Human Research Advisory Committee
Institutional Review Board

Investigators Handbook for Human Studies

UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES

ARKANSAS CHILDREN'S HOSPITAL

CENTRAL ARKANSAS VETERANS HEALTHCARE SYSTEM

REVISION DATE: MAY 21, 2003
Version Number 15
REVISIONS 5/21/2003

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Description of Changes:
- Updated Revision Date and Version Number.

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Description of Changes:
- Included new revisions in the 05/21/2003 Revisions Page.

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Description of Changes:
- Updated Table of Contents.

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Description of Changes:
- Page 1: Revised IRB Meeting Schedule and Submission Deadlines information.
- Page 6: Revised General Clinical Research Center (GCRC) information.
- Pages 1-19: Added new Revision Date of 5/21/2003 throughout entire Protocol Submissions section.
  Changed HRAC to IRB throughout entire Protocol Submissions section.
## REVISIONS 5/21/2003

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### Description of Changes:
- Removed the following HRAC Submission Forms because they are no longer used:
  - HRAC Protocol Form
  - Drug/Device Form
- The Request For Pharmacy Cost Impact UAMS Hospital and Clinics Form is now page 2.

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### Description of Changes:
- Added link to revised [HRAC Continuing Review Form](#).
- Added link to [Directions for Completing the HRAC Continuing Review Form](#).

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### Description of Changes:
- Added ACH web site.
- Updated Fax Number for ACH Research Pharmacy.
- Added ACHRRI web site.
- Added CAVHS web site.
- Added UAMS web site.
- Added GCRC web site.
- Added IRB web site.
- Added Office for Clinical Trials web site.
- Added Office of Research Compliance web site.
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**Description of Changes:**
- Revised Guidelines for Blood Draws using guidelines approved by Arkansas Children’s Hospital’s Patient Care Committee in September 2002.
# REVISIONS 4/28/2003

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**Description of Changes:**
- Changed HRAC to IRB
- Changed VA to CAVHS
- Collaborating With Other Institutions (Added CAVHS and ACHRI)
- Grant Initiated Research (Added grants information.)
- Changed the section The HRAC Submission Packet to Committee Approvals
- Added IRB Protocol Submissions Requirements Using ARIA
- Added How to Submit A New Behavioral Study Protocol
- Added How to Submit a New Biomedical Study Protocol

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**Description of Changes:**
- Added ARIA and HIPAA

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**Description of Changes:**
- Added links to the ACHRI Grant Submissions Forms
- Added links to the Industry Sponsored /Clinical Trials /Pharmaceutical Studies Forms
- Delete paper forms

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**Description of Changes:**
- Revised ACH phone numbers
- Revised ACHRI phone numbers
- Revised CAVHS phone numbers
- Revised UAMS phone numbers
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INTRODUCTION

WELCOME TO THE HUMAN RESEARCH ADVISORY COMMITTEE

The Human Research Advisory Committee (HRAC) is the body designated by the University of Arkansas for Medical Sciences (UAMS), Arkansas Children’s Hospital (ACH), the Central Arkansas Veteran’s Healthcare System (CAVHS), the Arkansas State Health Department (ASHD), and the Arkansas State Hospital (ASH) to approve the initiation of, and conduct periodic reviews of biomedical and behavioral research involving human subjects. This committee operates according to Federal, State, Institutional and Good Clinical Practices (GCP) guidelines. The IRB also recognizes the tripartite International Code of Harmonization (ICH).

AUTHORITY AND RESPONSIBILITY OF THE IRB

The IRB operates under a Federal Wide Assurance (FWA). This is an agreement between the HRAC and the Department of Health and Human Services (DHHS), which outlines the responsibilities of the HRAC for upholding the ethical principles regarding research involving human subjects. These principals are outlined in the report of the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research entitled, Ethical Principles and Guidelines for the Protection of Human Subjects of Research (known as the “Belmont Report”).

Research activities are overseen for DHHS by the Office for Human Research Protections (OHRP). Studies involving veterans are also overseen by the Office for Research Compliance and Assurance (ORCA). Other agencies that the IRB report to include; the Food and Drug Administration (FDA), the Office of Research Integrity (ORI), institutional officials, sponsors, and funding agencies.

Normally, the IRB will agree to serve as the institutional review board for other institutions only if a staff member or faculty appointee of UAMS, ACH, CAVHS, ASHD, or ASH is involved as a principle or sub-investigator. However, the HRAC will serve any state agency for a specific protocol by written request. Appropriate agreements between the committee and the requesting institution will be required.

The IRB was established to protect the rights and welfare of human participants in research conducted under the auspices of the UAMS, ACH, CAVHS and other state agencies. The HRAC has the authority to approve, disapprove or require modifications of research activities that fall within its jurisdiction. The HRAC may work in conjunction with other university or institutional committees; however, it reviews research projects independently based upon the principle that human participants will be adequately protected.
IRB MEMBERS

The Vice Chancellor for Academic Affairs and Sponsored Research at UAMS appoints members of the IRB, including the Chair. Appointments are for four-year periods. Federal requirements mandate that the HRAC must have at least five members of varying backgrounds to promote complete and adequate review of research activities commonly conducted at this institution. HRAC members must be knowledgeable about institutional commitments and regulations, applicable laws, standards of professional conduct, and practice. The HRAC membership must be diverse in matters of race, gender, and cultural background; and include at least one person in each of the following categories:

- The member’s primary concern is the scientific area
- The member’s primary concern is the non-scientific areas
- The member is not affiliated with the institution and is not an immediate family member or a person who is affiliated with the institution.
- A representative from the CAVHS R & D Committee

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

REPRESENTATION OF VULNERABLE POPULATIONS

When research involving vulnerable participants (i.e., children, prisoners, pregnant women, and individuals institutionalized or mentally disabled) is reviewed, the HRAC will include one or more members who have as their primary expertise the needs of the vulnerable population.

Example: Research involving children with behavioral disabilities requires the HRAC to involve a pediatric psychologist during discussion of the protocol at the HRAC meeting. Similarly, research involving inmates requires the HRAC to involve a prisoner or prisoner advocate during discussion of the protocol at the HRAC meeting.
PROTOCOL SUBMISSIONS

GENERAL INFORMATION REGARDING SUBMISSIONS

MEETING SCHEDULE AND SUBMISSION DEADLINES

Effective June 1, 2003, the Biomedical Institutional Review Board (IRB) meets on the first, third, and fourth Tuesdays of each month. Meetings are held at 2:30 p.m. in the Betsy Blass Board Room on the 10th floor of the Arkansas Cancer Research Center on the UAMS campus. The deadline for submission of protocols for IRB review is 10:00 a.m. two weeks prior to the scheduled meeting. Submissions not received in the IRB office by that day and time are held over for consideration at the next meeting.

The Behavioral and Social Sciences Institutional Review Board (IRB) meets the second Thursday of each month. Meetings are held at 8:00 a.m. in Room G160 at the Donald W. Reynolds Center on Aging on the UAMS campus. The Behavioral and Social Sciences IRB studies reviewed by this committee are considered medically non-invasive and include studies involving questionnaires, surveys, interviews, focus groups, etc.

PRIOR TO SUBMISSION

Prior to preparing a research application, investigators should determine the following.

- Does the project involve research?
- Will the project involve human subjects?

DEFINITION OF RESEARCH

Research is a systematic investigation, including research development, testing, and evaluation designed to develop or contribute to generalized knowledge, 45 CFR 46.102(d). Examples of research activity include: clinical trials, surveys, interviews, behavioral investigations, retrospective reviews of medical information, experiments with blood and tissue, and demonstration or service programs. The Food and Drug Administration (FDA) includes under the definition of reviewable research, the use of an FDA regulated product outside of its marketed use in the practice of medicine for the purposes of contributing to generalizable knowledge.

Example: Use of a cardiac medicine for the treatment of neurogenic pain could be considered experimental and subject to IRB review.

In determining whether a proposed activity is research, the following criteria can be applied:

- Is the proposed activity intended for release to the Scientific Community as a contribution to knowledge?
- Does the proposed activity involve an interaction or intervention with a living person that occurs solely for the purpose of the project?
• Will the proposed activity collect identifiable, private data/information in a form that is associable with the individual?
• Is the proposed activity portrayed (explicitly or implicitly) by university students, faculty, or staff as “research” or “experimental” investigation?
• Is the proposed activity intended to fulfill requirements for a master’s thesis, doctoral dissertation, or other research requirement?

If any one of the above criteria is answered “yes”, the protocol must be reviewed and approved by the IRB.

DEFINITION OF HUMAN SUBJECTS AND ETHICAL CONSIDERATIONS

A human subject is defined in Title 45 of the Code of Federal Regulations, Section 46.102 (f) as a living individual about whom a professional or student investigator conducting research obtains data through intervention or interaction with the individual or collects identifiable private information. Human subjects are also defined as an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A “subject” may be a healthy human or a patient [21 C.F.R. 56.102 (e)].

The Nuremberg Code is the first in a series of codes of ethical conduct for modern researchers. The use of human subjects for research demands that the investigator have a working knowledge of pertinent rules and regulations. One of the strongest threads binding the many rules and regulations together is the distinction between research subject (participant) and patient. If the activity that is planned for the subject is less effective or more dangerous than standard care, it is not “ethical” for that person to become a research subject except under notable exceptions. It is the ethical obligation of the investigator to make findings widely known and eliminate unnecessary risk to the former subject and patients.

In its review of human subject research, the IRB has jurisdiction over all aspects of research including:

• 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
• The protocol and summary of the research
• Any risks to subjects from the proposed research are reasonable in relationship to anticipated benefits
• Proposed changes to the research
• Unanticipated problems involving risk to the subject or others
• Continuing reviews
• Uses of investigational drugs and devices in emergencies
• Humanitarian uses of drugs and devices
• Determination of a protocol’s eligibility for waiver of full review
The submission of any study for initial review should address those issues listed above that are pertinent to the protocol.

**RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR WHEN SUBMITTING A STUDY FOR IRB APPROVAL**

It is the responsibility of the Principal Investigator (PI) to submit his/her proposed research for approval. The PI must assure that all persons performing research activities under his or her direction are properly credentialed by the institution to perform the procedures or interventions outlined in the research protocol. Approval by the IRB does not relieve the PI from the obligation to follow procedures and rules of the institution at which the research is to be undertaken.

It is the responsibility of the PI to assure that IRB approval of the protocol is continuous. Investigators must also maintain continuous approval from each institution where the research is being conducted. The study must be reviewed and re-approved by IRB not less than one year from the date of study approval. If this continuing review report (CRR) is not approved by the date specified, the study is considered out of compliance. No subjects may be enrolled until approval of the CRR is obtained from the IRB. If the PI does not respond to the IRB request for continuing review reports, the study will be terminated. Patterns of noncompliance by the investigator can trigger formal inquiries by the IRB.

The validity of the CRR information must be supported in the study records. It is the responsibility of the PI to monitor study records for completeness, accuracy, authenticity, and validity.

The PI (or his or her formally authorized designee) must sign ALL communication with the IRB. Communication not signed by the appropriate person will be returned.

At the conclusion of any study, the PI must furnish a final report to the IRB, including applicable data analysis and long-term follow-up, so that the study can be closed. The final report of study results should be received by the IRB no later than 90 days after the completion of the study. When a protocol is complete except for data analysis or long-term follow-up, the PI should indicate the status of the protocol on the CRR so that approval can be expedited. Studies are not to be closed until the investigator has determined that the study is ready to be closed.

