submitted.

2. No changes may be implemented until IRB, and as applicable Sponsor, approval is received. The only exception is a change necessary to eliminate apparent immediate hazards to the

research participants. In such cases, the Investigator will promptly inform the IRB, and as applicable the Sponsor, of the implemented change.

B. IRB Process:

1. Major Modifications – Will be reviewed by the convened IRB in accordance with IRB Policy 7.4.

2. Minor Modifications – Will be reviewed by an Experienced Reviewer in accordance with IRB Policy 7.5.

Department: UAMS Institutional Review Board
Policy Number: 8.2
Section: Change in Protocol
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; May 20, 2004

SUBJECT: Change in Principal Investigator

The IRB must be notified within 30 days of a change in the principal investigator. When changing investigators, please submit the following:

1. Protocol Amendment/Modification Form through ARIA.
2. A letter from the principal investigator indicating the change in responsibility.
3. A letter from the new investigator accepting the responsibility for the research, and the new investigator's CV if not already part of the study file.
4. Revised protocol, consent forms, HIPAA authorizations or advertisements, as applicable.
5. Revise FDA Form 1572 if applicable.

Any IRB project associated with a Principal Investigator (PI) who has left the University of Arkansas for Medical Sciences cannot continue without modification. These projects must be closed or a new PI must be signed to take full responsibility for the project and the subjects enrolled in the project. If the study cannot be closed because of safety issues related to participant involvement, it is mandatory that a local, affiliated investigator be named as PI.

If a significant difference in the background, training and expertise exists between the two PIs, the IRB may consider the change in PI to be a major revision, requiring a full Board review before the change can be officially implemented. A change in sub-investigators must also be reported to the IRB. It is the responsibility of the PI to notify the IRB when a sub-investigator is dropped from a study and when a new sub-investigator joins an IRB-approved project. Sub-investigator changes are considered minor revisions, but must also be approved before the change can be implemented.

Department: UAMS Institutional Review Board
Policy Number: 8.3
Section: Change in Protocol
Effective Date: July 31, 2002
Revision Date: May 20, 2004

SUBJECT: Off-Campus Duty Assignment (Sabbatical) or Leave of Absence

When the Principal Investigator (PI) is conducting a study and receives an off-campus duty assignment, a sub-investigator must be assigned to the research project throughout the duration of the sabbatical. Appropriate change in PI forms will need to be submitted to the IRB.

Department: UAMS Institutional Review Board
Policy Number: 8.4
Section: Change in Protocol
Effective Date: February 8, 2005
Revision Dates: NA

SUBJECT: Study Closure

POLICY: Once all study activities are complete and there is no longer a need to access identifiable participant information, Investigators should close the study out with the IRB within 30 days of decision to close study. Investigators may request closure of a study upon continuing review or by submitting a separate study closure form.

PROCEDURE:

1. Investigator:

1.1 If Investigator chooses not to close at the time of Continuing Review, a fully complete study closure form should be submitted through ARIA.

2. IRB Staff:

2.1 Upon receipt of Study Closure Form in ARIA, IRB Staff should verify study closure is appropriate. This may require comparison of information submitted on Closure form and last Continuing Review form and/or contacting the Investigator to resolve any outstanding issues.

3.3 Prepare a study closure letter for Chair review, approval and signature.

3.4 Place on next available agenda under Study Closures reported to the Committee.

Department: UAMS Institutional Review Board
Policy Number: 9.1
Section: IRB Decisions
Effective Date: July 31, 2002
Revision Date: August 26, 2004; June 1, 2005; April 5, 2007; March 5, 2008; July 28, 2008; January 24, 2011

SUBJECT: Range of IRB Decisions

Acknowledged: When approval is not required, submitted documents may be acknowledged.

Approved: The submission, including associated documents, is approved. The approval letter will list all documents approved with the submission. Studies may not begin until an initial approval letter is received. Modifications may not be implemented until the corresponding approval letter is received.

Not Yet Approved Major Revisions Required: The submission is not approved. There are Major Revisions required. The Investigator's response to those major revisions, also called contingencies, must be reviewed by the convened IRB. The IRB Letter to the Investigator will list the required revisions that must be addressed.

Major revisions request substantive clarifications or modifications that are directly relevant to determinations that must be made by the convened IRB. They are broad and unspecific such as "The IRB needs more information about why ARM 2 of the study is needed" or "The IRB is concerned that the PI has not done enough to reduce risks to human subjects. Please revise or explain" or "The consent form was written in a very scientific manner. Please revise so that it is understandable" or "the IRB is concerned that there are not enough resources to complete this project, please explain".

Studies may not begin until an initial approval letter is received. Modifications may not be implemented until the corresponding approval letter is received.

Not Yet Approved Minor Revisions Required: The submission is not approved. There are Minor Revisions required. The Investigator's response to those minor revisions, also called contingencies, may be reviewed by an IRB Chair or Experienced IRB Reviewer. The IRB Letter to the Investigator will list the required revisions that must be addressed.

Minor revisions are very specific and direct which allows the IRB Chair or Experienced IRB Reviewer to readily verify the revisions have been met. Some examples are "Please revise consent form page 4 to add the study procedures described in your protocol on page 2" or "Please add the PIs name to the consent form page one in accordance with UAMS IRB policy" or "Remove ARM 2 of the study to reduce the risk of heart attack" or "Please remove the second sentence from your recruitment advertisement as it is coercive".

Studies may not begin until an initial approval letter is received. Modifications may not be implemented until the corresponding approval letter is received.

Tabled: The submission lacks information necessary for the IRB to determine that the regulatory approval criteria are met. The IRB Letter to the Investigator will list the information needed and any required revisions. The Investigator's response must be reviewed by the convened IRB.

Declined: The research or modification as presented has serious deficiencies affecting the safety and welfare of the projected subject population. These deficiencies cannot be addressed. The IRB letter will provide the rationale for the decision. For new studies that are declined, the Investigator may choose to address the deficiencies but must do so under an entirely new study submission in ARIA. For modifications that are declined, the Investigator may not implement any of the proposed changes.

Suspended for Cause: An action taken by the IRB to temporarily stop some or all research procedures until the outlined requirements are met. The IRB can, at its discretion, take a range of actions regarding the conduct of a given protocol in order to better secure the protection of participants. This action is a suspension of IRB approval and must be reported in accordance with IRB Policy 2.6.

Terminated for Cause: An action taken by the IRB to permanently stop some or all research procedures. The IRB can, at its discretion, take a range of actions regarding the conduct of a given protocol in order to better secure the protection of participants. This action is a termination of IRB approval and must be reported in accordance with IRB Policy 2.6.

Department: UAMS Human Research Advisory Committee
Policy Number: 9.2
Section: IRB Decisions
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; August 26, 2004

SUBJECT: IRB Notification of Meeting Decisions

Upon completion of the review of any submission (new, modified, continuing review, etc.), regardless of exempt, expedited or full classification, the IRB office will prepare a letter noting the outcome of the review.

This letter will include:

- i. Outcome of the review by the Chair or IRB and if study is declined, suspended or terminated, the reason for the decision;
- ii. Date the decision was reached; and
- iii. Date of next scheduled continuing review, as appropriate.

Principal Investigator and Primary Study Contact will receive an email notification that a letter is available in ARIA. Any personnel listed on the study will have access to the letter in ARIA.

Department: UAMS Institutional Review Board
Policy Number: 10.2
Section: Principal Investigator Responsibilities
Effective Date: July 31, 2002
Revision Date: October 10, 2002; July 7, 2004; February 8, 2005;
June 1, 2005; March 5, 2008; July 28, 2008; January
24, 2011; March 11, 2011

SUBJECT: Information that must be reported to the IRB and IRB Actions

I. Policy

Federal regulations require the IRB to ensure that Investigators promptly report all “unanticipated problems involving risks to subjects or others” (UPIRTSO).

This policy identifies the types of events that Investigators must report to the IRB. The IRB will determine if the reported event is an unanticipated problem involving risk to subjects or others. If an event is determined to be UPIRTSO, IRB Policy 2.6 on reporting will apply. If an event is determined to be non-compliance, IRB Policy 12.6 will apply.

Reports submitted under this policy will be reviewed by an IRB Chair or Experienced IRB Reviewer.

II. Definitions

A. Related: For this policy, an event is “related” if it was caused by participation in the research activity or there is a reasonable possibility that the event may have been caused by the procedures involved in the research.

B. Risk: The probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a research study.

C. Unanticipated: A problem is “unanticipated” when it was unforeseeable at the time it occurred.

D. Unanticipated Adverse Device Effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

E. Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO): Any problem, event or new information that is:

- a) Unanticipated or unexpected;
- b) Related to the research; and
- c) Involves new or increased risks to subjects or others.

F. Unexpected: An event is “unexpected” when its specificity, nature, severity or incidences are not accurately captured in the approved consent form. Examples include a lower rate of response to treatment or a side effect that is more severe than initially expected.

III. Investigator Reporting Responsibilities

A. Time Frame: All events listed below must be reported in ARIA within 10 days of the event or notification of event if non-local. Events requiring reports under this policy which have resulted in death or are life-threatening should be reported immediately to the IRB office or IRB Chair.

Reporting requirements apply regardless of whether they occur during the study, after study completion or after subject withdrawal or completion.

B. Content of the Report: Each report should be submitted through ARIA and contain:

- 1. Description of the event including date and location;

10.2 Information that must be reported to the IRB and IRB Actions

2. Nature of the risk to subjects from the event, noting whether Investigator believes the event increases the risk to the subject or others;
3. How the event relates to the research;
4. Whether the Investigator believes the consent or protocol should be changed or if subjects should be notified.

C. Reportable Events:

1. Local adverse events that the Investigator determines are:

- a. Unexpected;
- b. Related to the research; and
- c. Involve new or increased risks to subjects or others.

An event must meet all three criteria to require reporting under this policy.

2. Non-local adverse events that have been determined to be unanticipated problems involving risks to subjects or others.

3. Unanticipated adverse device effects.

4. Any change or deviation made to the research without prior IRB approval in order to eliminate apparent immediate harm.

5. An accidental or unintentional change to the IRB-approved protocol that placed one or more subjects at increased risk or affects the rights and welfare of subjects or others.

6. Any new information that indicates an unexpected change to the risks or potential benefits of the research. This includes, but is not limited to,

- a. Revised Investigator Brochures, Package Inserts, Device Manuals
- b. Publications in the literature
- c. Data and Safety Monitoring Reports
- d. Interim results or other findings.

Examples include MedWatch reports indicating that a side effect is more frequent or severe than expected, or a publication showing that an arm of study is of no therapeutic value.

7. A breach in confidentiality that may involve risk to subjects or others. Examples include the loss of a laptop computer on which subject identifiers are stored or the loss of study records on a thumb drive.

8. Any complaint of a participant that indicates an unanticipated risk or any complaint that cannot be resolved by the research team.

9. Incarceration of a subject if study was not previously reviewed with the anticipation of enrolling prisoners.

10. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol

11. Restrictions, suspension or termination of study by the sponsor, Investigator, funding agency, regulatory body, or institutional administration.

12. The premature completion of a study.

13. Notifications of pending audits, inquiries or investigations by federal agencies.

14. Written reports from study monitor

15. Any other problem that was unexpected, related to the research and places the subject or others at a greater risk than previously known.

Other problems which do not meet the UPIRTSO definition should be submitted at the time of continuing review in summary format.

IV. IRB Responsibilities

A. Initial Review of Reports. An IRB Chair or Experienced IRB Reviewer will review each report and determine if the reported event is a UPIRTSO under this policy or a report of potential non-compliance using IRB Policy 12.5.

1. Event is not a UPIRTSO. If the Reviewer determines that the reported event does not meet the definition of a UPIRTSO, the Reviewer will acknowledge the report.

a. Minor Modifications Submitted. If any Minor Modifications were submitted with the report, the Reviewer will review and approve in accordance with the Expedited Procedure outlined in IRB Policy 7.5.

b. Minor Revisions Required. If the reported event requires Minor Revisions, the Reviewer will outline those requested modifications in a letter to the Investigator.

c. Major Modifications Submitted. If the modifications submitted with the report cannot be considered Minor Modifications, the Reviewer should notify the IRB staff that the report and modifications need to be placed in the "Updates to be Reviewed by Two Reviewers" section of an upcoming agenda.

d. Major Revisions Required. If the reported event requires what the Reviewer would consider major revisions, the Reviewer should prepare a Major Revisions Required letter and identify the revisions that are required. The response will be placed in the "Updates to be Reviewed by Two Reviewers" section of the agenda.

e. Event is report of Non-Compliance. The Reviewer should follow the requirements of IRB Policy 12.6.

2. Event is a UPIRTSO. The reported event will be placed on the next available agenda under the "Updates to be Reviewed by Two Reviewers" section. The Reviewer will determine if any subject or others are at immediate risk of harm. If so, the Reviewer may suspend the study immediately and notify the Investigator in accordance with IRB policy 7.9

B. UPIRTSO Review by Convened IRB. Two Reviewers will be assigned to review the UPIRTSO event and present the problem to the convened IRB in sufficient detail to allow the IRB to take appropriate actions. All Reviewers will have access to the entire study file. Actions that may be taken by the IRB:

1. Require modifications to the protocol
2. Require modifications to the information disclosed during the consent process
3. Require current subjects to be notified when information may relate to subjects' willingness to continue to participate in the research
4. Require current subjects to re-consent participation
5. Require additional information be provided to past subjects
6. Request the research be audited by the Office of Research Compliance
7. Require monitoring of the consent process
8. Require more frequent continuing reviews

10.2 Information that must be reported to the IRB and IRB Actions

9. Require additional monitoring from an independent monitor

10. Refer to other organizational entities as appropriate. Examples include, but are not limited to, working with the HIPAA Office if the problem involves an unauthorized use, loss, or disclosure of Protected Health Information; requiring specific research education training in conjunction with the research education office or involving the Organizational Official.

11. Suspend the study for cause in accordance with IRB policy 7.9

12. Terminate the study for cause in accordance with IRB Policy 7.9

C. UPIRTSO Reporting. All events determined to be UPIRTSOs will be reported in accordance with IRB Policy 2.6

Department: UAMS Institutional Review Board
Policy Number: 10.3
Section: Principal Investigator Responsibilities
Effective Date: January 24, 2011
Revision Date:

SUBJECT: Protocol Content and IRB Submissions

I. PURPOSE

The purpose of this policy is to define what must be submitted to the IRB and the minimum requirements that should be included in a Protocol.

II. POLICY

The IRB or Experienced IRB Reviewer must have sufficient information in order to determine whether the criteria for approval of research are met.

Protocols which do not have the minimum content may be rejected. Grant applications generally will not contain sufficient information for IRB purposes. Incomplete ARIA submissions may also be rejected.

A pre-review contingency letter will be sent to the Investigator outlining the items that must be addressed.

III. PROTOCOLS

A. All Protocols. Heading titles may vary in order or description and sections may be combined in some protocols, however, all protocols must include the following content:

1. Each page should include page numbers, protocol version number, date, protocol name or descriptive identifier and the PI or Sponsor name.
2. Title of the protocol. This title should match the one entered into ARIA.
3. Background and Significance/Rationale. Establishes the significance of the topic to be researched and provides conceptual framework for addressing the hypothesis (es). Justifies proposed methods for intervention and assessment. Should include a statement placing the study in the context of the development or proposed use of the test article (if applicable).
4. Protocol Summary. Provides a brief synopsis of study, generally no more than 1-2 pages. Usually includes Background; Aims/Objectives; Study Design; Study Population; and Statistical Plan or Data Analysis.
5. Specific Aims/Objectives. This should clearly state the hypotheses to be tested and the objectives or specific aims.
6. Study Design and Procedures. Must provide details of clinical study design, including an in-depth narrative of the methodology to be employed. Flow charts or study calendars may be used to describe procedures and tests. Identify if any procedures are already being performed for diagnostic or treatment purposes.
7. Study Population/Data Source. This should include the study inclusion/exclusion criteria; expected number of subjects to be enrolled and age range of the subjects. If the study is a chart review only, the source of the data and data elements must be listed.
8. Ethical Considerations. This should include a description of the informed consent process or justification for waiver as appropriate. For protocols not under the Investigator's control, this must be addressed in the submission.

9. Risks and Benefits. This should provide the expected risks and benefits of the study procedures and the procedures taken to minimize those risks. Provisions to protect subject privacy and the confidentiality of the data should also be addressed.

10. Statistical Plan. Provide details of Statistical Considerations. In addition to proposed statistical analyses, when appropriate, this section should include a justification of the sample size and a statement regarding power based on one or more of the primary outcome measures.

11. Data Handling and Recordkeeping. Provides information on the method(s) for data collection and specifies data collection tools. Should also address confidentiality, de-identification of data, data storage, and security measures.

12. Study Registration and Publication. Provides information on the planned dissemination of data, including plans for publications, presentations, and website registration (i.e. www.clinicaltrials.gov).

13. References.

B. As Appropriate to the Study. Depending on the nature of the research, the following elements may be required for protocol review:

1. Safety or Efficacy Assessments. Provides details for how adverse events, serious adverse events, and/or unanticipated adverse device effects will be captured and reported.

2. Additional Safeguards to Protect Vulnerable Populations

3. Test Article Description and Status. Provides a brief description of the investigational product/device. If applicable, include information on formula/strength, route of administration, dosing schedule, and manufacturer/make/model (devices).

4. Recruitment Plan. Describe how potential subjects will be identified and approached.

5. Monitoring Plan. May be addressed in protocol, ARIA Submission or separate monitoring plan. Describe safety tracking plans, plans for interim data monitoring, and stoppage rules. Identifies any special committees (i.e. DSMB) that will be involved in making safety assessments.

6. Multi-Site Protocols where UAMS is the lead site must address minimal training requirements required of those from other sites, how IRB approvals from other sites will be managed and how information will be managed between the sites, including reporting unanticipated problems involving risks to subjects or others, modifications to study or documents.

7. Quality Control and Quality Assurance – Required for FDA regulated studies. Describe any Quality Assurance or Quality Control systems to be used. If such systems are not pertinent to your study, please indicate that as well.

8. Abbreviations.

IV. ARIA Submission

A. Documents. In addition to a completed ARIA Original Submission Form or Modification Form, Investigators must also submit the following documents, if applicable to the study:

1. Protocol

2. Consent Forms or Information Sheets

3. Description of the Consent Process. This may be included in protocol, submission form, separate SOP but must include:

- a. The person (people) who will conduct the consent interview
- b. The person who will provide consent or permission (e.g. subject, parent, LAR)
- c. Any waiting period between informing the prospective subject about the study and obtaining consent.
- d. Steps taken to minimize the possibility of coercion or undue influence.
- e. The language used by the person (people) obtaining consent.
- f. The language understood by the prospective subject or LAR

4. DHHS Model Consent

5. HIPAA Authorization

6. Grant Application.

7. Surveys, Questionnaires or any other research-related materials that will be seen by the subject.

8. Investigator's Brochure, Package Insert or Device Manual

9. Letter from FDA or RSC regarding test article status.

10. Advertisements, flyers or other materials used for recruitment purposes

11. Approvals from any other required institutional committees (e.g. ACHRI, PRMC, COIC).

12. Letters of Assurance from other research sites

13. A simplified CV or accurate completion of profile in ARIA providing same information.

B. Personnel. All individuals engaged in the research as UAMS, ACH or other institution subject to the oversight of the UAMS IRB must be listed as personnel in ARIA with a description of their role and qualifications. Failure to list the personnel in ARIA may result in delays in access to patient information systems and audit findings.

Department: UAMS Institutional Review Board
Policy Number: 12.5
Section: Quality Assurances
Effective Date: March 5, 2008
Revision Date: January 24, 2011

SUBJECT: Reports of Potential Non-Compliance

Reports of potential non-compliance may be in the form of, but not limited to, audit reports, deviations, violations, adverse event reports, publications and complaints.

These reports can come from investigators, members of the research team, research compliance, study sponsors, OHRP, FDA, participants, committees on campus and interested third-parties. Potential non-compliance may also be discovered during regular IRB review.

Process

IRB Staff (including the Chair or Reviewers) shall review all reports of potential non-compliance by the following methods:

1. Compile information. If additional information is needed, contact the person who made the initial report and any other person involved to make sure all the facts are available.

2. Ask the following questions:

a) Does this information represent an action of non-compliance? If yes, refer to IRB Policy 12.6 regarding findings of noncompliance.

b) Is this information unanticipated AND does it indicate that participants or others are at increased risk of harm? If yes, place on IRB agenda and follow IRB Policy 10.2 and report as required by IRB Policy 2.6.

If the answer to both questions is no and the report is in the form of an audit, assign to IRB agenda as audit report to be acknowledged. For all other reports, process the report for acknowledgment by an expedited reviewer.

3. If IRB Staff is unable to answer the questions in step 2, IRB staff will consult with IRB Director or IRB Chair for determination.

Department: UAMS Institutional Review Board
Policy Number: 12.6
Section: Quality Assurances
Effective Date: March 5, 2008
Revision Date: January 24, 2011

SUBJECT: Findings of Non-Compliance under IRB Policy 12.5

I. Policy

When IRB Staff, Chair or Reviewers determine that information reported and reviewed under IRB Policy 12.5 rises to the level of noncompliance, these findings of noncompliance shall be classified using the federal regulation criteria for classification of noncompliance events.

II. Process

The IRB Staff (including the Chair) shall use the following format for each issue of noncompliance:

Classify – Report – Remediate - Follow Up Reports

Classify:

1. Minor Non-compliance: Unintentional or willful failure to comply with applicable Federal Regulations, UAMS IRB policies and procedures, UAMS and/or other institutional policies and procedures, or the determinations of the UAMS IRB that does not meet the definition of serious or continuing non-compliance.

2. Serious Non-compliance: An action or omission which places, or could place, a subject at risk of significant harm or affects the rights and welfare of human participants or violates the basic principles of the Belmont report to which the institution has promised to adhere. This category may also include actions that could compromise the validity and integrity of the research data.