The PI is responsible for abiding by the Investigator's Agreement, (Appendix P) that includes the following items:

- No subjects will be recruited or entered into a protocol until the Investigator has received an approval letter from the IRB.
- No modification of the protocol or consent form will be initiated without prior written approval from the IRB, except when necessary to eliminate immediate hazards to the subjects.
• The PI will provide a prompt, written report to the IRB regarding any deviation from the protocol and/or consent form, adverse events that are serious, unanticipated and related to the study, or a death occurring during the study.
• Annual status reports for the protocol (CRR) will be completed and returned with the time limit stated on the forms.
• If the study involves any funding or resources from outside sources, the Grants Coordinator in the appropriate Institutional Research Administration Office will be contacted regarding a contract. Subjects cannot be enrolled prior to completion of the contract, unless specified by the institution.
• If the study involves industry sponsored trials at the VA, the PI must contact the Biomedical Research Office.
• Informed consent will be obtained from all subjects using the method approved by the IRB for the research protocol.
• The IRB office will be notified within 30 days of a change in the PI or of the closure of the study.
• The PI will sign a statement regarding the protection of human subjects and vulnerable populations. (Appendix P)

Failure to abide by the approved research plan can lead to suspension or termination of studies or to suspension of the PI’s research privileges by the IRB.

PLANNING THE IRB SUBMISSION

Investigators should understand that the human research must be carried out under a research plan or “protocol” that has been submitted and approved by the IRB. All changes in the protocol must be approved by the IRB before implementing, unless the change is urgently required for the subject’s safety.

If an investigator chooses to submit a funded grant proposal as a research protocol for IRB approval, human use descriptions used in that grant proposal will then be considered the active research plan. Similarly, changes in the IRB grant must be approved in the same manner as any other research protocol. The IRB does not recommend using a grant proposal as a research protocol; submission of a separate research proposal is encouraged.

Plans for human research should reflect careful and unhurried consideration on the part of the Investigator. Specifically, the questions that the PI proposes to answer and the precise methodology needed to obtain those answers must be included in the research plan. Approval or clearance from various bodies located in all of the institutions where the research will occur is required prior to beginning your study. Ideally, the investigator will present appropriate letters of approval with the protocol submission to the IRB for review. If gaining institutional committee letters cause a significant delay, the investigator may submit copies of his letters requesting approval with the submission to the IRB. A checklist to assist the investigator in preparing the IRB submission is included in Appendix D.
Protocols submitted to the IRB require documentation concerning the following:

**Sub-investigators**
If the study requires collaboration from another area, a sub-investigator from that area can be designated. The sub-investigator should be consulted and familiarized with his/her responsibilities. A copy of the sub-investigator’s vita or resume should be included in the study records and be available if requested by the IRB. If an FDA form is required for the study, it must be kept updated if there is a change in sub-investigators.

**Ionizing Radiation**
If the study includes ionizing radiation, it is the investigator’s responsibility to obtain approval from the Radiation Safety Committee in each institution where the research will be performed if approval is required.

**Oncology Research**
If the study involves oncology, the protocol may need to be submitted to the ACRC Protocol Review and Monitoring Committee (PRMC). The PRMC reviews all cancer protocols conducted under the auspices of the Arkansas Cancer Research Center for scientific merit, subject availability, and available resources. It is the responsibility of the PI to submit oncology protocols to the PRMC for approval in addition to IRB approval. *Clinical protocols that are NOT cancer-related, but have an ACRC member as a principal investigator do not require PRMC approval.*

**Recombinant DNA and/or biohazardous protocols**
If the study involves the use of recombinant DNA or biological vectors, the institution’s Biosafety Committee (IBC) should be notified. Projects that require UAMS Biosafety Committee Approval before protocol submission to IRB include:

- Protocols involving DNA or recombinant DNA sequencing
- Experimentation using BL2 or BL3 infectious microorganisms
- Experimentation using carcinogenic (known or suspected) or highly toxic compounds.
- 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 <100ng/kg.
- Modification of the germline genes of animals (transgenic)
- Human gene therapies even if recombinant DNA is produced elsewhere.

The UAMS Biosafety Committee completes its review of protocols as soon as possible after they are received. If the proposal involves the CAVHS, contact the VA research Office to submit to the VA Research Safety Committee. A list of contact numbers for the institutional subcommittees can be found in Appendix O.
General Clinical Research Center (GCRC)

The GCRC is a National Institutes of Health (NIH) funded grant primarily intended to leverage federal funding for investigator-initiated, human-based research and serves the research communities of UAMS, CAVHS and ACH. The GCRC provides investigators with specialized research space, dedicated research nursing support, dietary consultation and metabolic kitchen, biostatistical support, informatics consultation, design and maintenance, and specialized core laboratories.

Protocols are reviewed by the GCRC Advisory Committee (GAC) and must be received by the second Friday of each month for review on the first Friday of each subsequent month. In addition to GAC approval, each protocol must gain both IRB approval and R&D Committee approval prior to initiation on the GCRC. For more information, please access the GCRC web site at http://www.uams.edu/gcrc or call 501-257-5399.

Grants and Funding Sources

Studies done at UAMS must be submitted to the Office of Research and Sponsored Programs (ORSP). Studies conducted at CAVHS must also be submitted to the Biomedical Research Foundation. At ACH, the studies are to be submitted to the Arkansas Children’s Hospital Research Institute. Funds are usually not released until IRB approval and institutional approval is obtained.

Pharmacy

If the proposed research involves the use of a pharmaceutical, the pharmacy in each institution where the research will take place must be consulted. ACH, CAVHS, and UAMS all have policies requiring dispensing of all investigational drugs through their pharmacies. All pharmacies require cost impact Information forms to be completed (Appendix E). The receipt, storage, and dispensing of drug will be overseen by each institution’s pharmacy. Each pharmacy requires information about the protocol and a copy of each subject’s informed consent documents. A list of Pharmacy Contacts is located in Appendix O.

VA R & D Committee

The Central Arkansas Veterans Healthcare System (CAVHS) Research and Development (R&D) Committee is responsible through the Chief of Staff to the facility Director for maintaining high standards throughout the facility’s R&D program. These standards include those concerning the scientific quality of research and development projects, human rights, laboratory safety, and welfare of animals used in research. It advises the Director on professional and administrative aspects of the R&D program. All R&D activities within the facility, whether funded or un-funded, are within its purview.

Individual investigators are responsible for ensuring that all of their research activities are approved by the CAVHS R&D before they begin the project. Projects reviewed by the CAVHS R&D committee must have received all applicable sub-committee reviews before they can be approved as a CAVHS R&D project. Investigators and their staff
are responsible for adhering to all applicable regulations regarding the proper use and handling of hazardous materials (i.e., radioactive materials), animal welfare, human subject protections and laboratory fire and safety rules. In particular, investigators conducting protocols with human subjects must also have received credit for training in the mandatory instruction on human subject protections.

According to the VA MP3, Part I, Chapter 9, each VA must organize it's own Human Investigations Studies Sub-committee (HIS) of the R&D committee OR it must obtain the services of an IRB from its affiliated University. CAVHS currently has an inter-institutional agreement (IIA) with the University of Arkansas for Medical Sciences for IRB services. Under this agreement, that committee reviews all human subject research protocols and their decision is binding on all VA human subject protocols. From VA Headquarters perspective, the UAMS IRB functions as a “sub-committees” of the CAVHS R&D committee. The CAVHS R&D committee makes the final determination on what research is or is not conducted at CAVHS, which includes the Ft. Roots (North Little Rock) facilities. Any questions regarding research conducted at CAVHS should be directed to the Administrative Officer CAVHS Medical Research Service at 501-257-4819.

PLEASE NOTE: If you plan to conduct your study at more than one institution, an approval letter or a copy of the application letter for each institution’s appropriate committee will be required with the IRB submission.

Example: You plan to conduct a pulmonary study involving frequent chest x-rays and computerized tomography (CT) scans on subjects admitted to the VA and UAMS hospitals. An approval letter from or letter of application to each institution’s radiation safety committee will be required with your submission to the IRB.

A contact list for these committees and other resources at the various institutions covered by the IRB is listed in Appendix O.
INFORMED CONSENT REQUIREMENTS

No investigator may involve humans as subjects in research unless the investigator has obtained the informed consent of that subject or the subjects' legally authorized representative or a waiver has been granted by the IRB. An investigator will seek informed 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. The informed consent document must include the following:

- A clear and concise explanation of the research to be conducted and the procedures to be employed
- Be written in language appropriate for the targeted subject population (e.g.; 8th grade reading level, English and foreign language versions for a multi-cultural study)
- Clear and precise language detailing all potential risks or discomfort and procedures to minimize such risks, duration of participation, and benefits of participation
- A statement defining the right of the subject to withdraw at any time without affecting medical care
- A statement describing alternatives to the proposed research activity, if any exist
- A statement that the data/information will be kept confidential
- A statement of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject
- A statement that the subject is fully informed and agrees to participate on a purely voluntary basis

The IRB also requires specific elements to be included in each consent form in order to comply with federal, state and institutional regulations. Appendix H includes a checklist to use when constructing the informed consent document. The link to the CAVHS consent form template is located in Appendix H. Please follow these instructions carefully while preparing your consent and assent forms.

Informed Consent and Assent Documents

The informed consent form must provide signature lines for subject, investigator, person obtaining consent, and witness. However, an investigator cannot serve as both the person obtaining consent and the witness. The IRB recommends, but does not require, the principal investigator’s signature on all subject informed consent documents. If the principal investigator is unable to sign a subject’s informed consent document, only an approved sub-investigator may sign the investigator line.

If children are involved, signature lines should be provided for the child and for the parent(s). All signatures must be dated. A line for the time consent is obtained may also be appropriate
in drug or device studies. A member of the study team may serve as the witness. The PI should retain copies of the completed consent forms for a period of at least three years following termination of the protocol.

The Investigator must retain the original signed consent form document in the study file and provide a copy to the subject.

The IRB requires that each subject be given a copy of the informed consent document. A copy of the subject’s informed consent must be placed in the medical records. *Pharmacies at each institution may also require a copy of the signed informed consent and protocol before dispensing study drug.*

Additionally, the *process* of informed consent must be documented by an entry in the research and medical records. A progress note should be made that includes:

- The date the subject was entered into the study
- The title of the study
- The name of the principal investigator
- The name of the person obtaining the informed consent
- The subject had an opportunity to ask questions about the research

*Note: CAVHS has special requirements for documentation and filing of informed consent. The Investigator should consult the VA R & D Standard Operating Procedures for complete information.*

If a pharmaceutical company commits to payment of any medical expenses resulting from research injury, the investigator must furnish a letter from the pharmaceutical company to the IRB confirming that commitment. The letter should be signed and dated by a duly authorized official of the company. The letter and consent form must state the extent to which the payment of medical expenses, injuries, and other losses will be made and include any conditions for payment (e.g. refusal to pay prior to submission for payment by subject’s insurance carrier or other third party). If the company agrees to pay only after claims are submitted to the insurance carrier or other third party, the claim submission will indicate that the injury is the result of an adverse drug reaction as part of an investigational trial.

Each page of the consent form should be numbered and dated. (The date will change with each revision of the consent form.)

**EXCEPTIONS FROM THE STANDARD INFORMED CONSENT PROCEDURES**

**Emergency Research Protocols Where Prospective Informed Consent is Waived**

It is possible to have a protocol involving enrollment of subjects in life-threatening situations when a signed informed consent is not feasible prior to use of an investigational test article. 45 CFR part 46.101(i) and 21CFR 50.24 provide specific requirements that must be met by both the IRB and Investigator who will conduct research in emergency research protocols.
Both the Investigator and a second physician not otherwise participating in the clinical investigation must certify in writing all of the following:

- The subject is confronted by a life-threatening situation necessitating the use of the test article
- Informed Consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the subject
- Time is not sufficient to obtain consent from the subject’s legal representative
- There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject
- Risks and benefits of the experimental treatment are reasonable in light of what is known about the condition and risks and benefits of other therapies

The IRB must approve a protocol that has requested waiver of consent for emergency research prior to administration of the test article.