3. Continuing Non-Compliance: A pattern of repeated actions or omissions that indicate a deficiency in the ability or willingness to comply with Federal Regulations, UAMS and/or other institutional policies and procedures, or the determinations of the UAMS IRB or affects or could affect the rights and welfare of human subjects or violate the basic principles of the Belmont report to which the institution has promised to adhere.

If during review Scientific Misconduct is suspected, which is fabrication, falsification, or plagiarism in proposing, performing or reviewing research, or in reporting research results, report the preliminary findings to the VC for Academic Affairs.

Report:

Report any incident of Serious or Continuing Non-Compliance to the IRB Chair immediately because subjects may be at risk. The IRB office must follow UAMS IRB Policy 2.6 for reporting all incidents classified as Serious or Continuing Non-Compliance.

Add report to next available IRB agenda as an "Update to be Reviewed by Two Reviewers" to allow the IRB to deliberate concerning remediation of the problem. All reviewers will have access to all available information.

Remediate:

While not limited to the following, IRB determinations may include:

- Requiring additional information to make a determination.
- Requiring additional investigator or study staff education.
- Requiring changes in study design or methodologies
- Suspension of any or all of the following study activities:

12.6 Findings of Noncompliance under IRB Policy 12.5

- i. Recruitment of subjects
- ii. Screening and enrollment activities
- iii. Research interventions and interactions or
- iv. Follow up activities
- e. Suspension of the investigator's research privileges
- f. Termination of the investigator's research privileges
- g. Termination of the study for cause
- h. No further action may be needed if the investigator has presented an adequate corrective action plan.

Additional protections may include, but are not limited to:

- a. Revision or modification of the protocol, consent or other study processes
- b. Verification that subject selection is appropriate
- c. Direct observation of the informed consent process by the ORC or individual IRB members
- d. Require that current subjects be re-consented to participation
- e. Enhanced monitoring of the research activity through such mechanisms as: the employment of data safety monitors or a data safety monitoring board, or continued evaluation by the ORC.
- f. Request an off-cycle data and safety monitor or board review
- g. Request further directed reviews by ORC of targeted areas of concern
- h. Require the investigator to issue a status report after each subject receives an intervention
- i. Modify the continuing review cycle
- j. Require the Investigator, and his or her staff, to receive focused education relevant to the area of non-compliance
- k. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation
- l. Notification of other groups such as the CCTR, PRMC, *etc*

Appropriate and timely communication to affiliate institutions involved will occur through the entire process.

Follow Up Reports

Because reporting under IRB Policy 2.6 requires very prompt turn-around, a preliminary report is often sent. After the IRB reviews non-compliance issues and decides on further remediation, a follow up report may be required in accordance with IRB Policy 2.6

Department: UAMS Institutional Review Board
Policy Number: 13.1
Section: Confidentiality
Effective Date: July 31, 2002
Revision Date: June 10, 2004; January 24, 2011

SUBJECT: Confidentiality Protections

I. Purpose

To identify studies in which Certificates of Confidentiality may be required as an additional confidentiality protection. Confidentiality refers to how a subject's identifiable information will be handled.

II. Sensitive Research

Research may be considered sensitive if it involves the collection of identifiable and sensitive information. Examples of the information which might be considered sensitive include, but are not limited to:

- a. Information relating to sexual attitudes or behaviors;
- b. Information relating to the use of alcohol, drugs or other addictive products;
- c. Information pertaining to illegal conduct;
- d. Information that if released could reasonably be damaging to an individual's financial standing, employability, or reputation within the community;
- e. Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatization or discrimination;
- f. Information pertaining to an individual's psychological well-being or mental health;
- g. Genetic information.

III. Certificates of Confidentiality and Exceptions

Certificates of Confidentiality are issued by federal agencies, such as the NIH or FDA, as a means to protect the researcher from compelled disclosures, such as by subpoena, of identifying information or characteristics of research subjects.

The Confidentiality Certificate does not govern the voluntary disclosure of identifying characteristics of research subjects but only protects subjects from compelled disclosure of identifying characteristics by the researcher. Researchers, therefore, are not prevented from the voluntary disclosure of matters such as child abuse or a subject's threatened violence to self or others. However, if a researcher intends to make such voluntary disclosures, the consent form should clearly indicate this.

IV. Procedure

For studies determined to be collecting sensitive information, the IRB may require the PI apply for a Certificate of Confidentiality as an added protection. The investigator should note in the IRB application if he or she plans to apply for a Certificate of Confidentiality. The submission must outline any conditions under which confidential information will be voluntarily disclosed, such as to meet mandated reporter requirements. The informed consent document must accurately reflect those conditions, including any voluntary disclosure by the researcher.

The IRB is required to determine whether the risks to subjects are minimized, informed consent is appropriate, and privacy and confidentiality protections are adequate.

Department: UAMS Institutional Review Board
Policy Number: 13.2
Section: Confidentiality
Effective Date: July 31, 2002
Revision Date: June 10, 2004

SUBJECT: Confidentiality in Archived Data- Social Science

The Principles

Social scientists have a deep and genuine commitment to preserve the anonymity of the subjects whom they study in the course of their research. Most often applied to individuals who consent to be interviewed in surveys, this commitment extends also to groups, organizations, and entities whose information is recorded in administrative and other kinds of records.

The social sciences broadly defined (as well as a number of professional associations) have promulgated codes of ethics that require social scientists to ensure the confidentiality of data collected for research purposes. (See, for example, the "Ethical Guidelines for Statistical Practice" of the American Statistical Association, which stresses the appropriate treatment of data to protect respondent confidentiality.) Both the rights of respondents and their continued willingness to voluntarily provide answers to scientific inquiries underlie this professional ethic. That ethic applies to all participants in the research enterprise, from data collectors to archivists to secondary analysts who use such data in their research.

Sets of regulations also bind all of us in the research enterprise to measures intended to protect research subjects as well as data obtained from such subjects. These regulations range from federal and local statutes to rules instituted by universities and colleges.

The Practice of Protecting Confidentiality

Two kinds of variables often found in social science datasets present problems that could endanger the confidentiality of research subjects. Most familiar are the **direct identifiers** that may have been collected in the process of survey administration. These include items such as names, addresses (including ZIP codes), telephone numbers (including exchanges), Social Security numbers, and other linkable identification numbers such as driver license numbers, certification numbers, etc. Data collectors should remove all such identifiers when preparing public use datasets.

Another category of variable can often be problematic as well: these are the **indirect identifiers** that might be used in conjunction with respondent attributes and publicly available information to identify individual respondents. This category is harder to deal with, since it includes items that are often quite useful for statistical analysis (indeed, that is probably why such information was collected in the first place), and is dependent on the content of the data collection and the nature of the research subjects included in the dataset. Some examples of these indirect identifiers are detailed geography (e.g., state, county, or Census tract of residence), organizations to which the respondent belongs, educational institution from which the respondent graduated (and year of graduation),

exact occupations held, place where the respondent grew up, exact dates of events, detailed income, and offices or posts held by the respondent.

How to Handle Indirect Identifiers

If, in the judgment of the principal investigator, a variable might act as an indirect identifier (and thus could be used to compromise the confidentiality of a research subject), the investigator should "treat" that variable when preparing a public use dataset. Typical kinds of treatment commonly used are:

- Removal--Eliminating the variable from the dataset entirely.
- Bracketing--Combining the categories of a variable.
- Top-coding--Restricting the upper range of a variable.
- Collapsing and/or combining variables--Merging the concepts embodied in two or more variables by creating a new summary variable.

Excerpted from "Guide to Social Science Data Preparation and Archiving", Inter-University Consortium for Political and Social Research

Department: UAMS Institutional Review Board
Policy Number: 14.1
Section: Recruitment Practices
Effective Date: July 31, 2002
Revision Date: June 24, 2004

Subject: Selection of Subjects

Overview: The requirement for an equitable selection of subjects helps ensure that the burdens and benefits of research will be fairly distributed. When the National Commission for the Protection of Human Subjects recommended that the IRB be required to make this determination, they noted that questions of equity have only recently been associated with scientific research. In the 19th and early 20th centuries, the burdens of research fell largely upon poor patients in hospital wards, while the benefits flowed primarily to private patients. This inequity was starkly revealed in the Tuskegee syphilis study, in which disadvantaged blacks in the rural south were recruited for studies of the untreated course of a disease that was by no means confined to that population. Such unjustified over utilization of certain segments of the population led the National Commission to recommend that selection of research subjects be scrutinized to determine "whether some classes (e.g., welfare patients, racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position or their manipulability, rather than for reasons directly related to the problem being studied."

Easy availability, compromised position, and susceptibility to manipulation often overlap. For example, psychology students are readily available for psychological research, medical students are readily available for medical research, prisoners, patients in mental institutions, and military personnel are readily available for a variety of research activities, and employees of drug manufacturing companies are readily available for pharmaceutical research. Subjects selected from these populations are also compromised to the extent that their jobs, promotions, grades, etc., are dependent upon those who might be recruiting them for research. This circumstance makes them susceptible to manipulation.

Patients may also be susceptible to real or imaginary pressure to participate. If an investigator also serves as a patient's primary physician, he or she may feel obliged to participate in the research out of a desire to please, gratitude, or fear that failure to do so will result in hostility or abandonment. Patients who are dependent upon a particular facility for their care (e.g., Veterans Hospitals, Indian Health Service Hospitals, or community health clinics) may feel that they will be treated less well or with less favor if they refuse to participate in research.

With these caveats in mind, investigators and the IRB must be careful not to *overprotect* vulnerable populations so that they are excluded from participating in research in which they wish to participate, particularly where the research involves therapies for conditions with no available treatments (such as HIV). So too, patients with serious or poorly understood disorders may want to participate frequently in research designed to provide a better understanding of their condition. The fact that the subject may be either a patient of the principal investigator or a patient in the clinic or hospital where the investigator conducts the research should not preclude them from the opportunity to choose to participate as often as they wish.

Just as the inclusion of disproportionate numbers of racial or ethnic minorities in research studies might overburden these groups without affording them the benefits that will result from

the research, so will under representation of these groups in study populations ensure that they will not benefit from the research. The National Institutes of Health (NIH) requires that its research grantees include minorities and women in study populations "so that the research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study." If a proposed project includes a study population in which women and minorities are not appropriately represented, the investigator must provide "a clear compelling rationale for their exclusion or inadequate representation". See IRB [policy 17.6](#) and [policy 17.8](#) for further discussion of this issue.

Evaluation Guidelines Regarding Equitable Selection of Subjects:

1. Will the burdens of participating in the research fall on those most likely to benefit from the research?
2. Will the solicitation of subjects avoid placing a disproportionate share of the burdens of research on any single group?
3. Does the nature of the research require or justify using the proposed subject population?
4. Are there any groups of people who might be more susceptible to the risks presented by the study and who therefore ought to be excluded from the research? Are the procedures for identifying such individuals adequate?
5. To the extent that benefits to the subjects are anticipated, are they distributed fairly? Do other groups of potential subjects have a greater need to receive any of the anticipated benefits?
6. To the extent that participation in the study is burdensome, are these burdens distributed fairly? Is the proposed subject population already so burdened that it would be unfair to ask them to accept an extra burden?
7. Will any special physiological, psychological, or social characteristics of the subject group pose special risks for them?
8. Would it be possible to conduct the study with other, less vulnerable subjects? What additional expense or inconvenience would that entail? Does the convenience of the researcher or possible improvement in the quality of the research justify the involvement of subjects who may either be susceptible to pressure or who are already burdened?
9. Has the selection process *overprotected* potential subjects who are considered vulnerable (e.g., children, cognitively impaired, economically or educationally disadvantaged persons, patients of researchers, seriously ill persons) so that they are denied opportunities to participate in research?
10. If the subjects are susceptible to pressures, are there mechanisms that might be used to reduce the pressures or minimize their impact?
11. Is the reimbursement provided equitable to subject or is it potentially coercive, diminishing the subject's voluntariness?

NIH requires the use of a prospective screening and enrollment log to verify appropriate subject selection. Most clinical trials do the same. The ICH guidelines consider a screening and enrollment log an essential document.

Department: UAMS Institutional Review Board
Policy Number: 14.2
Section: Recruitment Practices
Effective Date: July 31, 2002
Revision Date: October 10, 2002; June 24, 2004; February 8, 2005;
January 24, 2011

SUBJECT: Subject Compensation

I. Policy

Compensation or payment to research subjects for study participation is not considered a benefit. Rather, it should be considered compensation for time and inconvenience. Compensation may not include a Sponsor coupon good for a discount on the purchase price of the study product once it has been approved for marketing.

The amount and schedule of all payments should be presented to the IRB at the time of initial review. The IRB will review both the amount of payment and the proposed method and timing of disbursement to assure that neither are coercive nor present undue influence.

Each institution (UAMS, ACH/ACHRI, etc.) has its own policies regarding the appropriate handling of payments to research subjects. The PI is responsible for following the appropriate policies.

II. Investigator Process

A. For studies which provide compensation to subjects for participation, the Investigator must address the following in the submission to the IRB.

1. Timing and Method of Payments. Investigators must disclose when the payments will be made and the payment method to be used.

Credit for payment should accrue as the study progresses and not be contingent upon the subject completing the entire study. Subjects should be paid in proportion to their time and inconvenience as a result of participation in the research study.

Unless it creates undue inconvenience or a coercive practice, payment to subjects who withdraw from the study may be paid at the time they would have completed the study (or completed a phase of the study) had they not withdrawn. For example, in a study lasting only a few days, an IRB may find it permissible to allow a single payment date at the end of the study, even to subjects who had withdrawn before that date.

2. Completion Bonus. If a study completion bonus is offered, it must be reasonable.

While the entire payment should not be contingent upon completion of the entire study, payment of a small proportion as an incentive for completion of the study is acceptable, providing that such incentive is not coercive.

The IRB will determine whether the amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.

3. Disclosure of Payments in Consent Document. All information concerning payment, including the amount, schedule and type of payment(s) must be set forth in the informed consent document.

4. Advertisement of Payments. Advertisements may state that subjects will be paid or compensated, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type. See IRB Policy 14.3 for more information regarding advertisements.

B. Alterations in Payments. Any alterations in subject payment or payment schedule must be reported to the IRB prior to implementation as Modification.

Department: UAMS Institutional Review Board
Policy Number: 14.3
Section: Recruitment Practices
Effective Date: July 31, 2002
Revision Date: October 10, 2002; June 24, 2004; February 8, 2005;
January 24, 2011

SUBJECT: Advertisements for Study Subjects

I. Policy

The UAMS IRB is responsible for ensuring the equitable selection of research participants with the proper safeguards in place to protect the rights and welfare of the participants. In fulfilling this responsibility, the UAMS IRB will review the methods and materials that investigators use to recruit subjects.

Advertisements used to recruit subjects should be seen as an extension of the informed consent and subject selection processes. Therefore, the UAMS IRB will review all advertisements to ensure that the information is not misleading to subjects, especially when a study will involve persons with acute or severe physical or mental illness or persons who are economically or educationally disadvantaged.

Advertisements may also be subject to communication and marketing policies and practices of an Institution. If changes are requested under those policies, the revised advertisement may not be used until the IRB has approved the modification.

II. Investigator Process

A. Investigators wishing to advertise for subjects must submit:

1. The information contained in the advertisement.
2. The advertisement method
3. The final copy of printed advertisements. Draft copies may be submitted with initial submission. However, the IRB requires a copy of the final product before use.
4. The final audio or video advertisement. Transcripts may be submitted with initial submission. However, the IRB requires a copy of the final product before use.

B. Advertisements should be limited to:

1. The name and address of the Researcher and the Research facility
2. The purpose of the research, specifically stating that it is research
3. The eligibility criteria, in summary form, that will be used to admit subjects to the study
4. A brief list of the benefits to the subject for participating in the study
5. The time or other commitment required from the subject
6. The location of the research and the person to contact for further information

C. Advertisements, regardless of form, may not:

1. Be misleading or coercive, either in wording or visual effects
2. Promise a Favorable Outcome
3. Promise "Free Medical Treatment" if the intent is simply that there is no charge to partake in the research project.

4. Imply any benefits beyond what is outlined in the consent and protocol
5. Use terms such as “New Treatment”, “New Drug”, “New Medication” without explaining that the test article is investigational
6. Emphasize amount of payment for participation
7. Make claims, either explicitly or implicitly, that a drug or device is safe or effective for the purposes under investigation, or that the drug or device is in any way equivalent or superior to any other drug or device.

III. IRB Process

Advertisements will be reviewed for compliance with this policy to ensure that the selection of subjects is equitable.

Department: UAMS Institutional Review Board
Policy Number: 14.4
Section: Recruitment Practices
Effective Date: July 31, 2002
Revision Date: June 24, 2004; January 24, 2011

SUBJECT: Compensation to Investigators & Health Care Workers for Enrolling Subjects

I. Background

The use of special enrollment incentives in human subject research creates an unacceptable potential for conflicts of interest that may influence the equitable selection of subjects. This does not refer to subject compensation or payment to Institutions or Investigators for the actual costs associated with performing the research. Rather, this refers to the use of special incentives, bonuses or other similar forms of compensation provided to institutions or investigators as a mechanism for enrolling subjects in research, including clinical trials. These incentives may have an adverse effect on human subjects because they may erode the informed consent process and increase the likelihood that ineligible persons are enrolled as subjects in the research.

II. Policy

Enrollment incentives may not be accepted by Institutions, Investigators or research personnel conducting human subject research under the oversight of the UAMS IRB.

III. Examples

The following is a non-exclusive list of examples that are not permitted in human subject research under this policy:

1. Entering into a research agreement that contains a provision to provide incentives for enrolling human subjects.
2. Accepting or requesting an enrollment incentive for enrolling human subjects..
3. Fees that significantly exceed the actual costs of recruiting human subjects.
4. Bonuses, milestones, or similar forms of additional payments for over-enrollment or accelerated enrollment of human subjects or for retention of human subjects.
5. Bonuses, milestones or similar forms of additional payments for early IRB approval.
6. Use of per subject payment rates that vary based only upon the number of human subjects enrolled, including increased per subject payments for over-enrollment of subjects.
7. Extra-contractual benefits such as unrestricted research gifts, medical or office equipment, authorship rights, journal subscriptions, educational stipends, payment of conference fees, software, personal gifts, favors, or similar inducements provided in exchange for enrolling human subjects.
8. Finder's fees or other payments for referral of subjects.
9. Obtaining human subjects through recruitment firms or persons whose practices are not consistent with this policy.

Department: UAMS Institutional Review Board
Policy Number: 14.5
Section: Recruitment Practices
Effective Date: August 12, 2004
Revision Date: N/A

SUBJECT: Subject Enrollment Defined

Definitions:

Accrual goal - The proposed total number of subjects that are to be screened and/or enrolled in a research study.

Enrolled subject – A volunteer who gives informed consent to participate in a study.

Human subject - An individual who is or becomes a participant in research, either as a recipient of the test article/treatment or as a member of a control group, or who is a participant on whom identifiable data is being collected. A subject may be either a healthy individual or a patient.

Ineligible subject - A volunteer who gives informed consent to participate in the study, but who is found to be ineligible to participate in the study (e.g., based on study-required screening tests, revised laboratory report, etc.) and whose participation was terminated.

Screen Failures – Subjects who were evaluated for participation in a study but did not meet the criteria found in the study protocol. This subject may or may not have signed a consent form depending upon the specifics of the IRB approved protocol.

IRB Review

A new IRB application must state the number of subjects to be accrued, *i.e.*, the accrual goal. When initial IRB approval is issued, approval is granted to accrue only the number of subjects listed in the application.

If the accrual goal is reached, subsequent accrual must cease. Accrual of subjects beyond the initially approved number is considered non-compliance with the terms of the project approval. Careful records of subject accrual, screening and/or enrollment should be kept to avoid inadvertent non-compliance.

If the Principal Investigator (PI) anticipates that a portion of the subjects will not be eligible to continue in the study after a screening process, the accrual goal should be estimated accordingly. Subjects who are entered in the screening portion of a project count towards the approved accrual goal. If the PI anticipates that the study will require screening of twice as many subjects as will actually continue in a trial, the requested accrual goal should take this into account.

During the course of the study, all proposed changes in the accrual goal must be submitted to the IRB for approval, through the modification section in ARIA, with an accompanying justification. Any increase in the accrual goal cannot be implemented until IRB approval has been obtained.

If the PI wishes to amend the accrual goal at the time of continuing review, he/she should clearly indicate this request as part of the continuing review and await the final decision of the IRB before proceeding with additional accrual beyond the original accrual goal. All requests for increased enrollment must be accompanied by a justification for the increase.

Department: UAMS Institutional Review Board
Policy Number: 15.1
Section: Consent
Effective Date: July 31, 2002
Revision Date: August 25, 2004; June 1, 2005; September 22, 2005;
April 5, 2007; May 13, 2008; July 28, 2008; January
29, 2010; February 1, 2010; June 3, 2010; January
24, 2011; March 11, 2011

SUBJECT: Elements of Informed Consent

I. Purpose

The purpose of this policy is to outline the required elements for the informed consent process. The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective. The required elements for the assent process, when children are involved, are referenced in IRB policy 17.1, Children in Research.

II. Definitions

A. **Coercion** occurs when an overt threat of harm is intentionally presented by one person to another to obtain compliance.

B. **Exculpatory language** is language that waives or appears to waive any legal rights of the subject or that releases or appears to release the Institution, Sponsor or Investigator from liability.

C. **Informed consent process** assures that prospective human subjects will understand the nature of the research and can knowledgeably and voluntarily decide whether or not to participate in the research. Informed consent is an ongoing process. The informed consent document is not consent in and of itself; it serves as written documentation of what has been communicated.

D. **Legally Authorized Representative (LAR)** means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in research. See UAMS IRB Policy 17.13 Legally Authorized Representatives and 17.1 Research in Children for further information.

E. **Mandated Reporter** is anyone required to report suspected abuse. You are a mandated reporter if you are a: child care worker or foster care worker; coroner; day care center worker; dentist; dental hygienist; domestic abuse advocate; domestic violence shelter employee; domestic violence shelter volunteer; employee of DHHS; employee working under contract for DYS; foster parent; judge; law enforcement official; licensed nurse; any medical personnel who may be engaged in admission, examination or treatment; mental health professional; osteopath; peace officer; physician; prosecuting attorney; resident intern; school counselor; school official; social worker; surgeon; teacher; court appointed special advocate - staff member or volunteer; juvenile intake or probation officer; child advocacy center employee; clergyman.