Obtaining Informed Consent in Emergency or Compassionate Situations

Patient care situations may arise in which an investigator requires use of a non-approved drug or device in a life-threatening situation with insufficient time to submit a protocol for approval to the IRB or obtain informed consent. Please refer to the “Special Situations” section of the Handbook that elaborates on IRB requirements for these conditions.

Waiver of Written Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent for some or all subjects (45 CFR 46.117c) if it finds that:

- The only record linking the subject to the research would be the consent document, and the principal risk to the subject is the potential harm resulting from a breach of confidentiality. In that event, each subject should be asked if he/she wishes to have documentation linking the subject with the research. The subject’s wishes will govern OR
- The research presents no more than a minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. In cases where the requirement of documentation is waived, the IRB may require that the investigator provide the subject with a written statement regarding the research.

The Investigator may request the IRB’s ruling on waived consent at the time the protocol is submitted.
Waiver of the Requirement to Obtain Prospective Informed Consent From Subjects in Non-Emergency Research

Federal regulations allow the IRB the ability to grant a waiver from the requirement to obtain any consent from research subjects in non-emergency research, but only under specific circumstances and only when the decision is made at a convened meeting.

If an investigator believes neither written nor oral consent can be obtained from any subjects without jeopardizing the conduct of the project, arguments to support this position should be articulated in the application. Consent waivers will be discussed during a meeting of the convened IRB.

In order to grant a waiver, the IRB must document that it believes the request meets the following criteria:

a) The research involves no more than minimal risk to the subjects
b) The waiver will not adversely affect the rights and welfare of the subjects
c) The research could not be practicably carried out without the waiver
d) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

ADVERTISEMENT FOR SUBJECT RECRUITMENT

Studies may require the use of print, television, Internet or radio advertisement in order to accrue the subject population. Advertisements used for recruitment of subjects to participate in research protocols must be submitted to the IRB prior to use. Any type of advertising for research subjects that is intended to be seen or heard by possible subjects is considered to be part of subject selection process. The IRB must review both the information contained in the advertisement and the mode of its communications.

Advertisements should not be coercive and should not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. No claims should be made, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other drug, biologic or device. Such representation would not only be misleading to potential participants but would also be a violation of the FDA regulations concerning the promotion of investigational drugs and investigational devices.

Advertisements should not use the terms “New Treatment,” “New Medication,” or “New Drug” without stating that it is "Investigational".

Advertisements should not promise "free medical treatment," when the intent is only to say participants will not be charged for taking part in the investigation. The IRB will determine if
the promise of treatment without charge is coercive to financially constrained participants. Advertisement may state that participants will be paid, but should not emphasize the payment or the amount to be paid.

**Advertisements must include**
- The name and address of clinical investigator and/or research facility
- The condition under study and/or the purpose of the research
- In summary form, the criteria that will be used to determine eligibility for the study
- A brief list of participation benefits, if any (e.g., a no cost health examination)
- The time or other commitment required of the participants
- The location of the research and the person or office to contact for further information.

**COLLABORATING WITH OTHER INSTITUTIONS**

Collaboration with other institutions may be conducted at various levels. The IRB should be notified of the level of collaboration in order to ensure appropriate procedures are instituted.

If Institutional Review Board (IRB) review is required at each collaborating institution, there are options to providing required review as per Federal regulations. If the collaborating institution has a federally approved IRB, that IRB will review the study unless they request that the UAMS IRB be the IRB of record.

If a research project at UAMS is to be carried out in conjunction with another institution or entity, such as CAVHS or ACHRI, and the IRB will be responsible for the review of the project, the IRB incurs certain aspects of liability that require additional information from the investigator. Usually, a Letter of Agreement between the institutions or entity will be sufficient. However, a Federal Wide Assurance (FWA) may also be necessary from the cooperating institution. A FWA is a document which formalizes an institution’s commitment to protect human subjects and is required by any institution that participates in Federally supported human subject research. Obtaining the FWA is usually the responsibility of the sponsor or investigator.

The local IRB must approve all research studies conducted by CAVHS participants through the CAVHS Cooperative Studies program with other VA hospitals across the country.

**GRANT INITIATED RESEARCH**

If a research study is grant initiated, it has to be first sent to the Grants office. Grants can’t be awarded until all approval letters are submitted. For example, if a research study is funded by a NIH grant, the PI has to submit the study to the NIH first then submit it to the IRB.
COMMITTEE APPROVALS

If you are doing the research entirely or partially at UAMS, you will need to submit the protocol to all of the committees that pertain to your research (e.g., Biosafety Committee, Pharmacy Committee, etc.) before you can apply to the IRB. Do not start any research until all approval letters have been received.

Once all committee approvals, grants and budgets information, and appropriate education certification has been documented, the PI can assemble the documents required for IRB review. While planning for the IRB review, it is a good time to prepare your submissions for the other institutional research bodies where the trial will be conducted.

Research at Central Arkansas Veterans Healthcare System (CAVHS) requires approval by the VA Research and Development Committee (VA R&D). If research involves patients, medical records, personnel, space, or resources of CAVHS, please contact Tammy Gross, Administrative Officer for Research and Development, at 501-257-4816.

Research at Arkansas Children's Hospital requires approval by the Arkansas Children’s Hospital's Research Institute (ACHRI) prior to submission to the IRB. For more information, contact Jennifer Sharp, Legal and Human Protections Administrator, at 501-364-3571.

Other institutional research committees are listed in Appendix O.

IRB PROTOCOL SUBMISSIONS REQUIREMENTS USING ARIA

Effective January 2003, the PI must submit their entire protocol to the IRB for review using ARIA (Automated Research Information Administrator).

For assistance with obtaining an ARIA username and password or for assistance with submitting protocol using ARIA, please contact Connie Hendrixson, Grants Administrator, at 501-526-5494 or by email at HendrixsonConnieL@uams.edu.

The documents required for IRB Protocol Submissions have to be uploaded in ARIA or you CANNOT submit. All documents need to be in a PDF Format. If you will be submitting protocols, you will need to purchase a copy of the software Adobe Acrobat.

NOTE: The latest copies of Adobe Acrobat and Adobe Approval are now available for $30 through UAMS IT Procurement for UAMS tagged PCs. To obtain more information or a copy of the software, please contact the Help Desk at (501) 686-8555.
Information from the following documents is needed for Protocol Submissions via ARIA.

1. HIPAA Authorization forms or a Waiver Form for HIPAA.
2. Protocol Summary (not to exceed two pages).
3. A copy of the consent form (see consent form directions in Appendix I).
4. A complete protocol containing details of the proposed research project, including:
   - Study background including scientific rationale and aims
   - Methods
   - A list of all procedures which are experimental
   - Anticipated risks and benefits to subjects and procedures to minimize risks
   - A discussion of human subject protection issues and methods
   - Number of subjects
   - Additional safeguards for the protection of vulnerable subject populations
   - Applicable confidentiality issues
   - Data analysis method
   - References
5. A copy of the investigational drug or device brochure (from the sponsor) if the protocol requires the use of an investigational drug or device.
6. A copy of the study Standard Operating Procedures (SOPs) if used in conducting the study.
7. If the study is being done at the CAVHS, a copy of the VA forms you plan to submit there.
8. If the study is being done at ACH, the review of protocol letter from Arkansas Children’s Hospital Research Institute (ACHRI).
9. A copy of any survey or questionnaire to be used in the research.
10. A copy of any advertisement to be used for subject recruitment.
11. A simplified CV of the PI.
12. Letters from appropriate committees, (i.e. Radiation Safety, PRMC, Biosafety Committees).
13. If the study is funded by a grant, a copy of the entire grant application is required.
HOW TO SUBMIT A NEW BEHAVIORAL STUDY PROTOCOL

1) Access the ARIA web site at https://aria.uams.edu/default.lasso
2) Select PI LOGIN.
3) Enter your Username and Password.
4) Click on the Login button.
5) The “Welcome To ARIA” page appears.
6) Select Profile and edit the information if needed.
7) Click the Continue button to return to the main menu.
8) Select New Submission.
9) Select a Protocol Type:
   Is this a Behavioral, or Biomedical Study?
10) Select Behavioral.
11) Click the Continue button.
   Complete the following steps by providing the requested information:
12) Contact Information.
13) Type of HRAC Submission.
14) General Protocol Information.
15) Study Type (Check all that apply).
16) Special or Vulnerable Populations represented in Protocol (Check all that apply).
17) Informed Consent.
18) HIPAA Information.
19) Protocol Design and Subject Specifications.
20) Significant Financial Interest Disclosure.
21) Click the Continue Button.
22) General Personnel Information.
23) Funding Information.
24) Institutions and/or Facilities Used in this Research.
25) Click the Continue Button.
26) Add New Document.
27) Type in Title of Document.
28) Type in Version 1.
29) Date.
30) Click the Add Document button.
31) Click the Add File button.
32) Select File.
33) Click the Browse button to find file on your computer.
34) Click the Upload File button.
35) Is this document acceptable? Yes or no
36) Click Yes.
37) Add documents that are needed for this New Submission.
38) When you are finished adding documents, click the Cancel button at the bottom of the document page.
39) Click the Continue button.
40) Read the Investigator’s Agreement.
41) Click on the “I AGREE” button. It becomes an electronic signature.
42) You will receive an email acknowledgement that the IRB has received the online submission form.

For assistance with ARIA, you can access the Tutorial Guide for ARIA Web Information System.
HOW TO SUBMIT A NEW BIOMEDICAL STUDY PROTOCOL

- Access the ARIA web site at [https://aria.uams.edu/default.lasso](https://aria.uams.edu/default.lasso)
- Select PI LOGIN.
- Enter your Username and Password.
- Click on the Login button.
- The Welcome Page appears.
- Review your profile and edit if needed.
- Select New Submission.
- Select a Protocol Type
  Is this a Behavioral, or Biomedical Study?
- Select Biomedical.
- Click on the Continue button.

Complete the following steps by providing the requested information:

1) General Protocol Information (Step 1 of 11)
   - Title
   - Type of HRAC Submission
   - General Information
   - Study Type
   - Special or Vulnerable Populations
   - Consent
   - Hit the Enter button
   - Key in HIPAA information

2) General Personnel Information (Step 2 of 11)
   - Personnel
   - Primary Contact Information

3) Institutions/Facilities Used in this Research (Step 3 of 11)
   - Locations

4) Funding Sources (Step 4 of 11)
   - Funding

5) Drugs, Devices, and Procedures (Step 5 of 11)
   - Drugs

6) Drugs, Devices, and Procedures (Step 6 of 11)
   - Investigational Devices
   - Approved Devices for Unapproved Use
   - Approved Devices for Approved Use

7) Drugs, Devices, and Procedures (Step 7 of 11)
8) **Risks (Step 8 of 11)**

- Surgical or Invasive Procedures
- Laboratory Considerations
- Radiation Safety
- Oncology Research
- Genetic Testing Confidentiality Considerations
- Biosafety Considerations

9) **Protocol Summary and Subject Specifications (Step 9 of 11)**

This section documents information about the research design. Please refer to the guide which contains a checklist of information required in the written protocol.