F. **Undue influence** occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance.

III. Policy

A. The Consent Process

1. Informed consent must be legally effective. If a subject is not able to consent on his/her own behalf due to age or cognitive ability, refer to UAMS IRB Policy 17.13, Legally Authorized Representatives, to ensure

permission is obtained from a legally authorized representative. Refer to UAMS Policy 17.1, Children in Research, for information on the process for obtaining consent and assent in children.

2. Informed consent must be sought only under conditions that a) provide the prospective subject or representative sufficient opportunity to consider whether or not to participate and b) minimize the possibility of coercion or undue influence.

3. Informed consent must be in a language understandable to the subject or legally authorized representative (LAR) and at a level understandable to all subjects. No complex scientific or technical language should be used without an explanation in lay or common terms. The consent document should be written in language that is at or below an eighth grade level.

4. Informed consent may not include any exculpatory language that waives or appears to waive any legal rights of the subject or releasing the Institution, Sponsor or Investigator from liability. Avoid phrases like “you give up all rights”, “you will not be compensated” or “I authorize the use” in the consent process.

5. Informed consent must be prospectively obtained and documented unless requirements outlined in UAMS IRB Policy 15.3, Waivers of Signed Informed Consent Documents and Waivers of Informed Consent Elements, apply.

6. Informed consent documents should be consistently written in the second person when referring to the subject or representative, with the exception of the final paragraph. Using terms such as “you” or “your” rather than “I” or “me” helps convey the voluntary nature of the process.

7. Informed consent for research studies should use terms like “participant” or “subject” and “research procedures” rather than “patient” and “treatment”.

B. Elements of Informed Consent.

1. Unless specifically waived by the IRB, the following elements must be addressed in the informed consent process and included in the written informed consent document.

- a. A statement that the study involves research.
- b. An explanation of the purpose of the research.
- c. The expected duration of the subject’s participation in the research.
- d. A description of the procedures to be followed.
- e. Identification of any experimental procedures.
- f. The number of subjects involved in the study.
- g. An age range for subjects to be studied.
- h. A description of any reasonable foreseeable risks or discomforts to the subject.
- i. A description of benefits, if any, to the subject or to others that may reasonably be expected from the research. Benefits refer to health or well-being, not payment for participation.
- j. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- k. A statement that significant new findings developed during the course of research, which may relate to the subject’s willingness to continue, will be provided to the subject.
- l. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, noting as applicable that certain entities, as outlined below, may inspect the records.

- i) The UAMS Institutional Review Board (IRB) must be listed;
- ii) The phrase "Other Institutional oversight offices" must be listed;
- iii) The Office for Human Research Protections (OHRP) a Federal agency must be listed;
- iv) Any funding source or sponsor that may access the records should be listed;
- v) If the study is subject to FDA oversight, the Food and Drug Administration must be listed;
- vi) If any member of the study team is a mandated reporter, an explanation of this limit to confidentiality must be present in the informed consent document. See section III (E) (4) of this policy for a suggested clause;
- vii) In studies where subject will be tested for HIV or other communicable diseases, a statement must be included that describes how the subject and Department of Health will be notified of a positive test result and that subject will be given information about counseling options if HIV positive or have any other communicable disease.

m. Contact information for both the research team as well as the IRB. The purpose of this contact information is to provide a means for the research subject to ask questions regarding the research or their rights as a research subject, to voice concerns, to file a complaint, or to notify the research team in the event of a research related injury. See section III (E) (2) of this policy for a suggested clause.

n. A statement that the participation is voluntary; that refusal to participate involves no penalty or loss of benefits to which the subject is otherwise entitled; that no rights have been waived; and that the subject may discontinue participation at any time without penalty or loss of benefit to which the subject is otherwise entitled. For clinical trials regulated by the FDA, see section III (C) (16) for issues related to subject withdrawal.

2. The subject or subject's legally authorized representative shall receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects prior to participation.

C. Additional Elements of Informed Consent When Applicable

1. All drug or device studies will include in the informed consent a statement that the particular treatment or procedure may involve risks, which are currently unforeseeable, to the subject, embryo or fetus if the subject is or may become pregnant.

2. If the study is greater than minimal risk, there must be an explanation as to whether or not any compensation and/or medical treatment is available for injury. See section III (E) (1) of this policy for a suggested clause.

3. If the Investigator anticipates the subject may be terminated from the study without regard to the subject's consent, the informed consent will include the specific anticipated circumstances under which the subject's participation may be terminated by the Investigator.

4. When there are anticipated consequences to withdrawing from a study that may put the subject at greater risk, the informed consent will include the specific consequences of the subject's decision to withdraw from the research and procedures for the orderly termination of participation by the subject.

5. When additional costs to the subject are anticipated as a result from participation in the research, the informed consent will describe these additional costs. See section III (E) (3) (a),(b),or (c) for a suggested clause.

6. If the study is being conducted at multiple sites, the informed consent will include the approximate number of subjects involved in the study locally and nationally.

7. If the study involves the use of a placebo, the informed consent will include a statement describing the use of a placebo and the probability of being assigned to the placebo arm.

8. When test articles (i.e., drugs, devices) are being used in the project, include a statement as to status of the article (i.e., FDA approved for use in cardiology patients aged 16 years and older), and whether or not the study is testing the safety or effectiveness of the test article. If the study is testing the safety or effectiveness of the test article, the consent form cannot make any claims that the test article is safe or effective.

9. If any information will be collected after the subject's active involvement, the informed consent document must state the duration of the collection.

10. If subjects are to be contacted for future research, the IRB requires that the informed consent document include a yes/no option to being contacted in a separate section of the consent form that allows the subject to consent to the primary study but decline to be re-contacted for future studies.

11. If data or specimens will be stored for future research, the protocol and consent must describe:

- a) How the data or specimens are to be stored,
- b) Why the information is being collected,
- c) The protocol must describe in detail the types of future research that are anticipated,
- d) How long the data or specimens will be stored,
- e) A description of how subjects may request to withdraw data or specimens.

12. If data or specimens are stored for future research, the IRB requires that a yes/no option be provided in a separate section of the informed consent document or in a separate document. The option should provide for future use of data or specimens in a way that allows a subject to consent to the primary study but decline to allow the storage of samples if s/he desires. See UAMS IRB Policy 17.11, Stored Data or Tissues.

13. In studies where ionizing radiation is used, include in lay terms the increase of radiation exposure over the current standard of care.

14. In studies where there is potential for gene linkage, an explanation of risks including social and financial will be included. See UAMS IRB Policy 19.1, Human Genetics.

15. All drug studies (except for Phase I studies) and all device studies (except for feasibility studies) require the informed consent documents and processes to include a specific statement that clinical trial information will be entered into the clinical trial registry databank maintained by the National Institutes of Health/National Library of Medicine (NIH/NLM). The FDA has emphatically stated that this clause must be exactly as follows:

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

16. For clinical trials regulated by the FDA, there are specific data retention requirements when a subject withdraws from the study.

- a) The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.
- b) A researcher may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and allow further data collection after their withdrawal from the interventional portion of the study. The discussion with the subject must distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review; and address the maintenance of privacy and confidentiality of the subject's information.
 - i) The subject's informed consent must be obtained for this limited participation in the study. If this situation was not described in the original informed consent, the IRB must approve a consent document for the limited participation.
 - ii) If a subject does not consent to continued follow-up of associated clinical outcome information, the researcher may not access the subject's medical record, or other confidential records requiring the subject's consent, for purposes related to the study. Researchers may

review study data collected prior to the subject's withdrawal and may consult public record, such as those establishing survival status.

NOTE: If Protected Health Information (PHI) is being collected, HIPAA requires an Authorization for Use, unless specifically waived by the IRB in its role as the privacy board. The requirements for a valid HIPAA authorization are in addition to the requirements for informed consent. You may incorporate the HIPAA required elements into your informed consent document or you may submit a HIPAA authorization as a separate document. See UAMS Administrative Guide 3.1.27 for the HIPAA Research Policy.

D. Format Requirements for Consent Form

1. All informed consent document pages must include the protocol title; or if the protocol title is more than two lines long, the full title is to appear on the first page and an appropriate protocol identifier, such as the IRB protocol number, may be used on all subsequent pages.
2. All informed consent document pages must include the name of the sponsor.
3. All informed consent document pages must include the institutions where the research is being conducted.
4. All informed consent document pages must include page numbers, date and version number.
5. The informed consent document must include lines for the signature and date of consent for:
 - a) Subject; and/or
 - b) Parent or LAR signature for studies enrolling children or individuals that are cognitively impaired (See UAMS IRB Policies 17.1, Research in Children; 17.2, Cognitively Impaired Persons; and 17.13, Legally Authorized Representatives. NOTE: Both Parent signatures are mandated by regulation for studies determined to be pediatric risk category 3 or 4.); and
 - c) Person obtaining consent (POC).
6. The last paragraph will address the voluntary nature of the study and that time has been given to ask questions and express concerns. See section III (E) (5) of this policy for a suggested clause.

E. Suggested Clauses. The following are suggested examples of language that may be considered acceptable. These clauses should not be considered required clauses. Any statement used must be applicable to the study and consistent with any sponsor or funding agreement.

1. Injury Clauses

a) For studies that do not have an Industry Sponsor: "In the event you are hurt by being in this research, treatment will be available. This treatment may include: first aid, emergency treatment and/or follow-up care. This treatment may be billed to you or your insurance company in the normal manner. Normally, no other form of compensation is available. If you think you have been hurt by this research, let the study Investigator know right away by calling <<<insert PI name and contact number>>> or <<<24 hour number when applicable>>>".

b) For studies that have an Industry sponsor who has agreed to pay for some injuries: "In the event you are hurt by being in this research, treatment will be available. This treatment may include: first aid, emergency treatment and/or follow-up care. The Sponsor agrees to pay for all reasonable and customary diagnosis, care, treatment, or hospitalization costs to address any injury or illness you may sustain as a result of your participation in the Study. Normally, no other form of compensation is available. If you think you have been hurt by this research, let the Study Investigator know right away by calling <<<insert PI name and contact number>>> or <<<24 hour number when applicable>>>. <<<Research Support Center will insert any additional negotiated language>>>. This language needs to match the Sponsor agreement and must be consistent with any other language in the consent form.

2. Contact Clause

"If you have questions during the study about the research, you should contact <<<PI name and contact number>>> or <<<24 hour number when applicable>>>. You may call the Institutional Review Board (IRB) at 501-686-5667 regarding a research-related injury, with questions about your rights as a research subject or to discuss any problems or concerns about the research. Also, you may call this number if you are unable to reach the Investigator or you wish to speak to someone not directly related to this study"

3. Additional Cost Clauses

a) "The study may include tests and procedures that are conducted solely for the research study. These tests and procedures will be paid for by the study Sponsor. There may be some tests and procedures which the Principal Investigator considers standard of care (meaning you would receive this care whether or not you are in the research study) and these tests and procedures are billable to you and your insurance company. Your insurance company may or may not agree with this determination. If your insurance company feels that the charges are for tests and procedures related to the research study they may deny payment, making you responsible for any charges that are not paid for by the study Sponsor. There is never any guarantee with any service that you will not incur some financial liability."

b) "The Principal Investigator or his/her representative will discuss with you any additional tests and/or procedures that may be required due to changes in your condition during your study participation. You have the right to refuse to have any additional tests or procedures. If you feel that you have been billed in error, please contact the Principal Investigator or his/her representative whose name and telephone number is included on this consent form."

c) "A summary (insert a narrative or table-formatted description with headings of "Covered by the Study" and "Payable by You or Your Insurance") of the standard and investigational study-related procedures is included below together with an indication of those items that will, or may, be your financial responsibility."

4. Mandated Reporter

"By law, the study team must release certain information to the appropriate authorities if at any time during the study there is concern that child abuse or elder abuse has possibly occurred or you disclose a desire to harm yourself or others."

5. Voluntary Participation

"The purpose and voluntary nature of this study, as well as the potential benefits and risks that are involved have been explained to me. I have been able to ask questions and express concerns, which have been satisfactorily responded to by the study team. I have been told I will be given a copy of the informed consent document."

IV. Procedures

A. Submission Process

1. At the time of initial submission, upload all informed consent documents (including assent documents or scripts as applicable) to be used. The form should include all of the elements required by the UAMS IRB and Federal regulations and each of the other elements as is appropriate to the type and nature of the study.
2. Investigators will describe the entire proposed consent process in the original submission. See UAMS IRB Policy 15.5, The Informed Consent Process.

B. After Initial Submission

1. In response to contingencies or after approval, submit any proposed changes to the informed consent document with changes highlighted and/or tracked along with a clean version of the informed consent

document as a “modification”. The IRB will administratively reject any modifications to documents that are submitted without an accompanying tracked change version.

2. Investigators must not use any consent form version prior to its approval by the IRB.

3. Each time the informed consent document is modified, the date and version number must be updated. Revised documents should replace previous version numbers and dates in ARIA with the next consecutive number and date of submission or revision.

4. The version number and date entered into ARIA during the upload of the document during the submission process is the number that will be displayed on the approval letter from the IRB. Therefore, the version number and date entered into ARIA should be the same as those appearing on the consent form.

5. When the IRB approves amendments to a previously approved consent form, the previous version must be retired and can no longer be used to consent subjects. The IRB will provide guidance regarding the need to re-consent current subjects using the new form in accordance with IRB Policy 7.4, Review by the Convened IRB and IRB Policy 7.5 Expedited Review.

6. The IRB does not generally stamp consent forms; but, if the Sponsor requires a stamped consent, the Investigator should contact the IRB office to obtain a stamped copy of the approved consent form.

C. IRB Responsibility

1. Review consent form document

a) Ensure all required UAMS elements are addressed as applicable to the research.

b) Ensure consistency with all other submitted forms such as protocol, advertisement, or investigator’s brochure.

2. Review consent process

a) Ensure process allows sufficient opportunity to consider participation and the possibility of coercion or undue influence is minimized.

b) Ensure process includes all elements necessary to protect the safety and welfare of the subjects participating in the study.

c) Ensure the review is documented sufficiently by referring to the consent form review checklist in the presentation of the protocol review during the IRB meeting.

3. Request revisions as necessary to ensure that proposed activities are clear and the intended subjects can make a fully informed decision.

Department: UAMS Institutional Review Board
Policy Number: 15.2
Section: Consent
Effective Date: July 31, 2002
Revision Dates: February 8, 2005; August 24, 2004; October 11, 2002

Subject: Consent Exceptions: Planned Emergency Situations

The University of Arkansas for Medical Sciences will not review requests for waiver of the requirement for consent in planned emergency research.

NOTE: This is not the same as Waiver of informed consent in Emergency Use of a Drug or Biologic which is addressed in Policy 18.3; or Waiver of informed consent in Emergency use of an Unapproved Medical Device which is addressed in Policy 18.4.

It is the policy of UAMS to not waive informed consent for planned emergency research under FDA regulations 21 CFR 50.24 and November 1, 1996 DHHS Waiver of Informed Consent Requirements in Certain Emergency Research.

Department: UAMS Institutional Review Board
Policy Number: 15.3
Section: Consent
Effective Date: July 31, 2002
Revision Date: February 8, 2005; June 1, 2005; March 13, 2008;
January 24, 2011

SUBJECT: Waivers of Signed Informed Consent Documents and Waivers of Informed Consent Elements

I. Policy

Upon determining that the regulatory criteria have been met, the IRB or Experienced IRB Reviewer may waive or alter:

- *The consent process
- *Parental permission
- *Written documentation of the consent process

The IRB or Experienced IRB Reviewer must document its findings justifying the waiver or alteration.

II. Waivers

A. WAIVER or ALTERATION of CONSENT PROCESS – Does not apply to research regulated by the FDA, except as outlined in IRB Policy 18.3. For research not subject to FDA regulations, the IRB may approve a waiver of some or all of the consent elements provided that the research fits into one of two scenarios:

- 1. Some or all elements of consent may be waived if all of the following apply:**
 - a. The research involves no more than minimal risk to subjects;
 - b. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
 - c. The research could not practicably be carried out without the waiver or alteration; and
 - d. Whenever appropriate, the subjects will be provided with additional pertinent information after they have participated in the study.

- 2. Some or all elements of consent may be waived if the project meets all of the following criteria:**
 - a. It is conducted by or subject to the approval of state or local government officials;
 - b. It could not practicably be carried out without the waiver or alteration;
 - c. It is designed to study, evaluate or examine one of the following four categories:
 - i. Public benefit of service programs;
 - ii. Procedures for obtaining benefits or services under those programs;
 - iii. Possible changes in or alternatives to those programs or procedures; or
 - iv. Possible changes in methods or levels of payment for benefits or services under those programs.

B. WAIVER of DOCUMENTATION of CONSENT. The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if the research fits into one of two scenarios.

1. Applies to both FDA and non-FDA research.
 - a. Research involves no more than minimal risk of harm to subjects; and
 - b. Involves no procedures for which written consent is normally required outside the research context.

2. Applies only to non-FDA Research.
 - a. The only record linking the subject and the research would be the consent document; and

- b. The principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.

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

C. Procedure – Applicable to all expedited and full review studies.

1. Investigators requesting a waiver or alteration under this policy must provide written rationale in the ARIA application that shows how the study meets each element of the requirements for either a waiver of written consent or a waiver/alteration of consent.

The requirement for justification applies even in cases where the Investigator needs to use deception due to the possibility that subjects would behave differently if they knew they were being observed.

2. The IRB will:

- a. Review the submission to see if it is subject to FDA regulations in order to determine regulatory options.

- b. Review the waiver request, taking into account the importance of the research, the extent to which privacy will be invaded, the sensitivity of the information to which the investigators will have access, plans for further contact of the subjects, and the feasibility of obtaining consent from all subjects.

- c. For studies requesting to use deception, first decide whether the information to be withheld would influence the decision of prospective subjects about participating in the research. Research should not be permitted at all if the subjects are not being informed of things they would consider material to a decision to participate. Also decide if subjects should be debriefed either after participating in research unwittingly or after knowingly participating in research that involved some form of deception. Then in order to grant the waiver, document the following three things:

- i. the study presents no more than minimal risk;
- ii. the waiver would not adversely affect the rights and welfare of subjects; and
- iii. the waiver is essential to the ability to carry out the research.

- d. Decisions on informed consent, waivers of informed consent, documentation of informed consent, or requirements for debriefing will be described in the letter to the Investigator and reflected in the IRB minutes.

Department: UAMS Institutional Review Board
Policy Number: 15.4
Section: Consent
Effective Date: August 25, 2004
Revision Date: July 28, 2008; January 24, 2011

SUBJECT: Non-English-Speaking Research Subjects and when Short Form of Consent Documentation is allowed

I. Policy

A valid consent discussion must be in a language understandable to the subject or the subject's Legally Authorized Representative (LAR). If English is not the subject or LAR's primary language, the consent process and consent document must be in a language the subject or LAR can understand.

UAMS allows the use of the short form to document consent only when non-English speaking subjects are unexpectedly encountered. IRB approval of the short form and associated consent process must be obtained prior to using a short form. The IRB website may provide short form consent templates in other languages. However, these templates cannot be used without IRB approval of an Investigator's entire consent process which may include the use of one of these templates.

II. Procedure when Study Anticipates Enrollment of non-English speaking subjects

A. If an Investigator anticipates the enrollment of non-English speaking subjects at the time of initial submission, or if during the course of the study it becomes apparent that non-English speaking subjects will be encountered, the Investigator must submit:

1. A translated consent document;
2. Translated copies of any other documents that will be provided to subjects, such as brochures, questionnaires, diaries, as applicable;
3. Certification of translation. This must include the name and credentials of the person or company who translated the documents and a certification that the document is an accurate translation. Certifications that the documents have been back translated are encouraged, although not required.
4. The consent process must also address how the Investigator will ensure that the initial consent process and ongoing communications will be in a language understandable to the subject or LAR, such as use of institutional interpreter services, bilingual staff, etc.

III. Procedure when non-English speaking subjects are not anticipated

A. In order for the IRB to allow the short form of consent documentation, the Investigator must submit a description of the entire consent process and how the Investigator will ensure that the consent process and ongoing communications are in a language understandable to the subject or LAR. Documents that must be submitted include:

1. The short form must be in the language of the subject or LAR and must state that the elements of disclosure required by regulations have been presented orally to the subject or the subject's legally authorized representative. The short form must have signature and date lines for the subject or LAR and a witness.

NOTE: The witness must be conversant in both English and the language of the subject or LAR. The witness must be present for the entire oral presentation of the consent.

2. A written summary that embodies the basic and appropriate additional elements of disclosure. The summary must have signature and date lines for the person obtaining consent and the witness.

NOTE: A copy of the signed short form and signed summary must be given to the subject or LAR.

IRB approval of the short form and associated consent process must be obtained prior to using a short form.

IV. IRB Procedure

The IRB must determine that the consent process and procedures for documentation are appropriate and that the requirements of this policy are met prior to approving the use of the short form of consent documentation.

The IRB should consider the likelihood of additional non-English speaking subjects and determine whether to place a limit on the number of subjects who may be enrolled using the short form of consent documentation.

Requests for use of the short form of consent documentation may be reviewed by expedited procedures only when the study meets the criteria for review and approval by expedited procedures.

Department: UAMS Institutional Review Board
Policy Number: 15.5
Section: Consent
Effective Date: April 5, 2007
Revision Date: March 5, 2008; January 24, 2011

SUBJECT: Informed Consent Process

I. Policy

In studies for which informed consent must be obtained, no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative (LAR). An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

This SOP describes, in general terms, the requirements for the informed consent process and the IRB's duty to monitor this process in certain situations.

Additional requirements may also apply in certain instances, such as the inclusion of children or the use of LARs, and are described in IRB Policies 17.1 through 17.13.

II. Procedure

A. Initial Submission. In the initial IRB submission, the PI will explain in detail the consent process, both initial and ongoing processes. The description of the process is to include, at a minimum:

1. The person who will conduct the consent interview;
2. The language used by those obtaining consent;
3. The person who will provide consent or permission;
4. The language understood by the prospective subject or LAR;
5. The timing of obtaining informed consent;
6. The waiting period between providing information about the research and obtaining consent;
7. Steps taken to minimize the possibility of coercion or undue influence;
8. The information to be communicated to the prospective subject or LAR.

B. Informed Consent Process Note. The Investigator, or study team, is also required to document the informed consent process in either the subject's research record or medical record. A note separate from the consent form itself that includes, at a minimum, the following items are required to document the informed consent process:

1. The date the subject was entered into the study
2. The title of the study
3. The name of the Principal Investigator
4. The name of the person or people obtaining the informed consent
5. Statement that the subject or LAR was given a copy of the signed form.

The following additional elements are strongly encouraged to fully document the process:

1. A description of anyone else present during the process (e.g. subject's spouse or other family; study coordinator; Principal Investigator).
2. The types of questions the subject had during the process or that the subject had no questions.
3. Any other details specific to that particular consent process, such as the reason for any date discrepancies on consent form signatures, that help complete the description of the process.

If a written consent form is used, the person signing that form as the person obtaining consent shall sign the consent process note. If no written form is used, or if the written form used does not include a person obtaining consent signature line, at least one of the people who obtained consent shall sign and date the consent process note.

A separate informed consent process note is required for each subject enrolled. However, the IRB may, at its discretion, approve different types of consent process notes for special consenting situations, such as group processes.

At the time of the informed consent process, each subject must be given a copy of the signed and dated informed consent document. For those subjects that have a medical record, a copy of the subject's informed consent should be placed in the medical record. The original should be retained by the PI.

C. Monitoring the Consent Process

The IRB has the authority to observe, or have a third party observe, the informed consent process in research projects as necessary. Monitoring the consent process may be warranted in studies that involve vulnerable populations, complicated procedures or processes, studies utilizing deception or in any situation where the IRB believes the consent process should be monitored to provide further protections.

Observations may be done by an IRB Reviewer or research compliance personnel. The consent process observation should take into account such things as time allowed for questions, how the study team assessed understanding, how the research was presented and whether results were promised.

Department: UAMS Institutional Review Board
Policy Number: 16.1
Section: Risk/Benefit Analysis
Effective Date: July 31, 2002
Revision Date: June 24, 2004; February 8, 2005; January 24, 2011

SUBJECT: Risk/Benefit Analysis

Risks to research participants posed by participation in research should be justified by the anticipated benefits to the participants or society. This requirement is clearly stated in codes of research ethics, and is central to the federal regulations. One of the major responsibilities of the IRB, therefore, is to assess the risks and benefits of proposed research. In doing so, it is necessary for the IRB to evaluate the proposed research for scientific validity. This does not require that the IRB undertake a peer review function and compare the proposed research to other research studies. However, it does require the IRB, either through its own expertise or outside consultants, to understand the background, aims, and research methods enough to address two specific regulatory requirements.

The primary or secondary reviewers assigned to a project should review the submitted information and determine that:

- 1) risks to participants are minimized by using procedures which are consistent with sound research design; and
- 2) risks to participants are reasonable in relation to the anticipated benefits, if any, to the participants and to society and the importance of the knowledge that may reasonably be expected from the study.

Definitions:

Benefit: A valued or desired outcome; an advantage.

Minimal Risk: A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

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

Pediatric Category 1: Minimal Risk

Pediatric Category 2: Greater than minimal risk, but presenting the prospect of direct benefit to individual participants

Pediatric Category 3: Greater than minimal risk and no prospect of direct benefit to individual participants but likely to yield important generalizable knowledge about the participant's disorder or condition.

Pediatric Category 4: Otherwise not approvable, but presents an opportunity to understand serious health or welfare problems of children

There are two sources of confusion in the assessment of risks and benefits. One arises from the language employed in the discussion: "Risk" is a word expressing probabilities; "benefits" is a word expressing a fact or state of affairs. It is more accurate to speak as if both were in the realm of probability: *i.e.*, risks and expected or anticipated benefits. Another point of confusion may arise because "risks" can refer to two quite different things: (1) those chances that specific individuals are willing to undertake for some desired goal; or (2) the conditions that make a situation dangerous *per se*. The IRB is responsible for evaluating risk only in the second sense. It must then judge whether the anticipated benefit, either of new knowledge or of improved health for the research participants, justifies inviting any person to undertake the risks. **The IRB should disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.**

The IRB's assessment of risks and anticipated benefits involves a series of steps. The IRB must:

1. Identify the risks associated with the research, as distinguished from the risks of therapies the participants would receive even if not participating in research
2. Determine that the risks will be minimized to the extent possible
3. Identify the probable benefits to be derived from the research
4. Determine that the risks are reasonable in relation to the benefits for participants, if any, and the importance of the knowledge to be gained
5. Assure that potential participants will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits.
6. Determine intervals of periodic review, and, where appropriate, determine that adequate provisions are in place for monitoring the data collected.

In addition, the IRB should determine the adequacy of the provisions to protect the privacy of participants and to maintain the confidentiality of the data and, where the participants are likely to be members of a vulnerable population (e.g., mentally disabled), determine that appropriate additional safeguards are in place to protect the rights and welfare of these participants (see IRB policy 17.1-17.9).

Identification and Assessment of Risks. In the process of determining what constitutes a risk, only those risks that may result from the research, as distinguished from those associated with therapies participants would undergo even if not participating in research, should be considered. For example, if the research is designed to measure the behavioral results of physical interventions performed for therapeutic reasons (e.g., effects on memory of brain surgery performed for the relief of epilepsy), then only the risks presented by the memory tests should be considered when the IRB performs its risk/benefit analysis. It is possible for the risks of the research to be minimal even when the therapeutic procedure presents more than minimal risk. The IRB should recognize, however, that distinguishing therapeutic from research activities can sometimes require very fine line drawing. Before eliminating an activity from consideration in its risk/benefit analysis, the IRB should be certain that the activity truly constitutes therapy and not research.

It is important to recognize that the potential risks faced by research participants may be posed by design features employed to assure valid results as well as by the particular interventions or maneuvers that may be performed in the course of the research. Participants in a study whose research design involves random assignment to treatment groups face the chance that they may not receive the treatment that turns out to be more efficacious. Participants in a double-masked study take the risk that the information necessary for individual treatment might not be available to the proper persons when needed. In behavioral, social, and some biomedical research, the methods for gathering information may pose the added risk of invasion of privacy and possible violations of confidentiality. Many risks of research are the risks inherent in the methodologies of gathering and analyzing data, although the more obvious risks may be those posed by particular interventions and procedures performed during the course of research.

A final potential risk to participants is the possible long-range effect of applying the knowledge gained through research. For example, information gained about associative memory may enable advertising companies to develop new techniques for encouraging arguably harmful consumer behaviors; associations between race or gender and intelligence may have profound effects on public policy. The regulations specifically provide, however, that the IRB should not consider such effects "as among those research risks that fall within the purview of its responsibility (45 CFR 46.111).

Classification of Risk. The risks to which research participants may be exposed have been classified as physical, psychological, social, and economic [**Levine**, Robert J. *Ethics and Regulation of Clinical Research*, 2d ed. Baltimore: Urban and Schwarzenberg, 1986, p.42].

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

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

Social and Economic Harms. Some invasions of privacy and breaches of confidentiality may result in embarrassment within one's business or social group, loss of employment, or criminal prosecution. Areas of particular sensitivity are information regarding alcohol or drug abuse, mental illness, illegal activities, and sexual behavior. Some social and behavioral research may yield information about individuals that could "label" or "stigmatize" the participants (e.g., as actual or potential delinquents or schizophrenics). Confidentiality safeguards must be strong in these instances. The fact that a person has participated in HIV-related drug trials or has been hospitalized for treatment of mental illness could adversely affect present or future employment, eligibility for insurance, political campaigns, and standing in the community. A researcher's plans to contact such individuals for follow-up studies should be reviewed with care.

Participation in research may result in additional actual costs to individuals. Any anticipated costs to research participants should be described to prospective participants during the consent process.

Minimal Risk and Especially Vulnerable Populations. DHHS regulations on research involving fetuses and pregnant women [45 CFR46 (Subpart B)], research involving prisoners [45CFR46(Subpart C)], and research involving children [45 CFR 46 (Subpart D)] strictly limit research presenting more than minimal risk. For more information about "Special Populations", see IRB policy section 17 "Special Populations".

Determination That Risks Are Minimized. Risks, even when unavoidable, can be reduced or managed. If there are precautions, safeguards, and alternatives that can be incorporated into the research activity to reduce the probability of harm or limit its severity or duration, the IRB should require these changes before approving the study. The IRB is responsible for assuring that risks are minimized to the extent possible. In reviewing any protocol, the IRB should obtain complete information regarding experimental design and the scientific rationale (including the results of previous animal and human studies) underlying the proposed research, and the statistical basis for the structure of the investigation. The IRB should analyze the beneficial and harmful effects anticipated in the research, as well as the effects of any treatments that might be administered in ordinary practice, and those associated with receiving no treatment at all. In addition, they should consider whether potentially harmful effects can be adequately detected, prevented, or treated. The risks and complications of any underlying disease that may be present must also be assessed.

The IRB should determine whether the investigators are qualified in the area being studied, and whether they serve dual roles (e.g., treating physician, teacher, or employer in addition to researcher) that might complicate their interactions with participants. For example, an investigator's eagerness for a participant to continue in a research project (to obtain as much data as possible) may conflict with the responsibility, as a treating physician, to discontinue a therapy that is not helpful or that results in significant adverse effects without countervailing benefit. Likewise, teachers or supervisors who conduct research could (wittingly or unwittingly) coerce student- or employee-participants into participating. Thus any potential conflicts of interest must be identified and resolved before IRB approval is granted.

Another way for the IRB to meet this responsibility is to assess whether the research design will yield the data the Investigator states it will; whether the sample size is too small to yield the expected results, or whether there is a way to evaluate the data being collected. Participants may be exposed to risk without sufficient justification. While good research design may not itself reduce or eradicate risks to participants, poor or faulty research design means that the risks are not likely to be reasonable in relation to the benefits, to the participant or society.

A useful method of minimizing risk is to assure that adequate safeguards are incorporated into the research design. Frequent monitoring, the presence of trained personnel who can respond to emergencies, or coding of data to protect confidentiality are examples. It may be necessary to exclude individuals or classes of participants (e.g., pregnant women, diabetics, people with high blood pressure) whose vulnerability to a drug or procedure may increase with the risks to them. In certain types of clinical trials, special provisions need to be made for monitoring the data as they accumulate to assure the safety of participants, or to assure that no

group or subgroup in a trial is compromised by a less effective treatment. Data monitoring should also be used to ensure that the trial does not continue after reliable results have been obtained. In large-scale drug trials, this often requires establishing a specialized data and safety monitoring board or committee to review the incoming data at stated intervals.

Assessment of Anticipated Benefits.

Direct payments or other forms of remuneration offered to potential participants as an incentive or reward for participation are **NOT** to be considered a "benefit" to be gained from research.

The benefits of research fall into two major categories:

1. Benefits to participants. Frequently, the research participants are undergoing treatment, diagnosis, or examination for an illness or abnormal condition. This kind of research often involves evaluation of a procedure that may benefit the participants by ameliorating their conditions or providing a better understanding of their disorders.

and

2. Benefits to society. Patients and healthy individuals may also agree to participate in research that is either not related to any illnesses they might have or that is related to their conditions but not designed to provide any diagnostic or therapeutic benefit. Such research is designed principally to increase our understanding and store of knowledge about human physiology and behavior. Research that has no immediate therapeutic intent may, nonetheless, benefit society as a whole. These benefits take the form of increased knowledge, improved safety, technological advances, and better health.

The IRB should assure that the anticipated benefits to research participants and the knowledge researchers expect to gain are clearly identified.

Department: UAMS Institutional Review Board
Policy Number: 17.1
Section: Special Populations
Effective Date: July 31, 2002
Revision Date: October 10, 2002; June 24, 2004; February 8, 2005;
March 13, 2008; June 11, 2008; January 24, 2011

SUBJECT: Children in Research

I. Policy

Special ethical and regulatory considerations apply to reviewing research involving children, to protect the minor subjects' interests and to protect children from harm. The IRB may approve research involving children only if special provisions are met in addition to the other criteria required for approval. The IRB must classify research involving children into one of four defined risk categories and document its discussions of the risks and benefits of the research study.

The definition of Pediatric Risk Category IV is provided in this policy for reference purposes. In accordance with the scope of the UAMS Human Research Protection Program Plan (HRPP), research that falls into pediatric risk category IV may not be conducted under the UAMS HRPP.

II. Definitions

A. Assent. A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. Assent is generally sought beginning at age 7. Assent is a process, not a form. However, assent can be documented either on a separate assent form specifically tailored to children (especially adolescents) or on the same document used to obtain parental permission. Only the child's signature (or hand-printed name) is required to fulfill the assent document requirement.

B. Children. In Arkansas, "children" includes all those who have not yet reached their 18th birthday and have not been legally emancipated. Emancipation may be obtained through judicial decree or based upon certain events such as marriage or military service. Marriage or military service does not automatically emancipate an individual and Investigators should seek guidance if the issue arises.

C. Guardian. An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. (See Policy 17.13 for Legally Authorized Representative (LAR) for definitions.) Court-appointed guardians must petition and receive express permission from the court in order to provide consent authorizing experimental medical procedures.

D. Parent. Federal Regulations define this as a child's biological or adoptive parent. Arkansas law allows a parent to grant permission for his/her biological, adopted or stepchild to undergo surgical or medical treatments or procedures. Note however that there are restrictions on who can consent on behalf of foster children (a.k.a. "wards") for the purpose of research. See the detailed information and Special Instructions Section below for more information.

E. Permission. The agreement of parent(s) or guardian to the participation of their child in research.

F. Wards: Children who are considered to be in the custody of the state. Foster children are in the custody of the Arkansas Department of Human Services (DHS) and therefore are wards of the state. As such, only DHS may provide consent for their participation in research. Specifically, since foster care is under the Division of Children and Family Services (DCFS), the Director of that division will review all requests for research projects. Foster parents cannot provide permission for a foster child to participate in research.

III. Categories

A. Pediatric Risk Category I: Research Not Involving More Than Minimal Risk. When the IRB finds that no greater than minimal risk to children is present, the IRB may approve the proposed research

only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth below.

B. Pediatric Risk Category II: Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Subjects. If the IRB finds that more than minimal risk to children is present by an intervention or procedure but that the intervention or procedure holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, the IRB may approve the research only if the IRB finds that:

1. The risk is justified by the anticipated benefit to the subjects;
2. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
3. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth below

C. Pediatric Risk Category III: Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to Individual Subjects, but Likely to Yield Generalizable Knowledge about the Subject's Disorder or Condition. If the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well being of the subject, the IRB may approve the research only if the IRB finds that:

1. The risk represents a minor increase over minimal risk;
2. 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;
3. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
4. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth below.

D. Pediatric Risk Category IV: Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children. If the IRB does not believe the research proposal meets any of the requirements set forth above, it may still approve the protocol but only if:

1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
2. The Secretary of the Department of Health and Human Services or The Commissioner of Food and Drugs, as applicable, 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, has determined either that the research in fact meets one of the categories set forth above, or all of the following:
 - a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
 - b. The research will be conducted in accordance with sound ethical principles; and
 - c. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth below.

IV. Investigator Procedures Investigators should:

A. Design research projects involving children in accordance with this policy, making provisions to obtain the assent of all children age 7 or older. If the study population is such that the children will not be able to provide assent at the age of 7 or at all, the Investigator should specify this in the assent provisions of the application.

B. Identify in ARIA the pediatric category of research that the Investigator feels the project best meets and upload permission and/or assent documents.

C. Special Instructions:

1. Wards (foster children). Investigators considering a research project specifically targeting these children must contact the DCFS Director before finalizing the protocol. The study must address special considerations. DCFS staff will assist you in efforts to protect this special population.

1. If a child in foster care is found to qualify as a participant in research targeting a general population, a copy of the consent form and a cover letter describing the following must be faxed to the DCFS's Director's office prior to enrolling the child:

- a. The nature of the project,
- b. The Principal Investigator and Research Coordinator's contact information (telephone numbers email addresses) and
- c. The timeframe you need for the consent process to be completed;

DCFS contact information is as follows:

Phone: (501) 682-8770

Fax: (501) 682-6968

700 Main Street P.O. Box 1437, Slot S560

Little Rock, AR 72203-1437

2. Minor participants who reach the age of majority while involved in on-going research: When a child who is enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by the requirements of 45 CFR part 46.408 regarding parental or guardian permission and subject assent.

a. The IRB may approve a waiver of informed consent under 45 CFR 46.116(d), if the IRB finds and documents that the required conditions are met. Unless the Institutional Review Board (IRB) determines that the requirements for obtaining informed consent can be waived, the investigator must seek and obtain the legally effective informed consent, as described in IRB Policy 15.1, for the now-adult subject for any ongoing interactions or interventions with the subjects.

IV. IRB Procedure The IRB must determine:

A. Whether Assent is required.

1. If the IRB determines one of the following conditions to be true, then the assent of the children is not a necessary condition for proceeding with the research:

a. The capability of some or all of the children is so limited that they cannot reasonably be consulted; or

b. The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.

c. The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at either 45 CFR 46.116(c) or 45 CFR 46.116(d).

2. If the IRB determines that assent is required, it must find that adequate provisions are made for soliciting that Assent when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child,

as the IRB deems appropriate. The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition. The IRB must also determine the process for documenting the assent.

B. Whether Parental Permission is required.

1. If the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or legally authorized representative permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements described above, provided both (i) an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and (ii) the waiver is not inconsistent with Federal, State, or local law. The choice of an appropriate mechanism would 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.

2. If the IRB determines that parental permission is to be obtained, then there must be adequate provisions for soliciting parent or guardian permission(s) as follows:

1. The IRB must consider if the permission of one parent is sufficient for research not involving greater than minimal risk when the provisions of Pediatric Risk Category I above are met. The IRB may require both parents' permission even in Category I research.

2. The IRB must consider if the permission of one parent is sufficient for research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects when the provisions of Pediatric Risk Category II above are met. The IRB may require both parents' permission.

3. When the research is approved under Pediatric Risk Category III above, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

3. If Wards of the State or Other Agency are to be involved, the IRB can only approve the research if it finds and documents that such research is: (a) related to their status as wards; or (b) conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research is approved, the IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian. 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 agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

Department: UAMS Institutional Review Board
Policy Number: 17.2
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January 24, 2011

SUBJECT: Cognitively Impaired Persons

I. Background

Additional safeguards must be in place to protect the rights and welfare of participants who may be vulnerable to coercion or undue influence such as those that are cognitively impaired. Individuals with psychiatric, cognitive, or developmental disorders, or those who are substance abusers may have limited capacity to understand the information presented and may not be able to make a reasoned decision about participation.

II. Policy

A. Research that is expected to include cognitively impaired participants must address how determinations will be made as to whether a participant has impaired decision making capacity to consent both before and during the research and how those participants will be protected.

B. Research with those that are cognitively impaired must fall in to one of two categories:

1. The proposed research is minimal risk. The investigator must demonstrate to the IRB that there is a compelling reason to include cognitively impaired individuals as subjects. Cognitively impaired individuals must not be subjects in research simply because they are readily available.
2. The research presents a potential of direct benefit to the participant. Cognitively impaired individuals may not be subjects in research that is greater than minimal risk, unless that research has a potential to directly benefit the subject and the potential benefits outweigh the potential risks.

III. DEFINITIONS

A. Cognitively Impaired (also known as Unsound Mind): The inability to perceive all relevant facts related to one's condition and proposed treatment so as to make an intelligent decision based thereon, regardless of whether the inability is only temporary or has existed for an extended period of time or occurs or has occurred only intermittently and whether or not it is due to natural state, age, shock or anxiety, illness, injury, drugs or sedation, intoxication, or other cause of whatever nature. An individual shall not be considered to be "of unsound mind" based solely upon the fact of his refusal of medical care or treatment.

B. Health care: Any care, treatment, service, or procedure to maintain, diagnose, treat, or provide for the patient's physical or mental health or personal care.

C. Legally Authorized Representative (LAR) An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures involved in the research. See Policy 17.13 for Arkansas LAR Policy.

III. INVESTIGATORS MUST:

A. Provide a proposed plan to assess the capacity to consent before and during the research.

B. If capacity to consent is likely to be found lacking and the research involves surgical or medical treatments and/or procedures that might be prescribed by a licensed physician, provisions to obtain the permission of an appropriate LAR should be made. Consult IRB Policy 17.13 for the list of appropriate LARs.

Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect cognitively impaired individuals. When appropriate, the IRB should consider whether other health care providers ought to be consulted to ensure that proposed research

procedures will not be detrimental to ongoing therapeutic regimens. The LAR must be given descriptions of both proposed research studies and their obligations as a LAR. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.

C. Identify any additional safeguards that are in place to protect the rights and welfare of the cognitively impaired subjects.

IV. IRB RESPONSIBILITIES

IRBs may only approve research involving persons with impaired decision-making capability when the following conditions apply:

A. The proposed research has all necessary safeguards in place to protect the rights and welfare of the cognitively impaired subjects.

B. For studies that are greater than minimal risk, the IRB must determine that there is a prospect of direct benefit to the cognitively impaired subject.

C. The informed consent process and document make provisions for seeking consent from a LAR.

D. The IRB should consider whether to require investigators to solicit prospective subjects' "assent" (the willingness and, to the extent possible, knowledgeable participation of those unable to give legally valid consent). The IRB should also determine whether a cognitively impaired person's refusal to participate in research should override consent given by a LAR.