- State the hypothesis, research question or purpose of the proposed research.
- Provide the relevant background pertinent to the research question or purpose including the rationale for the experimental procedure, drug, biologic and/or device (limit your answer to 150 words or less).
- Will you be Advertising for Research Subjects: Yes  No
- If yes, indicate the type of advertising and attach a copy of your advertisement for review:
  - Posted Circulars
  - Newspaper
  - Magazine
  - Television
  - Radio
  - Internet
- Will the subjects be recruited from an emergency room type setting: Yes  No
- Summarize the inclusion/exclusion criteria for the subject population.
- Describe the anticipated benefits to subjects in this research.
- Does the protocol exclude any vulnerable population (children, pregnant women, fetuses, prisoners or cognitively impaired persons that might benefit from the research) Yes  No
- If yes, describe the scientific and/or ethical justification for this exclusion below:
- Summarize the protocol methodology (what is to be done to the subjects), including analysis of study data.
- Summarize the risks and side effects (physical, psychological, financial and social) to subjects in this research. List any precautions you are taking to minimize these risks.
- Investigator’s assessment of risk category:
  - Adult Risk
  - Pediatric Risk 1 2 3 4
- List any cost/financial remuneration to the subject as a result of participating in this research. N/A
- If the protocol provides compensation to investigators or others for identifying and/or enrolling subjects, is it justified: Yes No N/A

- Significant Financial Interest Disclosure
  Please Check One
  Significant financial interests are defined as interest valued at greater than $10,000 or an equity ownership of more than 5% held by an investigator and the investigator’s spouse or dependent children.
  - N/A
  - Salary or Other Payment for Services
  - Equity Interests
  - Intellectual Property Rights
  - Other Significant Interest
  - Research Requires the Use of a Device, Drug, or System that is an Invention of the PI

  If you selected a value other than NA, please refer to your institution’s requirements for financial disclosure.

  Click on the Continue button

10) Adding documents in ARIA (Step 10 of 11)
  The documents must be in a PDF format to be uploaded.

11) Investigators Agreement (Step 11 of 11)
  The PI clicks on the I Agree button and it becomes an electronic signature. The PI will receive an acknowledgement that the IRB has received the online submission form.

For assistance with ARIA, you can access the Tutorial Guide for ARIA Web Information System.
IRB REVIEW REQUIREMENTS

The IRB is required by CFR 45 part 46.111 to consider all of the following during its review of proposed studies and continuing reviews:

- The IRB is required to assure that the selection of subjects is equitable and should be particularly cognizant of the special problems of research involving vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons or economically or educationally disadvantaged persons
- Risks to subjects are minimized through the use of procedures consistent with sound research
- Risks to subjects are reasonable and in relation to anticipated benefits and to the knowledge that may reasonably result
- Informed consent is correctly obtained and appropriately documented
- Subject privacy and confidentiality of the subject data is maintained
- The research plan makes adequate provision for the monitoring of data to ensure subject safety.

ASSIGNING STUDY RISK CATEGORY AND FREQUENCY OF CONTINUING REVIEW REPORTING

The IRB committee meetings include a discussion and vote on new protocols, major modifications, and studies submitted for continuing review. New protocols are assigned categories of risk and frequency of continuing review. In order to approve research, the IRB must determine the degree of risk.

Below is the definition of risk categories derived from 45 CFR 46.102.

<table>
<thead>
<tr>
<th>Minimal Risk</th>
<th>Greater Than Minimal Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity where the probability and magnitude of harm or discomfort anticipated in the research is not greater in and of themselves than those ordinarily encountered in daily life or during performance of routine physical or psychological examinations or tests.</td>
<td>Research involving greater risk of harm than ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, but presenting the prospect of direct benefit to the individual subjects; or the research presents no prospect of benefit to the subject, but is likely to yield knowledge about the disorder or condition</td>
</tr>
</tbody>
</table>

Protocols not eligible for expedited review will be reviewed by at least two IRB members chosen on the basis of expertise with the particular subject matter of the study. These individuals will serve as the primary reviewers and will be responsible for presenting the protocol to the convened IRB for discussion.
The IRB must deliberate on all studies classified as greater than minimal risk for the purpose of assigning the frequency of continuing review reports. The IRB may decide to review greater than minimal risk studies more frequently than every six months.

**TYPES OF IRB REVIEW FOR NEW PROTOCOLS**

There are three categories of review.

<table>
<thead>
<tr>
<th>Exempt Review</th>
<th>Expedited Review</th>
<th>Full Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Some research is exempt from IRB review. Examples of this category are listed in 45 CFR 46.101. NOTE: Exempt research must be registered with the IRB by submission of one (1) set of the required forms.</td>
<td>The proposed research is defined as minimal risk. Review by the fully convened IRB is not necessary. Approval may be given by the IRB Chair and reported to the next convened IRB meeting.</td>
<td>Research involves issues that do not qualify for exempt or expedited review. The research is reviewed by 2 primary reviewers who present their findings to a fully convened HRAC for discussion and vote.</td>
</tr>
</tbody>
</table>

**Exempt Review**

Studies that are classified as "exempt" do not required approval by the HRAC. Under the Health and Human Services (HHS) regulations [45 CFR 46.101(b)], some research is exempt from meeting the requirements set forth in the regulations. **These exemptions do not apply to any activity classified as greater than minimal risk or research involving prisoners, children, fetuses, pregnant women, or human in vitro fertilization** (See Research Involving Vulnerable Populations). Further, the exemption for certain research involving surveys or interview does not apply to research involving children. No research involving FDA regulated products is exempt under FDA regulations.

**Consent forms are usually not required for exempt studies.** The extent of the Consent Process will be determined by the HRAC. Information sheets and/or verbal consent should be utilized for studies involving human subjects. These should be submitted with the letter outlining the study.

If the HRAC Chair agrees that the study is "exempt," the investigator will receive a letter confirming the exemption. If the study does not qualify as "exempt", if the issue is not clear, or if any of the required approvals are missing, the investigator will be notified in writing as to what is required.

Research that falls into any of the categories listed below has been determined by HHS to be exempt from IRB review requirements under 45 CFR 46.101. However, they must still be registered with the IRB. The investigator is required to submit a letter to the IRB outlining the study and including any approvals that may be required.
Categories of Exemption

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

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 subject
   - 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

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

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 in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

5. Research and demonstration projects which are conducted by or subject to the approval of Department of Health and Human Services, Federal Agency heads, and which are designed to study, evaluate, or otherwise examine:
   - Public benefit or service programs
   - Procedures for obtaining benefits or services under those programs
   - Possible changes in or alternatives to those programs or procedures
   - Possible changes in methods or levels of payment for benefits or services under those programs

6. Taste and food quality evaluation and consumer acceptance studies, if:
   - Wholesome foods without additives are consumed, or
   - 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 a level found to be safe, by the FDA or approved by
the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Any research plan that involves both exempt and non-exempt research activities must be reviewed by the HRAC.

**Expedited Review**

Some types of research do not necessitate review by the convened HRAC. These types of studies may be approved by the HRAC Chair and reported to the convened HRAC at its next meeting. Decisions reached at the convened meetings may supercede any decisions made through the expedited review.

If the proposed research is minimal risk and is of a type that falls into one of the categories listed below (and published in the Federal Register by DHHS and FDA), the Chair may review and approve the research (expedited review).

There are nine categories of research that may be eligible for expedited review. The categories apply regardless of the age of subjects, except as noted. *They are as follows:*

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

2. Collection of blood samples by finger stick, heel stick, ear stick or venipuncture as follows:
   - From healthy, non-pregnant 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
   - From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week. (See Guidelines for Blood Draws in Pediatric and Adult Populations, Appendix R).
2. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:
   - Hair and nail clippings in a non-disfiguring manner
   - Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction
   - Permanent teeth if routine patient care indicates a need for extraction
   - Excreta and external secretions (including sweat)
   - Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue
   - Placenta removed at delivery
   - Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor
   - 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
   - Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings
   - 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:
   - 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
   - Weighing or testing sensory acuity
   - Magnetic resonance imaging
   - Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity
   - Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where weight and health of the individual are appropriate

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).

6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to: research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

8. Continuing review of research previously approved by the convened IRB as follows:
   - Where research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions and the research remains active only for the long-term follow-up of subjects
   - Where no subjects have been enrolled and no additional risks have been identified
   - 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.

The nine categories listed above should not be considered to be of minimal risk simply because they are eligible for an expedited review. Inclusion on this list means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involves no more than minimal risk to human subjects.

<table>
<thead>
<tr>
<th>Expedited review may NOT be used when</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.</td>
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</table>

The HRAC must uphold the standard requirements for informed consent (or its waiver, alteration, or exception) regardless of the type of review (expedited or convened) used.
Expedited Review Procedures

Expedited review procedures are allowed for certain kinds of research involving no more than minimal risk, and for minor changes to already approved research. The HRAC Chair or one of the members of the HRAC designated by the Chair will conduct expedited reviews. Protocols submitted for expedited review must include all of the materials required for full committee review.

An investigator may apply for expedited review, or the Chair may determine that the study is eligible for expedited review if it meets the regulatory criteria. If the Chair determines that the project submitted for expedited review requires full committee review, the investigator will be notified in writing.

When performing an expedited review, the reviewer(s) may exercise all of the authorities of the HRAC except that they may not disapprove the research. Research may only be disapproved by the convened HRAC. A list of the protocols that receive expedited review since the last meeting of the HRAC is included in the packet of materials given to HRAC members in preparation for each meeting of the HRAC. Members may request additional information on any project which has received approval or been amended through an expedited review process.

The HRAC may also approve minor revisions to already approved projects through expedited review (e.g., changes of an administrative nature, minor revisions in the text of an informed consent document or advertisement, corrections in the text of documents, and other minor changes). These can only be expedited if the changes do not increase the risks involved.

Similarly, Adverse Event Reports, that in the judgment of the Chair or an experienced reviewer do not appear to be serious or to be occurring with some frequency and do not appear to affect the degree of risk to subjects, may be reviewed by expedited review. However, all serious adverse event reports submitted by the Investigator will be presented on the agenda at the HRAC meetings.

Full Review

All applications except those qualifying for exempt or expedited status will be reviewed by the HRAC at one of its convened meetings. The HRAC utilizes primary review teams in conducting full reviews. A minimum of two reviewers will receive the full study protocol application. All committee members will receive copies of the HRAC application forms, protocol summary, and informed consent documents. The Primary Reviewers will present the protocol and issues to the convened HRAC for discussion before a vote for approval can be cast.

A quorum (51% of the specific committee’s voting membership including the chair, who votes only in the case of a tie) of members, including at least one non-scientific member, must be present for voting purposes on each review. After the vote, the investigator will be notified in writing regarding the status of the application.
HRAC REVIEW RESULTS

The HRAC will review research protocols and approve, disapprove, or require modifications before approval is granted. Investigators are notified in writing concerning all HRAC actions. *If the HRAC disapproves a study, it will notify the investigator of the reasons for the disapproval, and allow the investigator an opportunity to respond. The investigator may appeal to the HRAC to reverse the decision to disapprove a study, but no other authority may approve a study if the HRAC disapproves it.*

HRAC Review results of new protocols fall into the following categories:

- **Protocol Approved:** The project and its study tools, including the informed consent documents, are approved as submitted. Once the investigator receives the HRAC approval letter, the study may begin.
- **Protocol Approval Deferred (Major or Minor):** The project requires revisions. Minor revisions may be reviewed through the expedited process. Major revisions in the project as submitted must be addressed before the HRAC can grant approval. Protocols with approval deferred for major deficiencies must be re-reviewed by the convened HRAC before final approval is granted.
- **Protocol Tabled:** Serious deficiencies in a newly submitted protocol with issues to be addressed by the investigator before the HRAC can grant approval. Protocols that are tabled must be resubmitted to the HRAC as if submitting the protocol for an initial application (35 sets of all revised materials).
- **Protocol Disapproved:** The project has serious deficiencies affecting the safety and welfare of the projected subject population. Protocols that are disapproved may not be resubmitted to the HRAC. The protocol requires major revision of safety issues and a new protocol submission.

Any involvement of human subjects in research may not begin until the approval of the HRAC has been received.

NOTIFICATION OF INVESTIGATORS FOLLOWING REVIEW

The HRAC office notifies each investigator in written form of the review of their initial protocol submission, correspondence received by the HRAC office, protocol activities reported at the HRAC meeting, and continuing review process. The written form should be issued within 14 business days and outline the HRAC actions and any further issues which must be addressed by the principal investigator. Upon receipt of that written form, the PI should make the required corrections, modifications, or resubmission of a new protocol. During registration of the project and protocol submission, a project number will be assigned. This
number will be the UAMS tracking number for that protocol. Tracking numbers will also be linked to funding sources in the Office of Research and Sponsored Programs.

All correspondence with the HRAC must reference the Project Tracking number. Correspondence that does not identify the HRAC number may be returned without further action.

NOTIFICATION OF INSTITUTIONAL OFFICIALS

The minutes of the HRAC meetings reflect summarized discussion of protocol issues and documentation of the vote on each HRAC action. A copy of the HRAC minutes will be sent to the Vice-Chancellor for Academic Affairs and Sponsored Research.
AMENDING A PROTOCOL

PROTOCOL AMENDMENTS

During the course of a research activity, the sponsor and investigator may decide that elements of the research require modification. If an investigator or sponsor finds it necessary to deviate in any way from an HRAC approved protocol, consent forms, or eligibility requirements, an amendment or request in writing to the HRAC must be submitted with the changes highlighted. If a change affects the approved consent form, it will be necessary to submit a revised consent with changes highlighted. New consent forms must have the version and date revised. The protocol amendments will be considered by the fully convened HRAC.

Changes in the research may not occur until HRAC approval of the amendment is received unless there is an immediate threat to the health of the patient. If such a situation were to occur, it would be the PI's responsibility to immediately report the event to the HRAC as a protocol deviation and serve notice that an amendment to the protocol will be forthcoming.

Major changes to an existing protocol, such as a change in the aim of the study, or the degree of risk to the subject may require that a new protocol be submitted (usually with a new title) and the old protocol be closed.

After HRAC approval of the protocol amendment, a copy of the approval letter should be sent to the sponsor by the investigator. The VA R & D Committee will also require copies of protocol amendment approval for research at CAVHS. A copy of the submission, approval letters, and amendments should be kept in the study’s regulatory files.

Any changes or amendments to an already approved protocol must be submitted for review and approval by the HRAC prior to initiation unless a serious patient safety issue exists.
CONTINUING REVIEW

All protocols approved by the HRAC are subject to continuing review. The Office for Human Research Protections (OHRP) and the FDA require periodic re-evaluation of all approved research at intervals appropriate to the degree of risk and not less than once per year. The HRAC accomplishes this process through the continuing review form.

At the time of initial review, the convened HRAC determines how often research projects should be re-evaluated based on the level of risk. Assessment of level of risk includes physical, psychological, social and economic factors. Most research projects are re-evaluated once per year. Protocols more likely to be reviewed at least every six months include those found to present greater than minimal risk to vulnerable populations, those involving a significant risk device, or those involving high-risk relative to the disease status. The Principal Investigator will be notified in writing of the approval’s expiration date for continuing review at the time the protocol is initially granted approval. Continuing review reports are required for all active research projects approved by the HRAC even if all data analysis has been completed since the last approval unless the study has been closed by the HRAC.

The continuing review expiration date may change from year to year. Each time the convened HRAC conducts continuing review, the study calendar is reset to the date of the meeting.

Example: A study’s continuing review date expires on June 1, 2000. The HRAC convened on May 15, 2000 and granted protocol approval. The next continuing review approval will expire on May 15, 2001.

Notices are mailed to the PI approximately 8-12 weeks prior to the project’s continuing review expiration date with a required return deadline. However, unforeseen problems may result in a renewal notice not being received by the PI. Therefore, an investigator should not depend solely on HRAC notification as a prompt for submitting the CRR and request for renewal. Investigators are required to submit continuing review reports at least 5 weeks prior to expiration to allow sufficient time for processing the report prior to the project’s expiration.

Timely submission of continuing review reports (CRR) by the investigator is essential to the continuation of the study.
The HRAC utilizes primary review teams in conducting continuing reviews. A minimum of two reviewers will receive the review and the full protocol file, including any application for research and approved or proposed modifications. The Primary Reviewers will also receive and review the Continuing Review Form for the status and progress of the study as required by federal regulations. A copy of the currently approved informed consent and a new informed consent containing any proposed changes to the informed consent process and document must accompany the continuing review report. All committee members will receive copies of the continuing review form and informed consent documents. The Primary Reviewers will present criteria required for review to the convened HRAC with discussion of the protocol before a vote for continuing approval can be made. The HRAC will vote separately on each continuing review. The vote will be recorded in the meeting minutes.

Continuing review may be conducted by expedited review only where the study falls into one of the expeditable review categories and is minimal risk. Expedited review may also be used for continuing review if a study has been closed to accrual and intervention has been completed, but the investigator is still collecting follow-up data.

A copy of all continuing review reports (CRRs) and approval letters should be kept in the Investigator’s study regulatory file.

Continuing review rulings are as follows:
- **Protocol Re-approval**: Follows review of satisfactory information submitted by investigator regarding an ongoing project.
- **Protocol Re-approval Deferred (Major or Minor)**: The information submitted by the investigator regarding an ongoing project is not sufficient for re-approval. Additional information from the investigator is required. Minor revisions may be reviewed through the expedited process. Major revisions in the project as submitted must be addressed by the convened HRAC. This information must be received as requested by the HRAC or the study may be out of compliance and the investigator must stop enrollment.
- **Protocol Suspended**: Suspension follows review of information submitted by investigators regarding an ongoing project that addresses issues of concern or serious problems in risk/benefit analysis. Protocol enrollment and study procedures must stop until additional information can be reviewed by the convened HRAC.

All protocols not approved by the HRAC by the project’s continuing review expiration date are automatically suspended to subject accrual.
NOTIFICATION OF INVESTIGATORS FOLLOWING CONTINUING REVIEW

The HRAC office notifies each investigator in written form of the results of the committee’s action on the protocol’s continuing review submission. The written notice should be issued within 14 business days and outline the HRAC actions and any further issues which must be addressed by the principal investigator. Upon receipt of the written form, the PI should make the required corrections, clarifications or modifications, and resubmit them to the HRAC office.

If a study’s continuing review was performed before its approval deadline, but has approval deferred, subject enrollment may continue until the continuing review expiration date has passed. After the continuing review expiration date passes, the study enrollment must be suspended until the research has received final approval.

For studies where continuing review approval has lapsed, the HRAC will determine on a case-by-case basis if it is appropriate to suspend interactions and/or interventions in currently enrolled subjects. The study will be terminated 30 days after study suspension notification if no response has been received from the investigator.

If the HRAC’s review of a project requiring continuing review results in termination, a new HRAC application will be required to continue with the research. No new subjects may be enrolled, all ongoing research activities must stop, and subjects currently participating should be notified that the study has been terminated. The regulations make no provision for any grace period extending the research beyond the current expiration date.

Termination notices due to non-compliance with the federal regulations for continuing review will be sent to the PI, the Department Chair, and the Office of the Vice Chancellor for Academic Affairs and Sponsored Research. The HRAC must also notify study sponsors, the FDA and OHRP (if the studies are government funded). If the study is done at the VA, ORCA will be notified of termination.
RESEARCH RECORD-KEEPING AND REPORTING

RECORD-KEEPING RESPONSIBILITIES OF THE PRIMARY INVESTIGATOR

Proper record keeping is integral to the validity and reliability of data collected during research trials. The PI should oversee the general organization and design of study records, both paper and electronic, and assure that all records are authentic. All data recorded on study recording forms and procedures performed should be supported by documents filed in the study file. Each study involving human subjects must have a log listing those enrolled and those who were approached to enter the study with identifying information. Identifying information can be encrypted.

The PI is also responsible for the proper organization of regulatory documents; such as protocols, protocol amendments, HRAC submissions, CRR and approval letters, reports to all appropriate entities on adverse events, deaths, protocol violations and deviations.

Each study should have the following general records:

<table>
<thead>
<tr>
<th>Regulatory</th>
<th>Individual Subject Files</th>
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</thead>
<tbody>
<tr>
<td>Subject Log</td>
<td>Original signed informed consent form</td>
</tr>
<tr>
<td>Copies of all HRAC correspondence</td>
<td>Copies of study recording forms (CRFs)</td>
</tr>
<tr>
<td>Approved Protocol</td>
<td>Subject medical record number and emergency contact information</td>
</tr>
<tr>
<td>Approved Consent Form</td>
<td>Supporting Documentation for: *</td>
</tr>
<tr>
<td>HRAC Approval Letters</td>
<td>• Inclusion/Exclusion criteria</td>
</tr>
<tr>
<td>Other Institutional approvals</td>
<td>• Results of tests or procedures</td>
</tr>
<tr>
<td>Continuing review reports</td>
<td>• Adverse events</td>
</tr>
<tr>
<td>Investigator’s Brochure</td>
<td>• Deaths</td>
</tr>
<tr>
<td>Correspondence with sponsors</td>
<td>• Communications with subject and follow up exams</td>
</tr>
<tr>
<td>Special Committee approvals</td>
<td>• Protocol Violations</td>
</tr>
<tr>
<td>Study Standard Operating Procedures</td>
<td>• Protocol Deviations</td>
</tr>
<tr>
<td>Sample questionnaires</td>
<td></td>
</tr>
<tr>
<td>Sample study forms with instructions</td>
<td></td>
</tr>
<tr>
<td>Reports of deaths, protocol violations, protocol deviations and serious adverse events.</td>
<td></td>
</tr>
<tr>
<td>Drug Accountability Records</td>
<td></td>
</tr>
<tr>
<td>Drug/Equipment Shipping Receipts</td>
<td></td>
</tr>
<tr>
<td>Data Safety Monitoring Reports (if applicable)</td>
<td></td>
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</tbody>
</table>

*Completed study recording forms are not considered supporting documentation. Additional records are needed; Example A lab value recorded on a study form must be supported by a clinical laboratory report of that test.

These records and any other that assists in collection of data must be consistently maintained. The PI may delegate elements of record keeping activities, but remains responsible for accuracy, authenticity, validity and completeness of all study records.
Investigators should consult each specific protocol for the length of time that study records should be maintained.

If the study is being carried out at CAVHS, the Investigator has additional record keeping responsibilities. A complete list can be obtained from the VA R & D Committee. However, some of the additional requirements are:

- A Copy of VA Form 10-1086 must be sent to both the pharmacy and each time a subject is entered into the study.
- For pharmaceutical studies, a copy of the subject’s informed consent form should be sent to the Chief, Pharmacy Service.
- VA Form 10 -1426 Research and Development Information System Project Data Sheet (if the study is a VA Cooperative Studies Program) should be sent to the VA Research and Development Committee administrative assistant.