Department: UAMS Institutional Review Board
Policy Number: 17.4
Section: Special Populations
Effective Date: July 31, 2002
Revision Date: October 10, 2002; June 24, 2004; February 8, 2005;
January 24, 2011

SUBJECT: Subjects in Long Term Care

Aside from the regulatory requirement that IRBs provide additional protections for especially vulnerable persons, there are no specific regulations governing research with elderly subjects. The elderly are, as a group, heterogeneous and not usually in need of special protections, except in two circumstances: cognitive impairment and institutionalization. Under those conditions, the same considerations are applicable as with any other, non-elderly subject in the same circumstances. See IRB policy 17.2 for discussion of cognitive impairment.

Institutionalization: In the past, persons in nursing homes or other institutions have been selected as subjects because of their easy accessibility. However, conditions in institutional settings increase the chances for coercion and undue influence because of the lack of freedom inherent in such situations. Research in these settings should therefore be avoided, unless the involvement of the institutional population is necessary to the conduct of the research (*e.g.*, the disease or condition is endemic to the institutional setting, persons who suffer from the disease or condition reside primarily in institutions, or the study focuses on the institutional setting itself).

IRB Considerations: When a research study is undertaken at a nursing home, all necessary parties are informed and all documentation is maintained in a manner that meets all local, state, and federal research requirements.

1. The researcher must provide evidence that permission has been obtained from the nursing home administrator and medical director. In a chain of nursing homes, permission could be obtained from a regional or national administrator and medical director, but contact and approval should still take place at the local level with both the local nursing home administrator and local medical director.
2. If the study involves the engagement of the nursing home staff in the research, then the nursing home must submit a Federalwide Assurance (FWA) to the Office for Human Research Protections. The nursing home will need to identify the IRB that will serve as its IRB of record. UAMS may only be named the IRB of record with the approval of the Vice Chancellor for Research and an IRB authorization agreement with UAMS. If the study does not involve the engagement of the nursing home staff in the research, an FWA is not necessary and the nursing home management can decide how it will review the researcher's protocol for appropriateness.
3. The protocol should include documentation of how consent to participate in the study will be obtained. This description should state that if the resident is not competent to provide informed consent that the consent and assent requirements described in IRB Policy 17.2 will apply. The procedures used to obtain consent and assent should be detailed in the protocol. Finally, the procedure to be used to obtain consent to review nursing home records from resident/LAR should be described.

Department: UAMS Institutional Review Board
Policy Number: 17.6
Section: Special Populations
Effective Date: July 31, 2002
Revision Date: August 24, 2004

SUBJECT: Minorities

Federal regulations require the equitable selection of subjects [45 CFR 46.111(a)(3)]. In addition, NIH requires that applicants for all research grants, cooperative agreements, and contracts involving human subjects include minorities (and women) in study populations "so that research findings can be of benefit to *all* persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them." Investigators must provide a "clear compelling rationale for their exclusion or under-representation" Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources.

The inclusion 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. Most diseases affect all population groups, minority and non-minority alike. For generalizability purposes, investigators must include the widest possible range of population groups. Sometimes, however, minorities are subject to a differential risk. Some research, for example, relates to conditions that specifically affect various minority groups (e.g., sickle cell anemia or Tay Sachs disease), so that involvement of the relevant minority groups is imperative. Other research focuses on characteristics of diseases or effectiveness of therapies in particular populations (e.g., HIV transmission, treatment for hypertension), and may also concern conditions or disorders that disproportionately affect certain racial or ethnic groups. Exclusion or inappropriate representation of these groups, by design or inadvertence, would be unjust. Further, to the extent that participation in research offers direct benefits to the subjects (in HIV research, for example, the receipt of a promising new drug), under representation of minorities denies them, in a systematic way, the opportunity to benefit.

IRB Considerations: Research designs that include diverse study populations are highly desirable. The UAMS IRB will require investigators to justify protocols that call for homogeneous study populations. The UAMS IRB will be aware of the implications of various recruiting strategies, and be prepared to suggest alternative recruitment methods so as to ensure an appropriately diverse or focused subject population.

In addition to ensuring adequate appropriate representation of minorities in study populations (and guarding against inappropriate overburdening of minorities), the UAMS IRB must ensure that any special vulnerabilities of subjects are accounted for and handled appropriately. To the extent that prospective minority study populations are also economically or educationally disadvantaged, the UAMS IRB will safeguard their rights and welfare by making sure that any possible coercion or undue influence is eliminated (e.g., compensation that is not commensurate with the risk, discomfort, or inconvenience involved, or recruiting in institutional settings where voluntary participation might be compromised).

The UAMS IRB will also safeguard the consent process (and, indeed, the entire research relationship) to ensure open and free communication between the researcher and the

prospective subject. Consent documents must be written in language easily understandable to subjects; the possibility of illiteracy should be accounted for, as should the need for communicating in foreign languages. The informed consent documents should be available in English and other languages as appropriate to the subject population(s). Foreign language consent documents should be developed using quality control procedures such as translation from English to the other language and then back to English, to ensure that the information is correctly conveyed. The UAMS IRB will require a letter from the translator certifying that the foreign language consent is a faithful rendition of the approved English consent form. The role of cultural norms of subjects should also be addressed. The involvement of representatives from the target population(s) may also be pertinent to IRB review.

Department: UAMS Institutional Review Board
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Section: Special Populations
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Revision Dates: February 8, 2005; July 9, 2004; November 18, 2002

SUBJECT: Pregnant Women, Fetus, and Human In Vitro Fertilization

This policy applies to all research, development, and related activities involving: (1) the fetus, (2) pregnant women, and (3) human *in vitro* fertilization and is based on the Federal Regulations at 45 CFR 46 Subpart B. The requirements in this Policy are in addition to those imposed under the other IRB policies and other applicable federal, state and local laws.

Research involving women who are or may become pregnant should receive special attention from the IRB because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the UAMS IRB will determine when the informed consent of the father to the research is required. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society. Procedural protections beyond the basic requirements for protecting human subjects are prescribed in federal regulations for research involving pregnant women.

Definitions

"Pregnancy" encompasses the period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the fetus.

"Fetus" means the product of conception from the time of implantation (as evidenced by any of the presumptive signs of pregnancy, such as missed menses, or a medically acceptable pregnancy test), until a determination is made, following expulsion or extraction of the fetus, that it is viable.

"Viable" as it pertains to the fetus means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. If a fetus is viable after delivery, it is a premature infant.

"Nonviable fetus" means a fetus *ex utero*, which, although living, is not viable.

"Dead fetus" means a fetus *ex utero*, which exhibits none of the following: heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).

"*In vitro* fertilization" means any fertilization of human ova which occurs outside the body of a female, either through admixture of donor human sperm and ova or by any other means.

Procedure: Investigators submitting studies which fall under this policy should design their protocols, consents and processes with these additional requirements in mind in addition to the standard requirements for human research. The IRB must find and document the additional requirements below specific to the research activities proposed.

Additional Requirements For Activities Involving Fetuses, Pregnant Women, or Human In Vitro Fertilization. In addition to all other requirements for approval, the UAMS IRB will determine that:

1. Adequate consideration has been given to the manner in which potential subjects will be selected; and
2. Adequate provision has been made by the investigator for monitoring the actual informed consent process (e.g., through such mechanisms, when appropriate, as participation by the IRB or subject advocates in (i) overseeing the actual process by which individual consents are secured either by approving induction of each individual into the activity or verifying, perhaps through sampling, that approved procedures for induction of individuals into the activity are being followed, and (ii) monitoring the progress of the activity and intervening as necessary through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen).
3. No person on the research team should play any role in the determination of fetal viability.

Activities Directed Toward Pregnant Women as Subjects

1. No pregnant woman may be involved as a subject unless: (1) the purpose of the activity is to meet the health needs of the mother and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus is minimal.
2. Father's Consent. Research may be conducted only if the mother and father are legally competent and have both given their informed consent after having been fully informed regarding possible impact on the fetus, except that the father's informed consent need not be secured if: (1) the purpose of the activity is to meet the health needs of the mother; (2) his identity or whereabouts cannot reasonably be ascertained; (3) he is not reasonably available; or (4) the pregnancy resulted from rape.

Activities Directed Toward Fetuses *In Utero* as Subjects

1. No fetus *in utero* may be involved as a subject in any research activity covered by this Policy unless the IRB determines either: (1) the purpose of the activity is to meet the health needs of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus imposed by the research is

minimal and the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means.

2. Research may be conducted only if the mother and father are legally competent and have both given their informed consent, except that the father's consent need not be secured if: (1) his identity or whereabouts cannot reasonably be ascertained, (2) he is not reasonably available, or (3) the pregnancy resulted from rape.

Activities Directed Toward Fetuses *Ex Utero*, Including Nonviable Fetuses, as Subjects

1. Until it has been ascertained whether or not a fetus *ex utero* is viable, a fetus *ex utero* may not be involved as a subject in an activity covered by this Policy unless:
 - a. there will be no added risk to the fetus resulting from the activity, and the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means, or
 - b. the purpose of the activity is to enhance the possibility of survival of the particular fetus to the point of viability.
2. No nonviable fetus may be involved as a subject in an activity covered by this Policy unless:
 - a. vital functions of the fetus will not be artificially maintained,
 - b. experimental activities which of themselves would terminate the heartbeat or respiration of the fetus will not be employed, and
 - c. the purpose of the activity is the development of important biomedical knowledge that cannot be obtained by other means.
3. In the event the fetus *ex utero* is found to be viable, it may be included as a subject in the activity only to the extent permitted by and in accordance with the requirements of other parts of this Policy.
4. Research may be conducted only if the mother and father are legally competent and have both given their informed consent, except that the father's informed consent need not be secured if: (1) his identity or whereabouts cannot reasonably be ascertained, (2) he is not reasonably available, or (3) the pregnancy resulted from rape.

Activities Involving the Dead Fetus, Fetal Material, or the Placenta. Activities involving the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus shall be conducted only in accordance with any applicable State or local laws regarding such activities.

Modification or Waiver of Specific Requirements. Upon the request of the investigator (with the approval of the IRB), the Secretary of the Department of Health and Human Services may modify or waive any of the above requirements of this Policy.

Studies in Which Pregnancy is Coincidental to Subject Selection. Any study in which women of childbearing potential are possible subjects may inadvertently include pregnant women. Federal regulations require that, when appropriate, subjects be provided a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable as part of the informed consent process.

The IRB must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to ensure that non-pregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the investigator immediately should they become pregnant. In some instances, there may be potential risk sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

Department: UAMS Institutional Review Board
Policy Number: 17.9
Section: Special Populations
Effective Date: July 31, 2002
Revision Date: November 18, 2002; August 24, 2004; February 8, 2005; January 24, 2011

SUBJECT: Prisoners Involved in Research

I. Background

The special vulnerability of prisoners makes consideration of their participation in research particularly important. Prisoners may be under constraints because of their incarceration, which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply to reviewing research involving prisoners.

II. Policy

Research which involves the use of prisoners as subjects must meet the requirements of the general IRB Policies and the special ones outlined in this policy. The IRB may not approve research involving prisoners if these special provisions are not met.

Investigators submitting research with the intent to enroll prisoners must show in their application how their proposed study meets each of the elements under Subpart C, as outlined below in Section V.

If a subject becomes a prisoner while enrolled in a study that was not reviewed under Subpart C, follow the procedures outlined below in Section VI.

Research involving prisoners cannot be deemed exempt.

Research involving prisoners may only be expedited in limited circumstances as described below in Section VII.

III. IRB Composition when Prisoners Are Involved

In order for the convened IRB to review a protocol involving prisoners as subjects, two conditions must be met regarding the composition of the IRB:

1. A majority of the IRB Committee 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 Committee shall be a prisoner representative with appropriate background and experience to serve in that capacity. The prisoner representative may be listed as an alternate on the IRB roster for quorum purposes, but is a voting member of the IRB when needed.

If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved.

The IRB must meet the special composition requirements for all types of review of the protocol: initial review, major modifications and continuing review unless no subjects have been enrolled. If no subjects have been enrolled, the continuing review may be expedited under category 8.

IV. Definitions

A. Minimal Risk. As used in this policy, "Minimal risk" 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 healthy persons.

B. Prisoner. As used in this policy "Prisoner" means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under

a criminal or civil statute, individuals, including juveniles, detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing. Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, for example, arraignment or trial. When a prisoner is also a minor, such as an adolescent detained in a juvenile detention facility, IRB policy 17.1 regarding Children in Research will also apply.

Common examples of the application of the regulatory definition of prisoner are as follows:

1. Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration are prisoners; however, individuals who are receiving non-residential court-ordered substance abuse treatment and are residing in the community are not prisoners.
2. Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration are prisoners; however, individuals who have been voluntarily admitted to an institution for treatment of a psychiatric illness, or who have been civilly committed to nonpenal institutions for treatment because their illness makes them a danger to themselves or others, are not prisoners.
3. Parolees who are detained in a treatment center as a condition of parole are prisoners; however, persons living in the community and sentenced to community-supervised monitoring, including parolees, are not prisoners.
4. Probationers and individuals wearing monitoring devices are generally not considered to be prisoners; however, situations of this kind frequently require an analysis of the particular circumstances of the planned subject population. Contact the IRB when questions arise about research involving these populations.

V. Convened IRB Review Process

Research involving prisoners must be reviewed, and presented at a convened meeting, by a prisoner representative with a focus on the requirements of Subpart C. The prisoner representative will have access through ARIA to all submitted materials.

Subpart C requires seven specific findings, which the IRB Minutes will document, in order to approve research involving prisoners.

1. The research represents one of the permissible categories of research:
 - a. A study 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 subjects;
 - b. A study 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 subjects;
 - c. Research 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). Research in this category may proceed only after the HHS Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of his or her intent to approve the research; or
 - d. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well being of the subject. For Research in this category, if the IRB-approved proposal is a study in which some prisoners will be assigned

to a control group and these prisoners may not benefit from their participation in research, such research may proceed only after the HHS Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of his or her intent to approve the research. OHRP interprets control groups which may not benefit from research to include a control group receiving standard of care that the prisoners would otherwise receive, services as usual, or a placebo.;

- e. Certain epidemiological research conducted or supported by HHS. In this category, the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease.

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;

3. The risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;

4. Procedures for the selection of subjects 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;

5. The study information is presented in language, which is understandable to the subject population;

6. Adequate assurance exists that the parole board will not take into account a prisoner's participation in the research in making decisions regarding transfer to community supervision, 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.

Note: In order to make some of these seven findings, the IRB must be familiar with the specific conditions in the local prison(s) or jail site(s) that are pertinent to subject protections, before approving the Research.

Research Funded by DHHS: If the proposed research is funded by DHHS, the IRB will certify to OHRP that the IRB reviewed the research and made the seven findings. Final approval may not be granted until OHRP responds with an approval. If OHRP determines that the research does not fit into one of the permissible categories, the research involving prisoners may not proceed.

Federal Bureau of Prisons. The Federal Bureau of Prisons places special restrictions on research that takes place within the Bureau of Prisons. The IRB should follow the regulations at 28CFR 512 when reviewing such research.

VI. Procedure when subjects unexpectedly become Prisoners

A. Investigator actions: If a subject becomes a prisoner while enrolled in research that was not reviewed under Subpart C, the Investigator will notify the IRB immediately. The investigator should note whether he or she wants to terminate subject's enrollment or have the study re-reviewed under Subpart C. If the Investigator believes it is in the best interests of the subject to remain in the research study while incarcerated, the justification for this belief should be submitted to the IRB.

Otherwise, all research interactions and interventions with the now-incarcerated prisoner-subject must cease and no more identifiable private information about the now-incarcerated prisoner-subject may be obtained.

B. IRB actions:

1. Review the research under Subpart C; or
2. If the subject's participation in the research is to be terminated, the IRB should consider the risks associated. If the subject's participation cannot be terminated for health or safety reasons, choose one of the following options:
 - a. Keep subject active on the study until the Subpart C requirements are met. The IRB must promptly re-review the proposal in accordance with the requirements of subpart C, and send a certification to OHRP, along with justification for keeping subject enrolled, and wait for a letter of authorization in reply.
 - b. Remove subject from the study but find alternate mechanism to keep subject on study intervention, such as compassionate or off label use.

VII. Expedited Review of Prisoner Research

- A. Research involving interaction with prisoners.** Research involving interaction with prisoners may only be reviewed under expedited procedures when a determination has been made that the research involves no greater than minimal risk to the prison population being studied. While the normal expedited reviewers may also review, the prisoner representative must review the research and agree with the risk determination. The prisoner representative must also be involved in the review of all modifications and continuing reviews.
- B. Research which does not involve interaction with prisoners (existing data, chart reviews).** Research which does not involve interaction with prisoners but uses identifiable private information about prisoners may only be reviewed under expedited procedures when a determination has been made that the research involves no greater than minimal risk to the prison population being studied. Separate review by the prisoner representative may be requested but is not required. However, if the prisoner representative reviews the initial submission, then he or she must review subsequent modifications and continuing reviews.

Department: UAMS Institutional Review Board
Policy Number: 17.10
Section: Special Populations
Effective Date: July 31, 2002
Revision Date: August 25, 2004

SUBJECT: Students, Employees and Healthy Volunteers

Healthy Volunteers. Special concerns surround the involvement of healthy persons who volunteer to participate in research. Primarily, the principles involved are beneficence and respect for persons. In the *Belmont Report*, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research stated the two general rules that describe beneficent actions as: (1) do not harm; and (2) maximize possible benefits and minimize possible harms. Volunteers for whom no therapeutic benefit can result from participation in research should, therefore, be exposed to risks that are minimized to the greatest extent possible. While the minimization of risks is an important requisite for any research involving human participants, the altruistic motivation of the healthy volunteer's agreement to participate (*i.e.*, of contributing to scientific knowledge for the benefit of society) heightens the concern for the risks to which such participants should ethically be exposed.

The principle of respect for persons requires that research participants be, where capable of doing so, allowed to act autonomously and to express their right of self-determination. These principles are effectuated through the process of informed consent, which involves providing subjects with all relevant information about the study, including the risks and benefits involved, in clear and simple language, and ensuring that the information is understood and appreciated. In research involving healthy volunteers, particularly where the research involves more than minimal risk, the IRB must ensure that any monetary payments to subjects are not so great as to constitute an undue inducement. The IRB should seriously scrutinize the payment schedules to ensure that any compensation offered is commensurate with the time, discomfort, and risk involved. Where a research procedure involves serious discomfort and/or the real, though slight, possibility of serious harm, the IRB should pay particular attention to the proposed study population and whether it may comprise persons who are likely to be vulnerable to coercion or undue influence, such as persons who are educationally or economically disadvantaged. The federal regulations require that the IRB employ special safeguards under such circumstances [45CFR 46.111(b)].

One area where healthy volunteers are employed in research is in Phase 1 drug trials. The justification for the involvement of healthy subjects is the need for volunteers whose experience with the trial materials is more easily analyzed because of the existence of fewer confounding factors. While Phase 1 trials are the first use of experimental drugs and devices in humans, preliminary studies involving animals provide investigators with data indicating a high likelihood of safe use in humans. Studies have indicated that the risk of injury from participating in Phase 1 studies is small, about the same as the risk of being injured while working as an office secretary [Levine, Robert J. *Ethics and Regulation of Clinical Research*, 2d ed. Baltimore: Urban and Schwarzenberg, 1986, p. 42.]. The likelihood of risk, including the availability of animal data, should be scrutinized by the IRB.

Healthy volunteers, like students and employees, should be recruited through general announcements or advertisements, rather than through individual solicitations. Personal solicitations increase the likelihood that participation will be the result of undue influence, either because of the relationship between the recruiter and the prospective subject, or methods of communication employed by the recruiter that may act to persuade prospective subjects to participate, thus compromising the voluntariness of the agreement to participate.

Investigators and the IRB should carefully consider what will happen if and when a healthy volunteer should become sick or be injured during the research. As with any research involving human subjects, such issues should be clearly spelled out in the informed consent document, and should be reviewed carefully with the prospective subject. For example, subjects should be told: whether any medical treatments will be made available should injury occur and, if so, what they consist of; whom to contact should a research-related injury occur; and that they may discontinue participation at any time without penalty or loss of benefits to which they would otherwise be entitled [45CFR 46.116(a)(6-8)]. In addition, where appropriate subjects should be told whether they will be dropped from the study in the event of injury or illness, and whether they will be required to pay for treatment of research-related injuries or illness [45CFR46(b)(2-3)]. Where illness in healthy volunteers does occur, particularly during a drug study, investigation by an independent physician may be warranted. [See Fazackerley, Randall, and Pleuvry (1987).]

The issues raised by the involvement of healthy subjects in genetic research are discussed in Guidebook Chapter 5, Section H, "Human Genetic Research."

Students. Two questions that have been posed are whether students -- medical students, in particular -- should be allowed to participate in biomedical research (and whether special protections should be adopted to restrict their participation), and whether participation in research can appropriately be included as a course component for course credit. The problem with student participation in research conducted at the university is the possibility that their agreement to participate will not be freely given. Students may volunteer to participate out of a belief that doing so will place them in good favor with faculty (e.g., that participating will result in receiving better grades, recommendations, employment, or the like), or that failure to participate will negatively affect their relationship with the investigator or faculty generally (*i.e.*, by seeming "uncooperative," not part of the scientific community).

Consent must state that students are allowed to refuse participation or withdraw early from a study without affecting their academic standing at UAMS. Prohibiting all student participation in research, however, may be an overprotective reaction. An alternative way to protect against coercion is to require that faculty-investigators advertise for subjects generally (e.g., through notices posted in the school or department) rather than recruit individual students directly. As with any research involving a potentially vulnerable subject population, the IRB should pay special attention to the potential for coercion or undue influence and consider ways in which the possibility of exploitation can be reduced or eliminated.

Confidentiality is a concern raised by the involvement of students as subjects in research. The IRB should be aware that research involving the collection of data on

sensitive subjects such as mental health, sexual activity, or the use of illicit drugs or alcohol presents risks to subjects of which they should be made aware and from which they should be protected, to the greatest extent possible. The close environment of the university amplifies this problem.