**INVESTIGATOR’S RESPONSIBILITIES FOR TEST ARTICLE ACCOUNTABILITY**

A pharmaceutical product, device or any other investigational product must be received, maintained, stored, inventoried and accounted for by the investigator according to Federal Guidelines. The investigator is responsible for the control and documentation of all test articles. If investigational drugs are involved in a study, shipment from the sponsor must be coordinated through the institution’s pharmacy. Sponsors may ship investigational drugs directly to a subject only in very rare circumstances. It is also against federal law for anyone other than the sponsor to send investigational drugs or devices to an investigator. Arrangements with the pharmacy for the receipt of all investigational drugs should be completed prior to submitting the protocol for approval.

**Example:** You are new to the institution and plan to continue your study of implantable catheters. The protocol has received HRAC approval. You must receive a new batch of catheters from the sponsor. You cannot obtain them from your previous workplace.

The investigator must assure the maintenance of a drug or device record that is current and includes the following:

- Date of delivery and shipping Invoice including name and address of consignee, type and quantity of drug or device and date of shipment
- Inventory log, with unique code numbers, reflecting use by each subject
- Location and environmental conditions of storage
- Security of storage (tamper-proof)
- Expiration dates, if applicable of drugs and devices
- Records validating that appropriate personnel used the drug or device according to protocol
- For investigational drugs: Documentation should include the amount of drug that was dispensed, unused by the subject, wasted by the research staff and returned to the pharmaceutical company. Documentation records must also reflect subject identification, the reason for waste or return, and batch or lot numbers of returned materials.
• For Investigational Devices: Documentation of the device used, including batch, Lot or identification number, subject identification, patient materials provided, devices returned to company and malfunctioning devices.

The Investigator must assure that test articles are administered or dispensed under his or her personal supervision or the supervision of the appropriate competent personnel. Arkansas State Law requires that only a physician or pharmacist may dispense drugs. An Investigator shall not supply a test article to any other person for administration or to use upon subjects for any other purpose, without the prior authorization of the sponsor [CFR 812.110 (c)].

If the test article is a controlled substance, the Investigator must assure that it is legally, stored, dispensed and accounted for and take reasonable precautions against the drug’s diversion. Controlled substances must be administered only both those legally allowed to do so.

Unused test articles must be returned to the sponsor. Documentation of the shipment should be retained with the drug/device record. For studies conducted at the VA, the disposal of unused articles should be done through the pharmacy after a letter of direction sent by the PI.

Subject information regarding investigational drugs or devices

The investigator or his designee must explain the correct use of the investigational product to each subject. Subjects should be followed up periodically to assure that they are using the products correctly. Additionally, sponsors often include device product identifiers, including lot numbers. These should be given to the subject. A copy of lot numbers or unique identifiers should be recorded in each subject’s medical record. Drug information must be recorded in the subject’s drug dispensing log.

INVESTIGATOR HRAC REPORTING RESPONSIBILITIES

Communication between the Investigator and the HRAC is critical to the Institution’s ability to conduct research using human subjects. Timely communications from the PI and appropriate guidance by the HRAC and the institution where the research is being performed is necessary for the protection of the subject, the maintenance of research compliance and the elevation of the quality of the research. Appropriate reporting forms are available on the Internet and in the HRAC office. These forms must be completed and submitted to the HRAC. The website the form can be found at is: http://www.uams.edu/ORSP/forms.htm

COMMUNICATING WITH SUBJECTS

Serious adverse events, deaths, changes in protocol and other new information regarding a study may need to be reported to subjects. Letters of this nature must be approved by HRAC prior to mailing.
REPORTING RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR TO THE HRAC

The principal investigator is required to notify in writing both the HRAC of **ALL** of the following:

<table>
<thead>
<tr>
<th>Investigator Must Report</th>
<th>Time Frame for Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious and unanticipated adverse events</td>
<td>Within 7 days of event</td>
</tr>
<tr>
<td>Deaths</td>
<td>Within 3 days, if subject currently in protocol. Otherwise within 60 days of investigator’s notification of the death.</td>
</tr>
<tr>
<td>Protocol deviations</td>
<td>Immediately, if it represents a significant alteration in the approved protocol and/or if it affects the safety or welfare of the subject. Otherwise, report during continuing review.</td>
</tr>
<tr>
<td>Protocol Violations</td>
<td>Immediately, if it represents a significant alteration in the approved protocol and/or if it affects the safety or welfare of the subject. Otherwise, report during continuing review.</td>
</tr>
<tr>
<td>Changes in approved research procedures or protocol (amendments)</td>
<td>Prompt notification within 30 days</td>
</tr>
<tr>
<td>Noncompliance with conducting of research protocols</td>
<td>Immediately upon discovery of noncompliance</td>
</tr>
<tr>
<td>Restrictions, suspension, or termination of study by the sponsor or principal investigator</td>
<td>Within 3 days</td>
</tr>
<tr>
<td>Any activity which involves a potential or actual unanticipated risk to subjects or others</td>
<td>Within 7 days of activity</td>
</tr>
</tbody>
</table>

**Adverse Event Reporting**

Your responsibility as a clinical investigator includes the prompt reporting to the HRAC of serious and unanticipated side effects associated with the use of either investigational drugs or devices. Such adverse events must be reported promptly within seven (7) days while a subject is on a study protocol. A death occurring while a subject is on a study must be reported within three (3) days. A death of a subject that is not protocol related and part of long-term follow up (e.g. following until death on oncology protocols) should be reported within 60 days that the investigator is notified of the death. Reporting to the HRAC does not substitute for a principal investigators’ responsibility of reporting to a sponsor.
A **serious adverse event** is any adverse experience occurring at any dose that:

- Results in death
- Is life-threatening (places the subject at immediate risk of death from the experience as it occurred)
- Results in a persistent or significant disability/incapacity
- Results in or prolongs an existing in subject hospitalization (even if in the hospitalization is a precautionary measure for observation)
- Is a congenital anomaly/birth defect in offspring of subjects taking the product, regardless of time to diagnosis
- Represents other significant hazards or potentially serious harm to research subjects or others

**You MUST** report any death to the HRAC office if:

- Protocol requires reporting of the death to the study sponsor or the FDA
- The subject was being actively treated on an approved research protocol at the time of death
- During the course of long-term follow up after completion of the experimental (i.e. active treatment) portion of an approved study protocol, the investigator becomes aware of the death of the research subject.

**You do not** need to report the death of a subject if:

- The study protocol has been officially closed and a final report has been received and accepted by the HRAC.
- The study subject has completed participation in the protocol including long-term data collection (the study remains open).
- The study involves no physical risks to the subjects. This includes any protocol for which only invasion of privacy (data collection) concerns applies, but does not apply if any experimental treatment, procedures, medications, or devices were used. Examples: chart reviews, questionnaires, surveys, and videotaping.
- The experimental portion of the study involved collection of tissue or blood samples without long-term follow up or ongoing collection of additional subject information (i.e. ongoing invasion of privacy concerns), even if the samples are stored for future use and tests are performed at a future date.

**How to report a death or serious adverse event:**

The investigator must fill out the HRAC form entitled: Serious Adverse Event/Death Report (See Appendix M) and enclose a copy of any correspondence sent to the sponsor regarding the event. The investigator may also include any additional information related to the study. Remember to send a copy of the form and your report to your institution’s research committees, e.g. VA Research & Development Committee, ACHRI, etc.
Reporting Protocol Deviations

Protocol Deviations are study events that are not covered under the approved research protocol, which represent a failure to comply with the protocol.  Example: A subject does not have the kidney biopsy, which is required six months after beginning transplant medication because she is in the ICU. The PI should report a protocol deviation to the HRAC immediately, if it represents a significant alteration in the approved written protocol and/or affects the safety and welfare of the subject. Use the guide in Appendix M for reporting protocol deviations.  Note: Protocol deviations are often referred to as “protocol exceptions”.  For the purpose of HRAC reporting, the two are the same.

Reporting Protocol Violations

Protocol Violations are those events clearly occurring outside of the approved research activity, which also represent a failure to comply with the protocol. The terms protocol deviation and protocol violation are similar, although a protocol violation refers to more serious non-compliance, which more often leads to exclusion of subjects from eligibility analysis or their discontinuation from the study.

Example: Enrolling a subject in a cancer study when the subject has no histologically or clinically proven cancer is considered a protocol violation when a tissue diagnosis of cancer is a protocol inclusion criterion.

The PI must report protocol violations to the HRAC, the sponsor, and all participating institutions. The report must be issued immediately if the health of welfare of the subject was jeopardized. Refer to Appendix M when reporting protocol violations.

Reporting notification of pending audits or inquiries

Investigators conducting research involving human subjects are required to report ANY COMMUNICATION from a federal or state department or agency or sponsor that questions the conduct of research or suggests an impending inquiry audit or investigation. The PI should inform the HRAC chair or Administrator by phone immediately upon notification of inquiry. A formal written notice to the HRAC committee that includes a detailed description of the proposed inquiry is required from the PI. This notice should be received in the HRAC office no less than 3 days from the notification of the PI.
SPECIAL SITUATIONS

EMERGENCY USE

Emergency use is defined in 21 CFR 50.23 as the use of a test article (e.g., investigational drug or biologic) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain HRAC approval.

When a situation arises which, in the judgment of a physician, calls for the emergency use of an investigational drug or biologic in a single patient, an IND (Investigational New Drug) number is still necessary. The situation may arise when a patient does not meet the criteria of a study protocol, or where an approved study protocol does not exist. The usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for use (in this one patient) under the company's IND. Should the company elect not to name the physician as an investigator, the physician can contact the FDA directly for an IND. The physician will be placed in contact with a FDA physician familiar with the drug or biologic to review the proposed circumstances for use and the information to be submitted in the IND.

Emergency use of an investigational drug or biologic may be exempt from the FDA requirements for HRAC review. The investigator must seek verbal approval from the IRB Chairman and report to the HRAC within five working days by letter explaining the circumstances. The letter should include the following information:

- Diagnosis
- Proposed treatment
- Date of treatment
- Drug or device names, if applicable
- Patient’s name and age
- Hospital number
- Hospital name
- Date of verbal approval
- A copy of the signed consent form

Only one such Emergency Use should be given per research protocol. The PI is expected to submit a full protocol and informed consent documents for approval within 5 days before any further patients are included in the proposed research. The NIH will not accept patients admitted on emergency use as investigational subjects for a protocol.
COMPASSIONATE USE

21 CFR 812.35/36 (devices) and 21 CFR 312.34 (drugs) designate the allowed use of test articles in a situation characterized as “compassionate use”.

1. Compassionate use acknowledgments are given when:
   - A patient from UAMS, CAVHS, ACH, or one of the affiliated institutions is requested to be entered into an approved protocol from another institution
   - Patient enrollment is requested in an approved protocol at this institution but does not meet the eligibility criteria.

2. As with emergency approval, verbal acknowledgment may be granted by the HRAC Chair for one patient only, and within five days the investigator must submit a letter to the committee that includes:
   - A new protocol or amendment to an existing approved protocol
   - Patient's name and age
   - Hospital number
   - Hospital name
   - Date of acknowledgment and the date used
   - A copy of the signed consent form.

3. In the case of an amendment to an approved protocol, the investigator should give the exact full title of the approved protocol.

As with emergency acknowledgments, the NIH will not accept patients admitted on compassionate use acknowledgements as investigational subjects for a protocol.
GENETIC RESEARCH

The greatest risk to subjects participating in genetic research is the inappropriate release of personal and private information. Therefore, concerns for how investigators will maintain the confidentiality of the data and specimens collected during the conduct of the study is a primary concern to the HRAC.

The protocol and informed consent should address the following points:

- Study information is coded and personal identifiers maintained securely
- Consent forms include information about who will receive the data derived (e.g. the subject, family members, non-participation family members, family physician, other investigators)
- Information as to whether clinically relevant information may be uncovered during the course of the study and whether subjects will be given the opportunity to decline receiving this information
- If children are to be research participants, how will consent be obtained and how will data be handled
- Participants may derive no benefit from participation.
- Study data should not be recorded in the subject’s medical record; separate research records with controlled access are preferred.
- Whether there will be any possibility of individually identifying subjects
- Inform subjects of any special risks associated with their participation (e.g. changes in family relationships, risks to privacy, confidentiality, insurability, employability, immigration status, and paternity suits)
- Indicate if general study results will be made available to subjects
- Whether genetic counseling will be made available and who will pay for this counseling
- Length of time in maintaining specimens (limited, indefinitely) and/or discarding specimens
- Subjects’ wishes to be re-contacted if clinically relevant information is developed
- If the investigator intends to share specimens acquired during the research with other investigators, this information must be included in the consent form and participants given the choice whether they are willing to permit this or not
- Should there be a potential commercial value derived from the research, the subject must be informed as to whether they will be asked to waive any rights or control over the tissue so used
- If the research involves the manufacture of a drug or biologic that is to be administered as a part of research, the Investigator should follow the 21CFR 210 “Good Manufacturing Practices” if required.
MEDICAL DEVICES

USE OF MEDICAL DEVICES IN RESEARCH STUDIES

The HRAC considers an investigational device to be one that is not currently marketed in the United States. According to 21 CFR Part 812, two types of device studies exist. These types are “significant risk” (SR) and “nonsignificant risk” (NSR). An SR device is defined as “a study of a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.” An NSR device study is defined as, “one that does not meet the definition for a significant risk study”.

NSR is not to be confused with the term “minimal risk” and studies of this type are not eligible for expedited review.

STUDIES INVOLVING DEVICES KNOWN TO BE OF SIGNIFICANT RISK (SR)

Devices that are known to be SR require an IDE from the FDA. A list of known SRs can be found in the FDA website www.fda.gov/cdrh/d861.html.

For studies involving SR devices, an IDE and appropriate information concerning the history of the device’s use, proposed investigation plan, description of subject selection criteria and monitoring procedures must be included with the submission packet.

HRAC ROLE IN DISTINGUISHING BETWEEN SR AND NSR DEVICE STUDIES

The HRAC acts as the surrogate of the FDA with respect to the review and approval of NSR studies. If an investigator OR sponsor proposes the use of a device it claims to be NSR, the HRAC may agree and approve the study. If the HRAC grants approval of an NSR device, the study may begin immediately and no IDE will be required.

If the HRAC does not agree and believes the device poses significant risk, the study may not begin until both the HRAC and the FDA approve the investigation. The HRAC will notify the sponsor and investigator of the SR decision. The investigator will be required to obtain an IDE from the FDA. The study, if approved by HRAC, will be conducted as a SR device trial.

Information that the HRAC must review in making the determination between SR and NSR include the following (which should be provided with the initial protocol submission):

- Reports of prior investigations conducted with the device
- The proposed investigational plan
• Subject selection criteria
• Monitoring procedures planned for the study
• Sponsor’s risk assessment and rationale
• Sponsor’s statement detailing any other IRBs that have reviewed the proposed study and what determinations were made.
• Sponsor’s statement regarding any assessments of the device’s risk that may have been made by the FDA.

The HRAC’s risk determination is based upon the proposed use of a device in an investigation and not the device alone. Factors that must be considered by the HRAC when evaluating the risk of a device include:
• The nature of the harm that may result from the device
• Is the potential harm to subject’s life threatening?
• Could the potential harm to subjects result in permanent damage to or impairment of body structure or function?
• Could the use of the device necessitate medical or surgical intervention to prevent damage to body structure or function?
• If the subject must undergo a procedure as a part of the investigation study, e.g., a surgical procedure, the IRB must consider the potential harm from the procedure in addition to the potential harm of the device.

The FDA makes the ultimate decision in determining if a device study is SR or NSR. If it does not agree with HRAC’s decision that a device study presents an NSR, and IDE application must be submitted to the FDA. Likewise, if a sponsor or investigator requests an IDE from the FDA for a presumed SR device study, but the FDA classifies the study as NSR, the IDE application will be returned and the investigator should resubmit the study to the HRAC as an NSR with the returned application.

INVESTIGATOR’S RESPONSIBILITIES RELATED TO INVESTIGATIONAL DEVICES
21CFR 812.110 states that investigators may not obtain informed consent for the use of a device without first obtaining IRB and FDA approval. Investigators must assure that the device is placed under their direct supervision and supplied only to persons authorized to receive the device. If there is not a sponsor for an Investigational Device study, the Primary Investigator will be responsible for the internal monitoring and reporting functions of sponsors as listed in 21 CFR part 812. The Investigator is also responsible for the control, disposal and record keeping related to investigational devices. Investigators are also responsible for maintaining the case histories of the subjects involved in investigational device trials. Investigational devices may not be used outside the supervision of the investigator.

STUDIES OF DEVICES WITH THE FDA 510K DESIGNATION
FDA regulations allow a manufacturer/sponsor to claim that a new device is substantially equivalent to models that FDA has already approved for marketing. Safety and efficacy testing of 510 K devices, or use of 510K devices in clinical protocols, requires review by the
HRAC and approval before the study may begin. Application to the HRAC should include verification of the device’s 510K status.

**EMERGENCY USE OF INVESTIGATIONAL DEVICES**

If, in the opinion of the investigator, a situation exists where an investigational device is required to protect the life or physical well being of a subject in an emergency, outside of the investigational trial, the investigator should contact the HRAC Chairperson and request emergency acknowledgment. Emergency Use of Investigational Devices should be reported in writing to the sponsor and the HRAC immediately by the investigator. Ideally, communication with the sponsor and the HRAC should occur before any test article is used outside of the research context. If the investigator is the sponsor, he/she is required to notify the FDA of the emergency use within 5-working days of the event.

**HUMANITARIAN USE DEVICES (HUD) OR CUSTOM DEVICES**

Investigators who wish to use devices classified by the FDA as Custom or Humanitarian Use should consult the HRAC office for guidance before using such a device or submitting a protocol.

**INVESTIGATIONAL DEVICES THAT MAY BE ELIGIBLE FOR EXEMPTION**

Some investigational devices are exempt from the FDA regulations. These included certain diagnostic devices, minor modifications of marketed devices or custom devices. *Investigators should request guidance from the HRAC if unsure of the device status before use.*

All devices, including those exempt from FDA regulations, require review and approval by the HRAC before use in patients or subjects.
RESEARCH INVOLVING VULNERABLE POPULATIONS

Certain groups of human subjects are considered to be particularly vulnerable to coercion or undue influence in a research setting. These groups and their special attention during the research process are outlined in 45 CFR 46.111(b) and 21 CFR 56.111(b). The regulations identify additional requirements for review and approval of research involving fetuses, pregnant women, and human in vitro fertilization, 45 CFR 46 Subpart B, prisoners, 45 CFR 46 Subpart C, and children, 45 CFR 46 Subpart D.

Vulnerable Populations

- Children
- Wards of the State
- Prisoners
- Pregnant Women and fetuses
- Persons who are mentally disabled or otherwise cognitively impaired
- Economically or educationally disadvantaged persons

In reviewing research projects involving all categories of vulnerable subjects, the HRAC must ascertain that their use is adequately justified and that additional safeguards are implemented to minimize risks unique to each group. A summary of the additional requirements for review and approval of research involving children, prisoners, and pregnant women and fetuses is presented below.

CHILDREN

Federal regulations (Title 45 CFR Part 46, Subpart D) require that investigators explicitly address the measures taken to protect the rights and welfare of children participating in protocols.

DEFINITION OF CHILDREN

"Children" are defined 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." 45 CFR 46.402(a). In the state of Arkansas, "children" include any persons under the age of 18 (unless the child has been emancipated by court order, marriage, or is on active military duty). Almost all research protocols involving children requires full review by the convened HRAC.
Investigators submitting proposals to the NIH for human subject research must include children in the study unless there are scientific or ethical reasons not to include them. The proposals must specifically include a description of plans for including children. And, if children will be excluded, the application must present an acceptable justification for the exclusion. Investigators should review the NIH Policy and Guidelines before submitting their proposals.

*National Institutes of Health (NIH) Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects (March 6, 1998)*

Categories of research involving children

45 C.F.R. 46, Subpart D, classifies research involving children into one of four categories depending upon the risks and benefits of the proposed research, which can be approved as follows:

<table>
<thead>
<tr>
<th>Category of Risk to the Child</th>
<th>Research Examples</th>
<th>Consent Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1 Minimal Risk</td>
<td>Research on children's attitudes about food preferences, surveys about play activities,</td>
<td>One parent/guardian permission</td>
</tr>
<tr>
<td>Category 2 Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects</td>
<td>Clinical drug trials for a new anticonvulsant in children with seizure disorders. Investigation of coping strategies of children living in foster care, research on the effectiveness of drug-use intervention programs for children testing positive for drug use</td>
<td>One parent/guardian permission</td>
</tr>
<tr>
<td>Category 3 Greater than minimal risk and no prospect of direct benefit to individual subjects but likely to yield important generalizable knowledge about the subject's disorder or condition.</td>
<td>Research using a non-approved drug or device which will provide no direct benefit to the subject, but will likely provide important information concerning efficacy for future subjects.</td>
<td>Both parents’ permission, unless one is not reasonably available, deceased, unknown, legally incompetent, or does not have legal responsibility for care of the child.</td>
</tr>
<tr>
<td>Category 4 Otherwise not approvable, but presents an opportunity to understand serious health or welfare problems of children</td>
<td>Phase I drug study in seriously ill children</td>
<td>Generally not approved, requires a panel of experts</td>
</tr>
</tbody>
</table>
Category 1: "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 examination or tests. Minimal risk protocols on children are approvable in accordance with the general HRAC review criteria provided that adequate provisions are made for soliciting the assent of the child and parental permission.

Category 2: Research involving greater than minimal risk, but presenting the prospect of direct benefit to individual subjects. is approvable in accordance with the general HRAC review criteria if
- The risk is justified by the anticipated benefit to the subjects
- The relationship of risk to benefit is at least as favorable as any alternative approach
- Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

Category 3: Research involving greater than minimal risk and no prospect of direct benefit to individual subjects but likely to yield important generalizable knowledge about the subject’s disorder or condition. Such research is approvable in accordance with the general HRAC criteria if:
- The risks represent a minor increase over minimal risk;
- The intervention or procedure presents risks to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- 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
- Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

Category 4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. This research is generally not approvable by the HRAC without the appointment of and review by a separate panel of experts.

Assent of Children

Recruitment of children as study participants should occur in a non-coercive manner. All participants in the study should be fully informed in language and terms they are able to understand. Although consent from a parent (or parents/legal guardian) must be obtained before children are enrolled as research subjects, an investigator must also inform the child of the purpose of the voluntary nature of their participation.
“Assent“ means a child’s affirmative agreement to participate in research. A child who fails to object to participation is not necessarily assenting to participation. Assent is not passive.

The HRAC must determine for all studies involving children

- The age of subjects where assent is required
- How and at what age assent is to be documented

Assent must be accompanied by the signed informed consent of the parent (parents) or legal guardian of the child. The investigator must also inform the child of the purpose and the voluntary nature of their participation. This must be modified to the child’s age and ability to comprehend. The following allow guidelines for age ranges in obtaining assent from children. These guidelines are recommended and are not intended to replace any institutional policies and procedures regarding the assent of children.

- Children younger than 7 years of age:
  If appropriate as determined by the child’s age and cognitive development, the investigator should administer a simple oral explanation of the study procedures to be conducted.