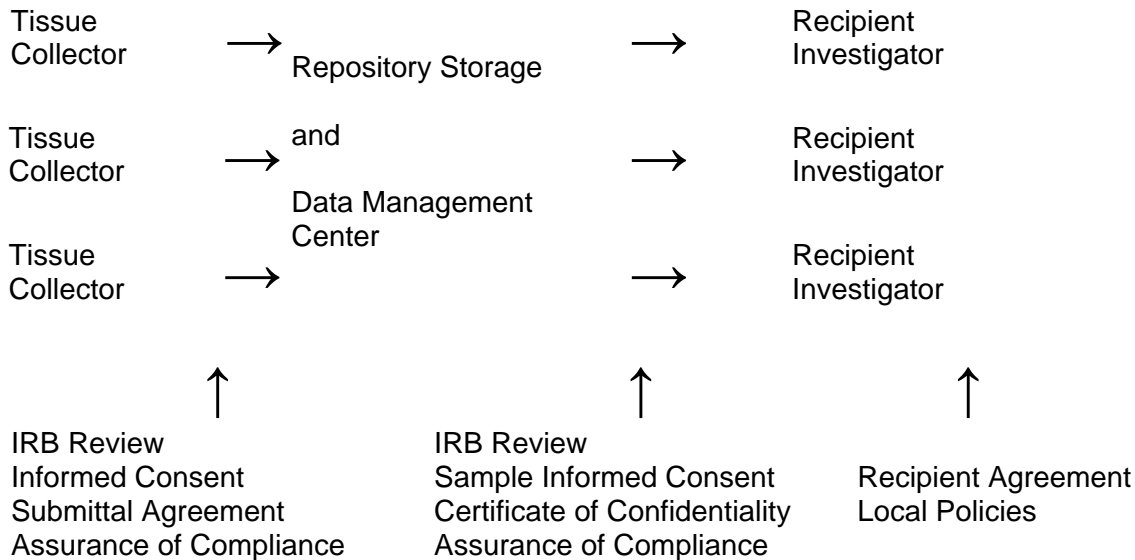
Employees. The issues with respect to employees as research subjects are essentially identical to those involving students as research subjects: coercion or undue influence, and confidentiality. Employee research programs raise the possibility that the decision will affect performance evaluations or job advancement. It may also be difficult to maintain the confidentiality of personal medical information or research data when the subjects are also employees, particularly when the employer is also a medical institution [Meyers (1979)]. For issues regarding compensation each Institution may have policies that apply. The investigator is responsible for following those policies.

Department: UAMS Institutional Review Board
Policy Number: 17.11
Section: Special Populations
Effective Date: July 31, 2002
Revision Date: August 25, 2004

SUBJECT: Stored Data or Tissues

Operation of the Repository and its data management center will be subject to oversight by the UAMS IRB. The IRB will review and approve a protocol specifying the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. The IRB will also review and approve a sample collection protocol and informed consent document for distribution to tissue collectors and their local IRBs. A Certificate of Confidentiality should be obtained to protect confidentiality of repository specimens and data.

1. Human Tissue Repositories collect, store, and distribute human tissue materials for research purposes. Repository activities involve three components: (i) the collectors of tissue samples; (ii) the repository storage and data management center; and (iii) the recipient investigators.
2. If supported by the Department of Health and Human Services (HHS), each component must satisfy certain regulatory requirements.



The Office for Human Research Protection (OHRP) formerly known as OPRR, provides the following guidance in response to requests from Institutional Review Boards, the National Institute of General Medical Sciences (NIGMS), and the research community.

1. **Local IRB Review.** Collection of data and specimens for inclusion in the NIGMS Human Genetic Mutant Cell Repository should be subject to oversight by local Institutional Review Boards (IRB) convened by the collecting institutions under OHRP-

approved Assurances.¹ The local IRB is familiar with the particular circumstances of its research setting and is in the best position to weigh critical considerations like local professional and community standards, institutional policies and resources, and the needs of differing patient or subject populations.

- 2. Informed Consent.** Written informed consent should be obtained from each donor-subject in accordance with Department of Health and Human Services (HHS) regulations at 45CFR46.116.

Included among the basic elements of informed consent should be a clear description of (i) the operation of the cell repository; (ii) the specific types of research to be conducted; (iii) conditions under which data and specimens will be released to recipient-investigators; and (iv) procedures for protecting the privacy of subjects and maintaining the confidentiality of data. Informed consent information describing the nature and purposes of the research should be as specific as possible. Where human genetic research is anticipated, informed consent information should include information about the consequences of DNA typing (e.g., regarding possible paternity determinations). Informed consent documents may not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights.

The Cell Repository should provide tissue collectors with an NIGMS-approved sample informed consent document containing these elements and with a sample protocol for tissue collection. The UAMS IRB may request copies of these sample documents to assist in their review of local informed consent documents and protocols.

- 3. Oversight of Repository Activities.** Operation of the NIGMS Human Genetic Mutant Cell Repository and its data management center will be subject to oversight by an Institutional Review Board convened by the Coriell Institute of Medical Research under an OHRP-approved Assurance of Compliance. The IRB should review and approve a protocol specifying the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. The IRB should also review and approve a sample collection protocol and informed consent document for distribution to tissue collectors and their local IRBs. A Certificate of Confidentiality should be obtained to protect confidentiality of repository specimens and data.
- 4. Submittal Agreement.** A written submittal agreement for tissue collectors should require written informed consent of the donor-subjects utilizing an informed consent document approved by UAMS IRB. It should also contain an acknowledgment that collectors 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.
- 5. Usage Agreement.** A written usage agreement for recipient-investigators should include the following: "Recipient acknowledges that the conditions for use of this research material are governed by the cell repository Institutional Review Board in accordance with Department of Health and Human Services regulations at 45CFR46. Recipient agrees to comply fully with all such conditions and to report promptly to the

cell repository any proposed changes in the research project and any unanticipated problems involving risks to subjects or others. Recipient remains subject to applicable State or local laws or regulations and institutional policies which provide additional protections for human subjects. This research material may only be utilized in accordance with the conditions stipulated by the cell repository IRB. Any additional use of this material requires prior review and approval by the cell repository IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an applicable OHRP-approved Assurance."

6. Under certain circumstances, collecting institutions may elect to rely upon the Cell Repository IRB at Coriell Institute. This requires a written Cooperative Amendment, signed by the collecting institution and the Coriell Institute, and approved by OHRP. Contact OHRP for details.

In response to requests from the National Institute of General Medical Sciences (NIGMS), the Office for Protection from Research Risks (OHRP) provides the following clarification regarding submission of "non-identifiable" materials to the Human Genetic Mutant Cell Repository.

As Chart 1 (attached) illustrates, human subjects are involved in research when the research involves (i) an intervention or interaction with a living individual that would not occur (or would occur in some other fashion) but for the research; **or** (ii) the use of identifiable private data or information in a form associable with a living individual [45CFR16.102(f)].

Human subjects would not be involved when material submitted to the Repository satisfies **both** of the following conditions:

1. The material, in its entirety, was collected for purposes other than submission to the Repository (e.g., the material was collected solely for clinical purposes, or for legitimate but unrelated research purposes, with no "extra" material collected for submission to the Repository).

and

2. The material is submitted to the Repository without any identifiable private data or information (i.e., no codes or linkers of any sort may be maintained, either by the Submitter or by the Repository, that would permit access to identifiable private data or information about the living individual from whom the material was obtained).

While OHRP requires neither an Assurance of Compliance nor a Certification of Institutional Review Board review [45CFR46.103(a),(f)] for activities that do not involve human subjects, local institutional requirements regarding review of such activities are, nevertheless, binding. Some institutions may require IRB or administrative review of all research activities involving human materials, even where "human subjects" are not involved.

OHRP offers the following guidance concerning operation of human cell repositories under Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR 46). The guidance assumes that repository activities include nonexempt human subjects research as defined under HHS regulations.

1. The operation of any HHS-supported human cell repository and its data management center should be subject to oversight by an Institutional Review Board (IRB) convened under an applicable OHRP-approved Assurance of Compliance. This IRB should set the conditions under which data and specimens may be accepted and shared. OHRP strongly recommends that one such condition stipulate that recipient-investigators not be provided access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained.
2. Collection of data and specimens should be subject to oversight by local IRBs convened under applicable OHRP-approved Assurances.
3. Written informed consent should be obtained from each donor-subject in accordance with HHS regulations at 45CFR46.116. Included among the basic elements of informed consent should be a clear description of (i) the operation of the cell repository; (ii) the specific types of research to be conducted; (iii) the conditions under which data and specimens will be released to recipient-investigators; and (iv) procedures for protecting the privacy of subjects and maintaining the confidentiality of data.
4. Informed consent information describing the nature and purposes of the research should be as specific as possible.
5. Where human genetic research is anticipated, informed consent information should include information about the consequences of DNA typing (e.g., regarding possible paternity determinations).
6. Informed consent documents may not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights.
7. OHRP recommends that the cell repository develop a sample collection protocol and informed consent document for distribution to collector-investigators and their local IRBs.
8. A written submittal agreement for collector-investigators should require written informed consent of the donor-subjects utilizing an informed consent document approved by the local IRB. It should also contain an acknowledgment that collector-investigators 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.
9. A written usage agreement for recipient-investigators should include the following:

"Recipient acknowledges that the conditions for use of this research material are governed by the cell repository Institutional Review Board in accordance with

Department of Health and Human Services regulations at 45CFR46. Recipient agrees to comply fully with all such conditions and to report promptly to the cell repository any proposed changes in the research project and any unanticipated problems involving risks to subjects or others. Recipient remains subject to applicable State or local laws or regulations and institutional policies which provide additional protections for human subjects.

This research material may only be utilized in accordance with the conditions stipulated by the cell repository IRB. Any additional use of this material requires prior review and approval by the cell repository IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an applicable OHRP-approved Assurance.

10. OHRP recommends that a Certificate of Confidentiality be obtained to protect confidentiality of human cell repository specimens and data.

Department: UAMS Institutional Review Board
Policy Number: 17.12
Section: Special Populations
Effective Date: July 31, 2002
Revision Date: April 15, 2004

SUBJECT: Terminally Ill Patients

In many contexts, research on terminal illness and its treatment requires the involvement of terminally ill patients when alternative populations for study do not exist or when involving alternative populations would be ethically unjustifiable. Two important reasons for concern regarding research involving terminally ill persons are: (1) they tend to be more vulnerable to coercion or undue influence than healthy adult research subjects; and (2) research involving the terminally ill is likely to present more than minimal risk.

Terminally ill patients are those who are deteriorating from a life-threatening disease or condition for which no effective standard treatment exists. It is generally considered unacceptable to ask such persons to participate in research for which alternative, not similarly burdened, populations of subjects exist. Nevertheless, it may often be necessary to involve terminally ill patients in research concerning their disease and its treatment. Further, terminally ill persons should not be excluded from research in which they may want to participate simply because of their status. Terminally ill individuals are a vulnerable population of research subjects, and, therefore, require additional protection against coercion and undue influence [45 CFR 46.111(b)]. If an IRB regularly reviews research involving the terminally ill, it should include among its members one or more individuals knowledgeable about and experienced in working with these subjects [45 CFR 46.107f].

With the appearance of HIV, concerns have emerged about circumstances under which persons with serious and life-threatening conditions may have access to research drugs through expanded access programs. The FDA's Parallel Track program and Treatment IND regulations seek to address these concerns. The IRB have a role both in considering circumstances in which terminally ill persons are appropriately excluded from research because they are a vulnerable group, and in providing persons who have no therapeutic alternatives the opportunity to receive the possible benefits of experimental interventions.

DEFINITIONS

Expanded Availability: Policy and procedure that permits individuals who have serious or life-threatening diseases for which there are no alternative therapies to have access to investigational drugs and devices that may be beneficial to them. Examples of expanded availability mechanisms include Treatment INDs, Parallel Track, and open study protocols.

Therapeutic Intent: The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinkage of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected.) This term is sometimes associated with Phase 1 drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some

improvement in the patient's condition as well as assessing the safety and pharmacology of a drug.

Phase I Trials: It is important to distinguish between risks that may be justified by anticipated benefits for the research subjects and risks associated with procedures performed purely for research purposes. A particularly difficult issue relating to research involving terminally ill patients arises in connection with the conduct of Phase 1 drug trials in which the drugs involved are known to be particularly toxic (e.g., a new form of cancer chemotherapy). In some of these studies, any benefit to the subject is, at best, highly unlikely. Despite the "therapeutic intent" of the investigators to benefit the subject, subjects may in fact experience a decline in health status, no improvements in terms of quality of life, or lengthened life for only a short time. It is extremely important that prospective subjects be clearly informed of the nature and likelihood of the risks and benefits associated with this kind of research. The challenge to the investigator and the IRB is to provide patients with an accurate description of the potential benefits without engendering false hope.

Group C Drugs: The FDA and the National Cancer Institute (NCI) developed a special category of drugs called "Group C." Group C drugs may be provided by oncologists to appropriate cancer patients through protocols outside the controlled clinical trial prior to the drug approval. In 1987, the FDA initiated a regulation establishing the treatment investigational new drug application (Treatment IND), and in 1992, instituted a policy providing for a "parallel track" mechanism [21 CFR 312.34]. Under a Treatment IND protocol, eligible patients have access to investigational new drugs intended to treat serious or life-threatening diseases; Parallel Track protocols enable persons with AIDS or HIV-related diseases who cannot participate in clinical trials to have access to investigational drugs.

IRB CONSIDERATIONS

The IRB should be satisfied that the nature, magnitude, and probability of the risks and benefits of the research have been identified as clearly and as accurately as possible. Special attention should be paid to the consent process, both in terms of the accuracy of the information to be provided and the manner in which consent is sought. As a general rule, accurate information concerning eligibility for participation (*i.e.*, diagnosis and prognosis), treatment options, and risks and benefits should be conveyed clearly and in a manner that will not either engender false hope or eliminate all hope.

The IRB must also consider including other information the patient might find relevant to making an informed decision to participate. For example, subjects should be told whether or not participation in the study is a condition for treatment at the institution; any costs to the patient of the research should be stated explicitly. The IRB should consider whether any payment might constitute an undue enticement, particularly if the subject population is economically disadvantaged. Patients should be provided with relevant information well in advance of making a decision about participation, and consultation with others such as family members, close friends, clergy, or medical consultants should be encouraged.

Department: UAMS Institutional Review Board
Policy Number: 17.13
Section: Special Populations
Effective Date: February 25, 2005
Revision Date: January 24, 2011

SUBJECT: Legally Authorized Representatives

I. Purpose

To describe who meets the criteria of a legally authorized representative and in what types of research under Arkansas law.

II. Definitions

A. *In Loco parentis* means one who puts him/herself in the situation of a lawful parent by assuming the obligations incident to the parental relation without going through the formalities necessary to a legal adoption.

B. Unsound Mind means and includes the inability to perceive all relevant facts related to one's condition and proposed treatment so as to make an intelligent decision based thereon, regardless of whether the inability is only temporary or has existed for an extended period of time or occurs or has occurred only intermittently and whether or not it is due to natural state, age, shock or anxiety, illness, injury, drugs or sedation, intoxication, or other cause of whatever nature. An individual shall not be considered to be "of unsound mind" for the purposes of this policy based solely upon the fact of his refusal of medical care or treatment.

C. "Other persons as may be authorized and empowered" would include an attorney-in-fact designated in a durable power of attorney for "health care". For purposes of the health care power of attorney statute, the term "health care" means "any care, treatment, service, or procedure to maintain, diagnose, treat, or provide for the patient's physical or mental health or personal care." An agent appointed under a power of attorney for health care would take precedence over any person listed above.

D. Court-appointed guardians also would be "authorized and empowered" to act on behalf of others, such as a minor or on behalf of a person of "unsound mind."

III. Policy

A. Research involving surgical or medical treatments or procedures. In Arkansas, in addition to other persons as may be authorized and empowered, the legally authorized representative for another person, for purposes of providing consent for research involving surgical or medical treatments or procedures, not prohibited by law, which might be suggested, recommended, prescribed or directed by a licensed physician, is any one the following:

1. Any parent, whether an adult or a minor, for his minor child or adult child of unsound mind. Child as used here includes biological, adopted, step or foster children. The father of an illegitimate child, however, cannot consent for the child solely on the basis of parenthood;
2. Any person standing *in loco parentis*, whether formally serving or not;
3. Any guardian, conservator, or custodian, for his ward or other charge under disability;
4. Any adult for a minor sibling or adult sibling of unsound mind;
5. If an authorized parent is absent, any maternal grandparent and, if the father is an authorized parent, any paternal grandparent, for a minor grandchild or for an adult grandchild of unsound mind;

6. Any married person, for a spouse of unsound mind; or

7. Any adult child, for their mother or father of unsound mind.

B. All Other Types of Research. For all other types of research, there is no legally authorized representative specifically designated under Arkansas law. Subjects requiring the use of LARs may only be entered into these types of research projects when the study meets the waiver of consent criteria outlined in IRB Policy 15.3 and is not FDA-regulated.

Department: UAMS Institutional Review Board
Policy Number: 18.1
Section: Drugs and Devices
Effective Date: July 31, 2002
Revision Date: April 15, 2004; February 8, 2005; January 24, 2011

SUBJECT: Review of Investigational New Drug (IND) Studies

A. Policy

Research that involves the use of a drug, other than a marketed drug in the course of medical practice, must have an investigational new drug (IND), unless the protocol meets one of the five exemptions. The IRB has the responsibility to evaluate all studies which involve the use of a drug for compliance with 21 CFR 312, Investigational New Drug Application.

All Investigator-initiated human research studies requiring an Investigational New Drug (IND) are subject to UAMS Administrative Guide Policy 12.1.10. Investigators proposing this type of study must work with the UAMS Research Support Center prior to submitting the study to the IRB.

B. Investigator Process for Study Drug with IND. For studies conducted under a valid IND, the Investigator must provide the IND# in the ARIA submission and submit documentation to confirm the validity of the IND. The following documentation is acceptable:

- a. Industry sponsored study protocol which includes the IND number;
- b. Written communication of the IND number from the Sponsor; or
- c. Written communication of the IND number from the FDA.

C. Investigator Process for Study exempt from the IND requirements. Investigators should provide sufficient information to show that the study meets one of the following exemptions as outlined in 21 CFR 312.2(b):

1. Approved Drugs. Research involving a drug that is lawfully marketed in the US is exempt if all of the following apply:

- a. The research is not intended to be reported to the FDA in support of a new indication for use nor to support any other significant change in the labeling for the drug;
- b. The research is not intended to support a significant change in the advertising for the product;
- c. The research does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- d. The research is conducted in compliance with the requirements for IRB Review and informed consent; and
- e. The research is conducted in compliance with the requirements of 21 CFR 312.7 regarding promotion and marketing.

See C6 below for the use of marketed drugs in cancer treatment.

2. Biological Products. Research involving blood grouping serum, reagent red blood cells or anti-human globulin is exempt if all of the following apply:

- a. The product is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and
- b. It is shipped in compliance with 21 CFR 312.160.

3. Placebo. Research involving use of a placebo is exempt from the IND requirements if the investigation does not otherwise require submission of an IND.

4. Bioavailability or bioequivalence study Bioavailability or bioequivalent studies are exempt provided:

- a. The drug product does not contain a new chemical entity as defined in 21 CFR 314.108;
- b. The drug product is not radioactively labeled;
- c. The drug product is not cytotoxic;

- d. The dose (single dose or total daily dose) does not exceed the dose specified in the labeling of the approved version of the drug product;
- e. The research is conducted in compliance with the requirements for IRB Review and informed consent; and
- f. The sponsor meets the requirements for retention of test article samples. See 21 CFR 320.31(d)(1).

Note: An IND is required when conducting a multiple-dose study on an extended release product on which no single-dose study has been completed.

5. Radioactive Drugs. Research involving radioactive drugs is exempt if a Radioactive Drug Research Committee, composed and approved by the FDA, determines the research meets the requirements in 21 CFR 361.1

6. Cancer Treatment. Marketed drugs that fit the requirements of FDA Guidance, “IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer”, may be considered exempt from 21 CFR 312.2(b). Investigators should read the Guidance and provide a letter to the IRB explaining how the proposed study meets the requirements for IND exemption under the Guidance.

D. Drug Storage and Dispensing. The UAMS Department of Pharmacy shall have oversight for the storage and use of any investigational drug used in human research at UAMS Medical Center. See Department of Pharmacy Policy and Procedure 5.16. For studies conducted at Arkansas Children’s Hospital, see PHAG030-A and PHAG030-B

For any other location, the Investigator must provide his or her plan to control the study drug. The plan must ensure that the drugs are used in an approved protocol and under the direction of approved study personnel.

E. IRB Review Process

The IRB will review research involving drugs in accordance with this policy, confirm that the study drug has an IND or the research meets one of the identified exemptions. In order to determine whether the drug storage and dispensing plans are appropriate, the ACHRI sign-off letter should indicate Pharmacy sign off. For UAMS studies, it should be evident that the study has gone through the Crimson review process which includes UAMS Research Pharmacy review.

Department: UAMS Institutional Review Board
Policy Number: 18.2
Section: Drugs and Devices
Effective Date: July 31, 2002
Revision Date: April 15, 2004; February 8, 2005; January 24, 2011

SUBJECT: Investigational Devices

I. Policy

Research that is conducted to determine the safety or effectiveness of a device must have an Investigational Device Exemption (IDE), unless the device meets the requirements for an abbreviated IDE or the protocol meets one of the exemptions from the requirement for an IDE.

All Investigator-initiated human research studies requiring an IDE are subject to UAMS Administrative Guide Policy 12.1.11. Investigators proposing this type of study must work with the UAMS Research Support Center prior to submitting the study to the IRB.

II. Definition

Device: An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory that:

- a. Is recognized in the official National Formulary, the United States Pharmacopeia, or any supplement to them.
- b. Is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in humans or other animals.
- c. Is intended to affect the structure or any function of the body of humans or other animals.
- d. Does not achieve any of its primary purposes through a chemical action within or on the body of humans or other animals, and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes.

Significant Risk Device: An investigational device that:

- a. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- b. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- c. 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
- d. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

III. Process

A. Investigator Process for Device with IDE. For studies conducted under a valid IDE, the Investigator must provide the IDE# in the ARIA submission and submit documentation to confirm the validity of the IDE. The following documentation is acceptable:

- a. Industry sponsored study protocol which includes the IDE number;
- b. Written communication of the IDE number from the Sponsor; or
- c. Written communication of the IDE number from the FDA.

B. Investigator Process for study submitted under an abbreviated IDE. In order for research to qualify for an abbreviated IDE, the Investigator must provide sufficient information to show that all of the following elements are met:

- a. The device is not a significant risk device with a brief explanation from the Sponsor of why the device is not a significant risk device.
- b. The device has not been banned.
- c. The device is or will be labeled in accordance with 21 CFR 812.5;
- d. The study will obtain the consent from each subject, unless waived by the IRB.
- e. The study complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;

- f. The study will maintain the records required under 21 CFR 812.140 and make the reports required under 21 CFR 812.150;
- g. The study complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

C. Investigator Process for study submitted under exemption from the IDE requirements. Investigators should provide sufficient information to show that the study meets one of the following exemptions as outlined in 21 CFR 812.2(c):

1. Research involves a device that was in commercial distribution before May 28, 1976 and the FDA did not consider the device to be a drug prior to that date. The device is being used or investigated in accordance with the indications in labeling in effect at that time.
2. Research involves a device that was in commercial distribution after May 28, 1976 but where the FDA has determined the device to be substantially equivalent to a device in commercial distribution prior to May 28, 1976. The FDA must not have considered the device to be a drug prior to that date. The device is being used or investigated in accordance with the indications in labeling in effect at that time.
3. Research involving a diagnostic device where the sponsor is in compliance with applicable requirements in 21 CFR Sec. 809.10(c). The device testing:
 - a. Must be noninvasive;
 - b. Must not require an invasive sampling procedure that presents significant risk;
 - c. Must not by design or intention introduce energy into a subject; and
 - d. Must not be used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
4. Research involving a device undergoing consumer preference testing, testing a modification of a device, or testing a combination of two or more approved devices. In order to meet this exemption, the device testing must not be for the purposes of determining safety and effectiveness and must not put subjects at risk.
5. Custom Devices may be exempt provided the research is not to test the safety or effectiveness of the device for commercial distribution. Custom device means a device that:
 - a. Necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist;
 - b. Is not generally available to, or generally used by, other physicians or dentists;
 - c. Is not generally available in finished form for purchase or for dispensing upon prescription;
 - d. Is not offered for commercial distribution through labeling or advertising; and
 - e. Is intended for use by an individual patient named in the order of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice.

E. Investigator Responsibilities for Investigational Device Studies

The Investigator is responsible for the tracking and oversight of FDA-regulated devices in research and must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the IRB. If the protocol does not address the storage and accountability plans as outlined below, the investigator should submit the Device Acknowledgement Form, found on IRB website, with the IRB Submission.

1. The investigational device must be used only by the Investigator or under his/her direct supervision.
2. The investigational device must be used only as described in the approved IRB protocol.
3. The Investigator must not supply the investigational device to any unauthorized persons.
4. The investigator must provide a plan for secure storage of the device and the proper disposal of or return of devices.
5. The investigator shall maintain the following accurate, complete and current records related to the device:
 - a. Correspondence with the IRB, sponsor, monitor, other investigators and FDA
 - b. Records of receipt, use or disposition of a device that relate to:
 - i. The type and quantity of the device, dates of receipt, and batch numbers or code marks
 - ii. Names of all persons who received, used, or disposed of each device
 - iii. The number of units of the device returned to the sponsor, repaired, or otherwise disposed of, and the reason(s)

- c. Records of each subject exposure to the device, including;
 - i. Informed consent
 - ii. All relevant observations
 - iii. Adverse device effects
 - iv. A record of the exposure of each participant to the investigational device, including the date and time of each use and any other therapy
- d. Dates and reasons for any deviations from the protocol

F. IRB Review Process

The IRB will review research involving devices in accordance with this policy; confirm that the device has an IDE, that the research meets one of the identified exemptions or the research meets the requirements for an abbreviated IDE; and that the device storage and accountability plans are appropriate.

For research conducted under an abbreviated IDE, the IRB must determine that the device is not a significant risk device. The minutes should document the reason for the determination.

If the IRB believes that a device submitted under an abbreviated IDE is a significant risk device, the study must be submitted to the FDA. Once the FDA approves, the IRB will then review the study.

Department: UAMS Institutional Review Board
Policy Number: 18.3
Section: Drugs and Devices
Effective Date: July 31, 2002
Revision Date: August 26, 2004; February 8, 2005; March 5, 2008;
January 24, 2011

SUBJECT: Emergency Use of a Test Article

I. Purpose

The purpose of this policy and procedure is to explain the limited circumstances where prior IRB approval is not required in the emergency use of a test article.

II. Definitions

A. Emergency Use means the use of a test article on a patient in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

B. Test Article means any drug, biological product or medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulations.

C. Life Threatening. Life threatening includes the scope of both life threatening and severely debilitating, as defined below:

Life threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and 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.

Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

III. Policy

The IRB acknowledges that there will be certain limited circumstances where IRB approval will not be obtainable prior to the first use of a test article. FDA requirements for emergency use must be met, and the IRB requires prior notification of test article use where possible. The IRB will acknowledge this one time use and require a follow up report within 5 days of the use of the test article.

Any subsequent use of the test article in a new patient will require full IRB review and approval prior to use. Submission of a protocol for review by the convened IRB is required within 30 days as a condition of emergency use.

If a test article has previously been acknowledged under the emergency use provisions, no subsequent uses in a new patient will be acknowledged without an approved protocol. Failure to submit a protocol within 30 days and any additional use of the test article will be treated as continuing non-compliance. For the safety of future patients, submit a protocol immediately after the first use.

Under FDA regulations, emergency use of a drug or biological product is considered a clinical investigation and the patient is considered to be a subject. The FDA may require data from an emergency use to be reported in a marketing application.

Under DHHS regulations, emergency use of a test article is not considered Human Research. Therefore, data from an emergency use cannot be used in any report of research activity subject to DHHS regulations.

IV. Procedures

An Investigator who intends to treat a patient with a test article in an emergency situation should:

A. Confirm situation meets the following emergency use requirements:

1. The patient is in a life-threatening situation
2. There is no standard acceptable treatment available
3. There is not sufficient time to obtain IRB approval.

B. Confirm test article status.

1. Drugs – Contact manufacturer to see if the drug can be made available for emergency use under the company's IND. If that is not an option, contact the FDA who may authorize shipment prior to IND Submission. The Research Support Center will provide assistance if needed.
2. Devices – FDA authorization is not required prior to the emergency use of an unapproved device. However, the manufacturer should be informed of the use in order to meet their IDE reporting requirements.

C. Consent Process. The Investigator should obtain consent from the patient or the legally authorized representative of the patient unless the PI and a physician who is not otherwise participating in the clinical investigation both make all of the following assurances, in writing:

1. Patient is in a life threatening situation;
2. All other available treatments are either unproven or unsatisfactory;
3. Patient is unable to give consent due to their medical condition ; and
4. There is no time to obtain consent from LAR.

If it is the Investigator's opinion that immediate use of the test article is necessary to save the patient's life and time does not permit seeking the opinion of a physician not otherwise involved, the Investigator should make the above determinations and proceed with the use. Within 5 working days after the use of the article, the Investigator must have the use of the test article reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

D. IRB Notification and Follow-up Report.

1. Notification. If possible, notify the IRB when a situation arises that calls for the emergency use of test article. The IRB will ask for confirmation that the situation meets the regulatory requirements for an emergency use. Information that may be requested includes the diagnosis, test article to be used, proposed use, and location of use. The IRB will acknowledge the intended use.

2. Follow-up Report. Within 5 days of the use of test article, the Investigator should submit a follow up report to the IRB that includes

- a. Name of test article used and date of IRB acknowledgement, if applicable
- b. Date, time and location of use
- c. Patient's diagnosis and outcome if known
- d. Any adverse events or unanticipated problems
- e. Copy of the signed informed consent. If consent was not obtained, provide the assurance letters from the Investigator and the independent physician as outlined in section C above.

3. IRB Review. The IRB will review the follow-up report to determine whether FDA regulatory requirements were met. If FDA regulations were not met, the matter will be handled according to IRB policies and procedures for non-compliance.

E. Protocol Submission. Within 30 days of first use, the Investigator must submit a New Protocol Submission in ARIA for review by the convened IRB.

Department: UAMS Institutional Review Board
Policy Number: 19.1
Section: Human Genetics Guidance
Effective Date: July 31, 2002
Revision Date: January 30, 2004

SUBJECT: Human Genetics

INTRODUCTION

Human genetic research involves the study of inherited human traits. Much of this research is aimed at identifying DNA mutations that can help cause specific health problems, developing methods of identifying those mutations in patients, and improving the interventions available to help patients address those problems. The identification of genetic mutations enables clinicians to predict the likelihood that persons will develop a given health problem in the future or pass on a health risk to their children. For many disorders, however, there will be a considerable time lag between the ability to determine the likelihood of disease and the ability to treat the disease.

The ethical issues raised by this scientific trend primarily concern the management of psychosocially potent personal genetic information. For researchers and IRBs, the major challenge in addressing these issues is the fact that genetic studies typically involve families; the research subjects involved in genetic studies are usually related to each other. As a result, research findings about individual subjects can have direct implications for other subjects, information flow between subjects is increased, and participation decisions are not made entirely independently. A second set of ethical issues emerges in cases in which the results of these studies are used to develop therapeutic interventions at the genetic level. Such concerns involve the special safety precautions and subject selection considerations required for gene therapy research.

Some of the areas described in this Section present issues for which no clear guidance can be given at this point, either because not enough is known about the risks presented by the research, or because no consensus on the appropriate resolution of the problem yet exists. Because of the uncertainties involved in genetic research, IRBs may not, for some time, be able to set clear standards for investigators. What IRBs can do, however, is ensure that investigators have thought through the factors that may affect the rights and welfare of human subjects (*e.g.*, risks to privacy, psychological risks, employment and insurance risks). IRBs should require investigators to explain their thoughts on these problems, how they plan to handle them, and how they plan to communicate them to subjects.

DEFINITIONS

Lod Score: An expression of the probability that a gene and a marker are linked.

Genotype: The genetic constitution of an individual.

Phenotype: The physical manifestation of a gene function.

Proband: The person whose case serves as the stimulus for the study of other members of the family to identify the possible genetic factors involved in a given disease, condition, or characteristic.

IRB CONSIDERATIONS

It may be useful to think of genetic research as being carried out on a continuum comprising four stages:

1. Pedigree studies (to discover the pattern of inheritance of a disease and to catalog the range of symptoms involved);
2. Positional cloning studies (to localize and identify specific genes);
3. DNA diagnostic studies (to develop techniques for determining the presence of specific DNA mutations); and
4. Gene therapy research (to develop treatments for genetic disease at the DNA level.

Unlike the risks presented by many biomedical research protocols considered by IRBs, the primary risks involved in the first three types of genetic research are risks of social and psychological harm, rather than risks of physical injury. Genetic studies that generate information about subjects' personal health risks can provoke anxiety and confusion, damage familial relationships, and compromise the subjects' insurability and employment opportunities. For many genetic research protocols, these psychosocial risks can be significant enough to warrant careful IRB review and discussion. The fact that genetic studies are often limited to the collection of family history information and blood drawing should not, therefore, automatically classify them as "minimal risk" studies qualifying for expedited IRB review.

Pedigree Studies. When investigators attempt to document and study the natural history of an inherited disease, condition, or characteristic, they do so by identifying individual members of families presenting the disease, condition, or characteristic and obtaining information about them and the other members of their family. The result is a pedigree analysis, which, in addition to tracing the natural history of a disease and documenting the range of symptoms involved, may also reveal information about family members that individual members may not have known about previously (e.g., the existence of previously unknown relatives or the presence of stigmatizing diseases, such as mental illness). It may also reveal information about the likelihood that individual members of the family either are carriers of genetic defects or will be affected by the disease.

Subject Recruitment and Retention. The familial nature of the research cohorts involved in pedigree studies can pose challenges for ensuring that recruitment procedures are free of elements that unduly influence decisions to participate. The very nature of the research exerts pressure on family members to take part, because the more complete the pedigree, the more reliable the resulting information will be. For example, revealing who else in the family has agreed to participate may act as an undue influence on an individual's decision, as may recruiting individuals in the presence of other family members. (Both would also constitute a breach of confidentiality. The problem of confidentiality will be dealt with later in this Section.)

Recruitment plans, some of which are described here, can attempt to address these problems; each approach has its own strengths and weaknesses. One strategy is to use the proband as the point of contact for recruiting. This approach insulates families from pressure by the investigator, but presents the risk that the proband may be personally interested in the research findings and exert undue pressure on relatives to enroll in the study. Furthermore, the proband may not want to act as a recruiter for fear that other family members will then know that he or she is affected by the

disease. Another approach is direct recruitment by the investigator through letters or telephone calls to individuals whose identity is supplied by the proband. Direct recruitment by the investigator may, however, be seen as an invasion of privacy by family members. A third approach is to recruit participants through support groups or lay organizations. Adopting this strategy requires investigator and IRB confidence that these organizations will be as scrupulous in their own efforts to protect subjects as the investigator would be. A fourth possibility is to contact individuals through their personal physicians. Prospective subjects contacted by their physician may, however, feel that their health care will be compromised if they do not agree to participate. In the end, the IRB must ensure that the recruitment plan minimizes the possibility of coercion or undue influence (38CFR16.116).

In contrast to inappropriate pressure placed on prospective participants to join the study is the possibility that a subject may agree to participate out of a misguided effort to obtain therapy. The purposes of the research and how subjects will or will not benefit by participation must be clearly explained. (See discussion below on informed consent).

Investigators and IRBs need to consider each of these concerns in arriving at a recruitment strategy that protects these various interests.

Defining Risks and Benefits. Potential risks and benefits should be discussed thoroughly with prospective subjects. In genetic research, the primary risks, outside of gene therapy, are psychological and social (referred to generally as "psychosocial") rather than physical. IRBs should review genetic research with such risks in mind.

Psychological risk includes the risk of harm from learning genetic information about oneself (*e.g.*, that one is affected by a genetic disorder that has not yet manifested itself). Complicating the communication of genetic information is that often the information is limited to probabilities. Furthermore, the development of genetic data carries with it a margin of error; some information communicated to subjects will, in the end, prove to be wrong. In either event, participants are subjected to the stress of receiving such information. For example, researchers involved in developing presymptomatic tests for Huntington Disease (HD) have been concerned that the emotional impact of learning the results may lead some subjects to attempt suicide. They have therefore asked whether prospective participants should be screened for emotional stability prior to acceptance into a research protocol.

Note that these same disclosures of information can also be beneficial. One of the primary benefits of participation in genetic research is that the receipt of genetic information, however imperfect, can reduce uncertainty about whether participants will likely develop a disease that runs in their family (and possibly whether they have passed the gene along to their children). Where subjects learn that they will likely develop or pass along the disease, they might better plan for the future.

To minimize the psychological harms presented by pedigree research, IRBs should make sure that investigators will provide for adequate counseling to subjects on the meaning of the genetic information they receive. Genetic counseling is not a simple matter and must be done by persons qualified and experienced in communicating the meaning of genetic information to persons participating in genetic research or persons who seek genetic testing.

Social risks include stigmatization, discrimination, labelling, and potential loss of or difficulty in obtaining employment or insurance. Changes in familial relationships are also social ramifications of genetic research. For example, an employer who knew that an employee had an 80 percent chance of developing HD in her 40s might deny her promotion opportunities on the calculation that their investment in training would be better spent on someone without this known likelihood. Of course, the company may be acting irrationally (the other candidate might be hit by a car the next day, or have some totally unknown predisposition to debilitating disease), but the risk for our subject of developing HD is real, nonetheless. One problem with allowing third-parties access to genetic information is the likelihood that information, poorly understood, will be misused. Likewise, an insurer with access to genetic information may be likely to deny coverage to applicants when risk of disease is in an unfavorable balance. Insuring against uncertain risks is what insurance companies do; when the likelihood of disease becomes more certain, they may refuse to accept the applicant's "bet."

Privacy and Confidentiality Protections. Special privacy and confidentiality concerns arise in genetic family studies because of the special relationship between the participants. IRBs should keep in mind that within families, each person is an individual who deserves to have information about him- or herself kept confidential. Family members are not entitled to each other's diagnoses. Before revealing medical or personal information about individuals to other family members, investigators must obtain the consent of the individual.

Another problem that arises in genetic family studies that is also common in other areas of research involving interviews with subjects is the provision by a subject of information about another person. In pedigree studies, for example, the proband or other family member is usually asked to provide information about other members of the family. The ethical question presented by this practice is whether that information can become part of the study without the consent of the person about whom the data pertains. While no consensus on this issue has yet been reached, IRBs may consider collection of data in this manner acceptable, depending on the nature of the risks and sensitivities involved. It may be helpful, for example, to draw a distinction between information about others provided by a subject that is also available to the investigator through public sources (*e.g.*, family names and addresses) and other personal information that is not available through public sources (*e.g.*, information about medical conditions or adoptions).

IRBs should require investigators to establish ahead of time what information will be revealed to whom and under what circumstances, and to communicate these conditions to subjects in clear language. For example, if the pedigree is revealed to the study participants, family members will learn not only about themselves but about each other. The possibility that family members who did not participate might also learn of the pedigree data should not be overlooked. Subjects should know and agree ahead of time to what they might learn (and what they will not learn), both about themselves and others, and what others might learn about them. One approach would be never to reveal the pedigree to participating subjects. Many investigators record their pedigrees using code numbers rather than names. IRBs should note, however, that when a study involves a rare disease or a "known" family, the substitution of numbers for names does not eliminate the problem.

Even where the protocol calls for providing certain information to subjects, participants in genetic studies should be given the option of not receiving genetic information about themselves or others that they do not wish to receive. In genetic research, the potential for psychosocial harm accruing to persons who express a desire not to receive information gained through the study and the uncertainties surrounding the disease-predictive value of the early phases of contemporary genetic research is felt to outweigh benefits of required disclosure. (A possible exception involving circumstances where early treatment of genetically-linked disease improves prognoses is discussed in the section on identifying and deciphering genes, below.)

Data must be stored in such a manner that does not directly identify individuals. In general, except where directly authorized by individual subjects, data may not be released to anyone other than the subject. An exception to requiring explicit authorization for the release of data may be secondary research use of the data, where the data are not especially sensitive and where confidentiality can be assured. IRBs should exercise their discretion in reviewing protocols that call for the secondary use of genetic data. Furthermore, when reviewing a consent documents, IRBs should note agreements made by investigators not to release information without the express consent of subjects. Subsequent requests for access to the data are subject to agreements made in the consent process. For studies involving socially sensitive traits or conditions, investigators might also consider requesting a certificate of confidentiality (see IRB policy 13.1).

Informed Consent. The information presented to subjects in the informed consent process should be as specific as possible. Subjects should be told both the known risks, as well as the uncertainty surrounding the risks of participation. Among the uncertainties is the likelihood that useful information will result from the study (it may not). Prospective participants often come into genetic studies with unrealistic expectations of how they will benefit from the study, and without an appreciation of low-probability risks that are not well-understood by anyone. To the extent possible, unrealistic expectations should be dispelled in the informed consent process.

The provision of relevant information should take place as a thoughtful discussion with prospective subjects. Through this process, subjects should be informed:

1. About the kind of information they will be provided (*e.g.*, that they will receive only information the investigator feels is significant and reliable, or that no genetic information will be provided) and at what point in the study they will receive that information;
2. That they may find out things about themselves or their family that they did not really want to know, or that they may be uncomfortable knowing;
3. That information about themselves may be learned by others in their family
4. Whether information they learn or information generated about them during the study may compromise their insurability;

5. That actions they may take as a result of their participation may expose them to risks (e.g., submitting insurance claim forms for reimbursement for costs of genetic counseling or procedures whose costs are not covered by the protocol);
6. About what assurances can be given to protect confidentiality and what lack of assurance can be given;
7. About the rights they retain and the rights they must give up regarding control over what can be done with tissue they donate (e.g., blood samples);
8. What the consequences of withdrawal from the study will be; and
9. Of any costs associated with participation (including, for example, the cost of genetic and/or psychological counseling, if those costs will not be covered by the investigator or the institution).

Information should be given to subjects in clear language, suitable to their age, cultural background, and physical and mental capabilities. Accommodations should be made for persons with learning disabilities (as distinguished from persons who suffer diminished mental capacity). The consent process should take place in the subject's native language, through an interpreter, if necessary; consent documents should be translated into the subject's native language. The IRB should satisfy itself that great care will be taken by the investigator to ensure that prospective subjects fully understand the risks and benefits involved in participation.

Disposition of DNA Samples. When tissue samples are to be collected for later DNA analysis, numerous issues must be addressed by investigators and IRBs. Primary among them are through what mechanism samples should be collected, who can have access to the samples and for what purposes, who owns the DNA, and how incorrect genetic information (due, for example, to faulty laboratory analysis) can be corrected. The American Society of Human Genetics' Ad Hoc Committee on DNA Technology has published a set of Points to Consider on DNA banking and DNA analysis (1987), with which IRBs may wish to acquaint themselves. While not all of the Society's recommendations may be directly applicable to the IRB's concerns, it is worth noting the importance the Society places on appropriate counseling and limited access to familial genotypes.

The genetic information (and tissue samples, where applicable) collected under a research protocol are of continuing importance to the families involved in the research. An important question for IRBs to consider is what will happen to the data (and samples) when funding for the research ends. Particular attention should be paid to protecting the confidentiality of the data and obtaining consent from the participants for any use of the data (and samples) that is not strictly within the original uses to which the participants agreed.

Withdrawal from Participation. Attention should be paid to subjects' rights when they decide to withdraw from participation in the study. The federal regulations clearly require that subjects be free to withdraw from participation without penalty or loss of

benefits to which they are otherwise entitled [38 cfr 16.116(a)(8)]. What the regulations do not address, however, is how to treat data or tissue samples obtained from subjects who subsequently withdraw from the study. A similar question was addressed by the California Supreme Court in the Moore case [*John Moore v. The Regents of the University of California* (1990)]. While *Moore* constitutes binding legal authority only in California and has not, as of this writing, been adopted in other jurisdictions, the court's findings may be helpful for exploring possible approaches to handling the treatment of data and tissue samples when a subject withdraws from a genetic study.

In *Moore*, the California Supreme Court held that cell lines established from a donated sample are not the property of the person who donated the sample. Extrapolating to the broader context of genetic research generally, the underlying principle would be that withdrawal releases the subject from providing further information or tissue samples, and perhaps requires the removal of the subject's identity from all research records, but does not require the investigator to eliminate the resulting data from the study or to destroy the cell line.

In pedigree studies, for example, investigators may respond to a request to withdraw by removing all information about that person and his or her spouse and children from the pedigree, but it is not clear that removal of the information is required by the human subjects regulations or any other legal principle.

Secondary Use of Tissue Samples. Where a new study proposes to use samples collected for a previously conducted study, IRBs should consider whether the consent given for the earlier study also applies to the new study. Where the purposes of the new study diverge significantly from the purposes of the original protocol, and where the new study depends on the familial identifiability of the samples, new consent should be obtained.

Vulnerable Populations. IRBs should ensure that the investigator conduct the research with sensitivity to the specific mental and physical manifestations of the particular disorders being investigated. Depending on the disease, and, therefore, the likely presenting population, investigators should be prepared to communicate effectively and with sensitivity with persons who have physical limitations (e.g., deafness or blindness), learning disabilities, cognitive impairments, or any other life circumstance that may affect their participation (e.g., severe pain).

The nature of genetic research raises some special concerns when the research will involve children, physically or cognitively impaired persons, older persons, or any subject population likely to have special needs. Not only must the IRB ensure that their participation is fully voluntary and informed, IRBs must also be sure to evaluate the risks and benefits of the research as they apply to these special populations. The risk of participation for an adult differs from that of children; persons who suffer from diminished mental capacities may be subject to different risks than persons who do not. If children will be involved in the research, IRBs should seriously consider consulting with experts in child development and others knowledgeable about risks to children and families. Similarly, if physically or cognitively impaired persons will be involved in the research, IRBs should consider consulting with experts who can advise them on the special concerns their participation raises. Where applicable, 45 CFR 46 Subparts B, C, and D (pertaining to women, fetuses, prisoners, and children) must be followed. The involvement of children in genetic research raises many concerns,

including pressure brought by family members on the child to participate and the potential for harm that may result from disclosure of genetic or incidental information. Even seemingly harmless research may actually present serious risks of harm to children. For example, interviewing children for genetic research on psychological disorders, such as schizophrenia or depression, or on alcoholism may inadvertently convey information about family members (the child may well wonder why he or she is being asked about alcoholism in the family) or cause self-doubt or stigmatization on the part of the child. Furthermore, disclosures of data to third-parties may result in children being labelled or stigmatized as, for example, potential alcohol abusers. IRBs must look carefully at both the questions that will be asked of children and the information that will be directly conveyed to them to determine whether the research involves more than minimal risk. The advisability of including children in studies of untreatable, fatal disorders such as HD has been strongly questioned [MacKay (1984), p. 3].

IRBs should also consider the mental capacities of participants in genetic research. In some diseases, such as Alzheimer Disease, patients will suffer loss of mental capacity over a period of time. In addition, it is possible that a family member might be comatose or legally incompetent for reasons unrelated to the disease under study. Special attention should be paid to methods of ensuring voluntary consent by the subject or the subject's legally authorized representative [38 cfr 16.102(c), 38 cfr 16.116]. Under the regulations, a "legally authorized representative" is defined as "an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research" [38CFR16.102(c)]. IRBs should pay particular attention to state and local laws relating to persons authorized to give permission for participation in research on behalf of prospective subjects, noting that such "proxy" consent to participation in research that does not involve a direct medical benefit may differ from consent to receive medical treatment. Where possible, the subject's assent should be sought; his or her dissent should be honored.

In appropriate circumstances the IRB might consider granting waivers of consent or alteration of the consent process. [See MacKay (1984), pp. 3-4, and Levine (1986).] The federal regulations allow for waivers or alterations in the consent process where the IRB finds that: (1) the research involves no more than minimal risk; (2) the waiver or alteration will not adversely affect the rights and welfare of the subject; (3) the research could not practicably be carried out without the waiver or alteration; and (4) whenever appropriate, the subjects will be provided with additional pertinent information after participation [38CFR16.116(d)]. Again, IRBs should carefully consider whether the research qualifies as "minimal risk."

Publication Practices. One final issue involving consent is the publication of research data. The publication of pedigrees can easily result in the identification of study participants. Where a risk of identification exists, participants must consent, in writing, to the release of personal information. Various authors have noted the problem of obtaining consent for the publication of identifying data, and have recommended that consent to the publication be obtained immediately prior to the publication, rather than as part of the consent to treatment or participation in research. [See, e.g., Rost and Cohen (1976) and Murray and Pagon (1984).] It is worth noting, however, that to address this concern, IRBs must also resolve the following questions: Who determines the risk of identification, and on what grounds? Who are defined as participants (is it

everyone listed in the pedigree, some of whom have been contacted by investigators, some of whom have had information about them provided by a family member)?

While IRBs must be careful to avoid inappropriate restrictions on investigators' research publications, some evaluation of publication plans is important as part of the IRB's overall interest in preserving the confidentiality of research subjects. One approach for investigators to use in evaluating their publication plans might be to work in a step-wise fashion: First, is publication of the pedigree essential? If publication of the pedigree or other identifying data (e.g., case histories, photographs, or radiographs) is essential, can some identifying data be omitted without changing the scientific message? (The practice of altering data — such as changing the birth order and gender — is controversial, and no clear professional consensus yet exists as to whether this is an appropriate practice.) Finally, if the pedigree must be published, and if identifying data cannot be omitted in an appropriate manner without changing the scientific message, subjects must give their permission for publication of data that may reveal their identity.

Another concern about publication is the potential for publicity of the research results, and the exposure of participants to such publicity. Consent by individuals to such publicity does not resolve the question. Because genetic research involves families, the agreement of one subject to participate in releases of information to the media (including interviews and the like) has significant implications for other members of the family, particularly where the research is of a sensitive nature. IRBs should ensure that the investigator has addressed this possibility.

Expedited Review and Exemption from Review. The expedited review process is available for minimal risk research where the research activity is limited to one of a specified category (as published in the *Federal Register*), including the provision of blood samples [38CFR16.110; *Federal Register* 46 (January 26, 1981): 8392]. In genetic studies that involve a blood draw, the additional psychosocial risks are likely to raise the risk beyond the "minimal risk" level allowable for expedited review. When an expedited review is requested, IRBs should review the question of minimal risk carefully.

With respect to exemption from review, the development of a pedigree through interviews with family members is likely to create identifying information, even where individuals will not be identified. Such research would not, therefore, qualify for exemption from review under the federal regulations [38 cfr 16.101(b)(2)].

Identifying and Deciphering Genes. Research focusing on identifying the specific genetic component of a particular disease, condition, or characteristic relies upon DNA analysis of tissue samples taken from the members of families in which the condition appears. Many issues raised by pedigree analysis are relevant to this stage of research as well: pressure or coercion in recruiting subjects; informing prospective subjects of the possible harms; minimizing psychological harm through counseling and education; protection of confidentiality (which is particularly problematic when family members constitute the subject population); control over the use of DNA tissue samples; and protecting particularly vulnerable persons, all of which were discussed in the previous section. Additional issues include: determining when the data constitute "information;" additional risks presented by this stage of research (e.g., the possibility of incidental findings); and possible conflicts between subjects' rights and investigators' duties with respect to revealing the results of the study to subjects [*i.e.*,

telling subjects whether they (or their relatives) carry the defect, and the meaning of their status with respect to the likelihood of suffering from the disease or passing it along to their children].

Access to Data: Interim Findings. An issue that must be resolved prior to beginning any genetic study is who will have access to the data and the stage in the research at which they will have access. The issue of information transfer is vitally important in all genetic research, but particularly in the first three stages of investigation. A crucial question investigators and IRBs must address is whether (and which) interim findings will be communicated to subjects.

Experts disagree about whether interim or inconclusive findings should be communicated to subjects, although most agree that they should not (that only confirmed, reliable findings constitute "information"). Persons who oppose revealing interim findings argue that the harms that could result from revealing preliminary data whose interpretation changes when more precise or reliable data become available are serious, including anxiety or irrational — and possibly harmful — medical interventions. They argue that such harms are avoidable by controlling the flow of information to subjects and limiting communications to those that constitute reliable information. MacKay (1984), writing about the development of genetic tests, argues against revealing interim findings, contending that preliminary results do not yet constitute "information" since "until an initial finding is confirmed, there is no reliable information" to communicate to subjects, and that "even...confirmed findings may have some unforeseen limitations" [p. 3]. He argues that subjects should not be given information about their individual test results until the findings have been confirmed through the "development of a reliable, accurate, safe and valid presymptomatic test" [pp. 2-3; see also Fost and Farrell (1990)]. Others have argued that all interim results should be shared with subjects, based on the principle of autonomy — that subjects have a right to know what has been learned about them.

These arguments are equally relevant at any of the first three stages of genetic research. IRBs should consider these arguments, weighing the possible harms and benefits. Investigators should determine, prior to initiation of the study, the point at which the data will be considered solid enough to be constitute information that should be provided to subjects. Investigators should further consider coding the data and separating the research records from individuals' medical records, so that neither the investigators nor the subjects may gain access to them [MacKay (1984), p. 3].

Reilly (1980) suggests that IRBs develop general policies governing the disclosure of information to subjects, to help make these determinations. He suggests that at least the following three factors be considered: "(1) the magnitude of the threat posed to the subject, (2) the accuracy with which the data predict that the threat will be realized, and (3) the possibility that action can be taken to avoid or ameliorate the potential injury" [p. 5]. IRBs should ask investigators to define three categories of disclosure: (1) "findings that are of such potential importance to the subject that they *must* be disclosed immediately;" (2) "data that are of importance to subjects..., but about which [the investigator] should exercise judgment about the decision to disclose....[i]n effect, these are data that trigger a duty to consider the question of disclosure;" and (3) "data that do *not* require special disclosure" [pp. 5, 12].

IRBs should consider whether the investigator's approach appropriately balances the risks and benefits involved in providing access to the data. Subjects should be told, as part of the consent process, whether, when, and what information they will receive. Any disclosures of genetic information should be accompanied by appropriate counseling by trained genetic counselors. However the IRB resolves this question, investigators should explain to prospective subjects the basis according to which they will decide which data will be disclosed to whom, and when those disclosures will be made.

Access to Data: The Subjects' "Right Not to Know." Subjects generally retain the right not to receive information about the results of a study that reveals their genetic status. A possible exception involves circumstances where early treatment of genetically-linked disease could improve the subject's prognosis. In such circumstances, investigators may have a duty to inform the subject about the existence of the genetic defect and to advise him or her to seek medical advice. [See, e.g., Andrews (1991).] (As of this writing, a legal duty of investigators to inform subjects about the existence of genetic defects has not been firmly established.)

Furthermore, the existence of a genetic defect that is linked to disease may have important implications for family members; can or should the confidentiality of subjects' data be compromised to allow other family members to be warned? The President's Commission (1983), addressed this question with respect to information generated from genetic screening. The Commission's discussion may also be relevant to information obtained as the result of genetic research, at stages that precede genetic screening. The Commission concluded that:

[the] ethical duty of [providing confidentiality] can be overridden only if several conditions are satisfied: (1) reasonable efforts to elicit voluntary consent to disclosure have failed; (2) there is a high probability both that harm will occur if the information is withheld and that the disclosed information will actually be used to avert harm; (3) the harm that identifiable individuals would suffer would be serious; and (4) appropriate precautions are taken to ensure that only the genetic information needed for diagnosis and/or treatment of the disease in question is disclosed [p. 44].

The Commission further advised that, to the extent possible, persons undergoing genetic screening should be asked to consent in advance to the disclosure of genetic information to relatives in the event that such useful information is discovered [pp. 43-44]. Whether a legal duty exists to warn relatives of possible genetic defects has not yet been established. [See Robertson (1992), pp. 92-94.]

Access to Data: Incidental Findings. IRBs should also ensure that investigators adequately deal with how they will handle incidental findings; that is, what will be done with genetic information that is learned during the course of the study that does not directly relate to the research. For example, in intergenerational pedigree analyses, questions of paternity or parentage can come up. DNA analysis will reveal information indicating that an individual's biological parents are not who he or she thought they were; blood typing may reveal similar information. DNA analysis may also reveal information about diseases or conditions other than the disease or condition under study. Prospective subjects should be informed during the consent process that the

discovery of such information is possible. Appropriate counseling should be provided to educate subjects about the meaning of the genetic information they have received, and to assist them in coping with any psychosocial effects of participation.

Access to Data: Secondary Use. Investigators should also address secondary use of research data (e.g., by other investigators, or by themselves for different research purposes). Where secondary uses can be foreseen, consent to the use should be sought. Express consent to access to data for secondary uses should be obtained for sensitive data and for circumstances under which confidentiality cannot be assured.

Research on Genetic Testing

Testing individuals to determine the presence of genetic defects falls into four basic categories:

1. Testing newborns to detect serious genetic diseases. The screening of newborns is considered to be of value to the extent that infants can benefit from early intervention. In the case of phenylketonuria (PKU), for example, a genetic disease for which a test is available, a special diet can prevent most of the serious effects of the disease (which include brain damage).
2. Testing for carrier status to identify individuals whose genetic makeup includes a gene or a chromosome abnormality that might have serious health implications for their children. Carrier testing is usually requested by adults who have some indication that they may be carriers of a genetically-linked disorder (e.g., because they are members of an ethnic group known to have a high incidence of the disorder, because a relative has a genetic disease, or because a spouse knows that he or she is a carrier). Testing will provide such persons information about the risks of being a carrier and of passing on either the disease or abnormal genes to their children. For recessive diseases, for example, a carrier will pass on the disease to their children only if the other biological parent is also a carrier of the same defective gene.
3. Prenatal testing is aimed at detecting the presence of genetic or chromosomal abnormalities in fetuses. Examination of the genetic makeup of the fetus is done through amniocentesis, chorionic villi sampling, blood sampling from the umbilical cord and blood samples from the mother.
4. Risk assessment testing (sometimes referred to as "presymptomatic testing") determines the probability that a person will develop a genetically-linked disease at some point in the future. The degree of certainty with which risk assessment tests can predict the likelihood of disease differs depending on the disease. For some diseases the actual gene has been located, making tests more accurate than for diseases for which only a marker has been found. Further, some markers are more closely linked to the gene than are others, thereby having a more predictive quality than others.

Protocols involving genetic testing raise somewhat different issues, depending on whether the tests are under development or are already established as reliable. IRBs are concerned with research aimed at developing genetic tests.

The ethical issues raised by the various kinds of genetic testing largely concern the concept of autonomy or self-determination. Before consenting to undergo genetic tests, whether new tests that are being developed, or already-established genetic

tests, subjects should fully understand what it is they are going to learn about themselves, what they are *not* going to learn about themselves, and how reliable the information will be. Subjects must have information on which to base their decisions whether or not to go ahead with the testing. When the research involves the development of a genetic test, however, the uncertainties involved make the consent process problematic: How does one adequately alert subjects to the psychosocial risks of testing when the point of the study is to try to help define those risks? Research on pre-test education in effect experiments with the informed consent process. Can subjects consent to research knowing that one of the risks is that they may not be adequately informed about what they are agreeing to? The federal regulations allow IRBs to approve consent procedures that do not include or that alter some or all of the elements of informed consent; one of the requirements is that the research must involve no more than minimal risk [38 cfr 16.116(d)]. Research that involves deliberate withholding of information or deception is reviewed pursuant to those provisions. Even where it is permitted, purposeful nondisclosure of pertinent information is allowed only to the extent necessary to conduct the study (*e.g.*, when disclosure of the information would affect the outcome of the study). Furthermore, subjects must consent to the nondisclosure; that is, they must be told that there is some relevant information about the study that they will not be told prior to consenting to participate (Levine 1986, p. 117).

In genetic testing research, however, the nondisclosure is not purposeful; rather, the nature and extent of the psychosocial risks involved is simply unknown. IRBs must look carefully at such studies to ensure that subjects are adequately protected. Investigators should provide the IRB their assessment of unknown risks. Subjects should be informed, in clear, understandable language, of the possibility of undisclosed risks, including any information the investigator has about their possible nature and extent.

Someone who possesses the appropriate medical and counseling expertise with which to explain the meaning of the test results should communicate research results to the subject. That person should ensure that the subject comprehends the information that has been provided to him or her, regardless of the time that may be involved. Furthermore, it may be appropriate to provide counseling not just for the subjects themselves, but also for their families. Consent to involve family members, should the need arise, should be sought as part of the consent to be tested.

Smurl and Weaver (1987) have developed a set of proposed ethical guidelines for the clinical testing of risk assessment tests for HD. IRBs reviewing investigations of risk assessment genetic tests should find their recommendations helpful. Many of their recommendations follow the arguments set forth in the discussions in the Guidebook on pedigree analysis and identifying and deciphering genes.

The misuse of genetic information due to misunderstanding its meaning is a risk faced by all participants in genetic research. Investigators can minimize this risk by working to educate not only subjects, but also the medical profession and the public about genetic testing. The term "diagnostic" is often used, but the term does not really apply. Genetic tests identify risks rather than "diagnose" the presence of disease. Discrimination in employment or in obtaining insurance are two areas that are of major concern, particularly where the genetic trait is one that is thought to indicate a predisposition to diseases or conditions caused by exposure to environmental agents.

Significant damage has been done by, for example, misperceptions about what it means to be a carrier of sickle cell trait. Persons who carry the sickle cell trait have been denied jobs or have been otherwise discriminated against. Education, together with protecting subjects against disclosure of genetic information, can help minimize the risk of discrimination.

Gene Therapy Research

Gene therapy attempts to treat genetic disease by altering an individual's cells. Gene therapy can involve treatment of either somatic (nonreproductive) cells or germline (reproductive) cells. Genetic changes made to somatic cells affect only the individual who has received treatment; genetic changes made to germline cells may be passed on to the patient's descendants. A distinction must be made between gene therapy designed to treat or eliminate disease or serious medical, psychological, or behavioral conditions (e.g., cystic fibrosis), and the "improvement" of human characteristics (e.g., height).

Gene therapy techniques involving somatic cells are aimed at curing genetic disease in individuals by inserting properly functioning genes into the individual's somatic cells [Walters (1989), pp. 220-221]. The approach for making genetic changes to germ line cells is to add new DNA to early embryos in an attempt to change the genes not only in the individual, but also the genes passed on to his or her progeny. Walters (1989) has described the process as follows:

In studies involving mice, for example, genes have been added to one-cell mouse embryos after the sperm had penetrated the egg but before the genetic material from the sperm and egg are joined within the same nucleus. If the experiment is successful, these added genes are then adopted by the embryo. As the embryo grows and the number of embryonic cells increases, the added genes become part of every new embryonic cell. Later, when the sperm or egg cells of the mouse develop, the added genes are included in approximately half of these reproductive cells. Thus, when the mouse reproduces, some of its progeny receive the added genes, and so on through the generations [p. 221].

After being reviewed and approved by the IRB and the local institutional biosafety committee, gene therapy protocols for research conducted at or sponsored by an institution that receives any support for recombinant DNA research from NIH must be reviewed by the Recombinant DNA Advisory Committee (RAC) at NIH. At present, the RAC will consider human somatic cell gene therapy protocols, but not germline cell gene therapy protocols. The process of review is as follows: The Human Gene Therapy Subcommittee conducts a public review of the protocol, then submits its recommendation to the RAC; if the RAC approves the protocol, it is forwarded to the director of NIH for final approval.

The RAC, through a Points to Consider Subcommittee, has established "Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA into Human Subjects." Among the ethical concerns that investigators must address are subject selection, informed consent, and privacy and confidentiality. Investigators must also justify the use of recombinant DNA techniques against alternative methodologies and delineate the risks and benefits of the research. A summary of the Points to Consider follows; IRBs would be well-served to follow a

similar line of inquiry when reviewing protocols that involve the transfer of recombinant DNA into human subjects.

Department: UAMS Institutional Review Board
Policy Number: 20.1
Section: Questions, Concerns, Suggestions and Complaints
Effective Date: September 1, 2007
Revision Date: January 24, 2011

SUBJECT: Questions, Concerns, Suggestions and Complaints

Purpose: This policy provides guidelines for individuals and offices on campus to present questions, concerns, and suggestions/complaints regarding the human subjects' protection program on campus.

Policy: As a general rule, the IRB Office Staff, IRB Chair, IRB Director, Office of Research Compliance, IRB Executive Committee, and the Vice Chancellors for Research and Institutional Compliance are appropriate members for addressing issues concerning the human subjects' protection program.

Procedure:

General Questions, Suggestions, and Concerns:

No specific order for addressing an issue is required; however, the following outline is a suggested path to follow until the issue is addressed. Response should be within two weeks to general questions, suggestions and concerns. If the question is not addressed within two weeks, move to the next level until you have reached one of the Vice Chancellors listed. Responses from the members can be written or verbal; however, this method is not an alternative method or substitute for the IRB approval process outlined in these policies. Phone numbers can be found on the IRB website:

1. IRB Office Staff
2. IRB Chair
3. IRB Director
4. Office of Research Compliance
5. IRB Executive Committee
6. Vice Chancellor for Research or Institutional Compliance

Specific, Significant Concerns or Issues that potentially involve risk

Some situations or concerns may require immediate action or a response from the institution. Examples are situations that involve one of the following: potential harm (physical or other) to subjects and/or study staff; potential high regulatory risk; potential high risk to institutional resources or operations; potential civil or criminal violations; indications that study disorganization may potentially jeopardize data integrity or subject safety. Initial reports of this kind of situation or concern should be made simultaneously to the IRB Chair, IRB Director, and the Office of Research Compliance. If the IRB or the ORC is a party to the concern in question, the office that is not involved should be notified, along with a simultaneous notification to the appropriate Vice Chancellor