- Children 7 years of age and less than 18 years of age:
  Written assent must be obtained from the child if it is an HRAC requirement. Assent of a child should be obtained in the presence of a parent/legal guardian and witness.

The HRAC encourages the Principal Investigator to submit classification information related to the study’s risk category, age required for assent and method of assent documentation in the initial study submission packet.

HRAC’s purpose is not to demand adherence to rigid criteria based solely on age, but to use the age ranges above as guidelines for approaching children after taking into account their emotional and cognitive development. For all children, but especially those with developmental disorders, the age ranges listed above refer to the cognitive rather than the chronological age.

The HRAC reserves the right to require both parents’ permission on selected protocols if the committee waives child assent or if additional requirements from the PI are deemed necessary by the convened IRB. The HRAC may consider a request from that PI that the permission of one parent is sufficient for research involving greater than minimal risk, if there is a clear prospect of direct benefit to the child-participant.
The requirements of parental permission may be waived in those cases where it is clear that the parents’ interests do not adequately reflect the child’s interests (e.g., research on child abuse or neglect). These research protocols require investigators to develop special procedures, which must be approved by the convened HRAC that protects the rights and welfare of the children asked to participate.

**There are NO exemptions for Research involving Children’s Participation in Surveys or Interviews**

Unlike research involving adults, the exemption at 45 CFR 46.101(b)(2) for research involving survey procedures, interviews, educational tests, or public observations (except where the investigator does not participate in the activities being observed) does not apply to research involving children. 45 CFR 46.401(b).

**Child Abuse Reporting**

The State of Arkansas requires the reporting of suspected child abuse or neglect. Investigators must abide by this law. If the protocol involves interviewing children about topics that might lead to a suspicion or to knowledge on the part of the investigator of child abuse or neglect, the child (and parent or guardian) must be informed of the reporting requirement as part of the informed consent process.

**The following sentence(s) should be integrated into the currently required Informed Consent Document among the statements about confidentiality and its limits:**

“We will attempt to maintain the confidentiality of any information you/your child give us in the course of this study. However, you should be aware of limits to the confidentiality of your information.”

“The researcher may also be required to report any child abuse or any intention you have to hurt yourself or others. The researcher, if ordered to do so by a court of law, may be required to disclose information you have provided.”

**WARDS OF THE STATE**

Where children are wards of the state or another agency or institution, additional restrictions apply. They may only be included in research that is related to their status as wards, or which is conducted in schools or other institutions in which a majority of children are not wards. If the HRAC approves research under this provision (45 CFR 46.409), it must appoint an advocate for each child that is a ward.

**EMANCIPATED MINORS**

There are exceptions to the rule of obtaining assent and seeking parental consent for individuals considered emancipated minors by the state of Arkansas. "Emancipated minors"
may include individuals under the age of 18, living on their own and financially independent from their parent or legal guardian, have borne a child, or are married. Consent is sought from an emancipated minor; not assent.

**PRISONERS**

45 CFR 46, Subpart C, provides additional safeguards for prisoners since "Prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and un-coerced decision whether or not to participate as subjects of research." A "Prisoner" includes any person who is sentenced to a penal institution under a criminal or civil statute as well as individuals detained in other facilities by virtue of statutes or commitment procedures, which provide alternatives to criminal prosecution or incarceration in a penal institution 45 CFR 46.303(c).

Research involving prisoners does not qualify for exemption from IRB review.

Categories of research involving prisoners (45 CFR 46.306(a))

- Studies regarding 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.
- Studies of prisons as institutions, or of prisoners as incarcerated persons, if those studies present no more than minimal risk or inconvenience to the subjects.
- Research on conditions affecting prisoners as a class after HHS publishes a notice in the federal register.
- Research on practices that are intended, and reasonably likely, to enhance the well-being of the subjects; however, if some of the prisoners will be assigned to control groups which will not benefit from the research, then the study must first be approved by HHS.

In addition to the general requirements for review, in reviewing prisoner research, IRBs are required by 45 CFR 46.305(a) to:

- Ensure that the membership of the IRB reviewing the protocol includes a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity, and that the majority of the HRAC is not associated with the penal institution involved. If no current member of the HRAC meets the prisoner or prisoners’ representative criteria, then the HRAC Chair will identify and recruit a qualified individual to fulfill this requirement and advise the HRAC. In addition, a majority of the HRAC members at the meeting must not be associated with the prison.
• Review that any advantages that prisoners will realize as a result of participating in the research, when compared to the general living conditions within the prison, are not so great as to impair prisoner’s ability to weigh the risks and benefits of participation and freely choose whether to participate.

• Review that the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.

• Review procedures for selecting subjects to determine whether they are fair, and free from arbitrary manipulation by prison authorities or prisoners.

• Review that control subjects will be selected randomly from among the group of eligible volunteers, unless the PI justifies a different procedure.

• Review the information presented during the recruitment and consent procedures to ensure that it is in a language, and level of complexity, that is understandable to the subject population.

• Ensure that the parole board will not take participation in the study into account, and that each prisoner will be informed that participation will have no effect on parole.

• Ensure that adequate provision will be made for follow-up care as necessary.

In addition, the FDA imposes specific restrictions on the use of prisoners in research involving FDA-regulated products. Use of prisoners in these studies is prohibited unless the specific requirements of this section are met (21 CFR Part 50, Subpart C.) When an HRAC reviews research falling within this category, its assurance provides for OHRP to be notified that the above criteria have been met.

Do not enroll a prisoner in an ongoing, HRAC approved study without the approval of the committee. If a study subject becomes a prisoner during the course of the research, notify the HRAC immediately.

PREGNANT WOMEN AND FETUSES

45 CFR 46, Subpart B, provides additional protections for research involving pregnant women. Pregnant women should not be excluded from research as participants if the risk to the fetus is minimal. If pregnant women are included in a research protocol, the informed consent must address the research activity and its possible impact on the fetus.

Researchers should obtain informed consent from both the pregnant woman and the father of the fetus. Consent by the father is not necessary if:

• The purpose of the study is to meet the health needs of the mother
• The identity or whereabouts of the father can not be reasonably ascertained
• The father is not reasonably available
• The pregnancy is the result of rape.

Research targeting pregnant women as subjects does not qualify for an exemption.
COGNITIVELY IMPAIRED

The participation of cognitively impaired individuals in research typically falls in categories that cannot be reviewed using exempt procedures. In addition, projects involving cognitively impaired individuals must specifically address how an individual’s capacity to give informed consent will be determined. Examples of cognitive impairment include: diagnosed mental retardation, dementia, and coma.

- The HRAC is not in a position to determine if an individual identified with a cognitive impairment has the capacity to give informed consent. However, the HRAC has developed a decision algorithm tool to assist investigators in making this determination. This is included in the Appendix I.

CAVHS permits the use of a surrogate consent process for persons who are cognitively impaired.

The HRAC advises the use of the decision algorithm when it is unclear if cognitive impairment may prevent a subject from giving informed consent.

ECONOMICALLY OR EDUCATIONALLY DISADVANTAGED

For research involving economically disadvantaged subjects, special care must be taken to assure that the financial inducements offered do not constitute the sole grounds for the subject participation in the research protocol. Financial inducements should also not be used to assume risks that subjects would not ordinarily incur.

The consent form for research involving educationally disadvantaged subjects should be written with special attention to assure that terminology has been sufficiently simplified. The investigator should discuss orally aspect of the study with the subjects to insure their understanding.

Illiterate English Speaking Subjects

An investigator into an HRAC approved study may enroll individuals, who can speak and understand English, but cannot read or write. The potential subject must be able to place a written mark on the consent form.

The subject must also be able to
- Comprehend the concepts of the study and understand the risks and benefits of the study as it is explained verbally, and
- Be able to indicate approval or disapproval for study enrollment.

If an investigator uses the above method to obtain consent, there must be documentation on the subject’s consent form specifying what method was used to communicate the
information and the specific means that the subject communicated agreement to study participation.

**EMPLOYEES AS SUBJECTS**

Employees may be recruited as study subjects. However, investigators should avoid using their own employees as research participants because of potential coercion and undue influence. The preferred method of recruiting employees for research studies is notices on institutional bulletin boards or third party notification, e.g. word of mouth. No directed advertising among one’s own employees should be used. Recruitment notices, including bulletin board or newspaper ads, are to be submitted to the HRAC before they are posted or submitted for publication.

**STUDENTS AS SUBJECTS**

Recruiting students as subjects represents a potential problem for investigators. Possible coercion is an issue from a student participating in a study conducted by his or her advisor. Undue influence is an issue whenever a student’s participation will be made known to someone who holds power over his or her academic status. How the investigator plans to handle potential problems of coercion and undue influence must be addressed in the initial submission of the study to the HRAC. In particular, activities that involve students who report directly to the investigator or attend a class for which the investigator has responsibility must be described.

**NON-ENGLISH SPEAKING SUBJECTS**

Non-English speaking subjects may not be excluded from therapeutic studies on the basis of language use if there is a possibility that they might benefit by participating in the study.

If a research subject does not understand English, the informed consent document should be in the language readily understood by the subject to meet the requirements of 21 CFR 50.20. If the principal investigator anticipates that consent interviews will be routinely conducted in a language other than English, the HRAC requires a translated consent document be submitted with the original protocol for approval. It is the investigator’s responsibility to ensure that the translation is accurate.

As required by 21 CFR 50.27, a copy of the consent document must be given to each subject. While a translator may be helpful in facilitating conversation with a non-English speaking subject, verbal translation of the consent document must not be substituted for a written translation.

If a Non-English speaking subject is unexpectedly encountered, investigators will not have a written translation of the consent document and must rely on oral translation. Investigators should carefully consider the ethical/legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented the subject’s consent will not truly be informed and may not be legally effective. If investigators enroll subjects without an IRB approved written translation, a "short form" written consent
document, in a language the subject understands, must be used to document that the elements of informed consent required by 21 CFR 50.25 were presented orally. At the time of consent for non English-speaking subjects, the

- Short form document should be signed by the subject or the subject’s legally authorized representative
- Summary (i.e., the English language informed consent document) should be signed by the person obtaining consent as authorized under the protocol, and
- Short form document and the summary should be signed by the witness

**Example:** You have a German-speaking subject in the Intensive Care Unit. He speaks no English. Your communication with him has been through a local clergyman. A German short-form version of the written consent document has been approved by the HRAC. A summary of the English Language Informed Consent Document is given to the clergyman who translates this to the subject. The German short-form version of the written consent document must be signed by the subject (or subject’s legally authorized representative) and the witness. The clergyman must sign the English language informed consent document approved by HRAC.

A sample short form document is included in Appendix J.
PAYMENT/REIMBURSEMENT OF RESEARCH SUBJECTS

Federal regulations and the various codes of ethics governing human subject research require that no “undue inducements” be offered potential research subjects in order to secure their participation in a study. Payment is not considered a benefit of study participation. To comply, the HRAC has adopted the following guidelines regarding payments to subjects:

- Subjects should not be induced to participate in research primarily by the prospect of financial gain. Payment is not a benefit. It is compensation for services.
- There must be parity in compensation for completion of research activities whether subjects, controls, or active participants.
- Investigators who plan to provide any payment/reimbursement to subjects for any reason must indicate this clearly in the informed consent, which must be approved by the HRAC.

Special Considerations for CAVHS Subject Reimbursement

CAVHS policy prohibits paying subjects to participate in research when the research is an integral part of subjects’ medical care and when it makes no special demands on the subject beyond those of medical care. Payment may be permitted with prior approval of the HRAC, in the following circumstances:

- No direct subject benefit (and standard of practice is to pay subject)
- When other subjects in a multi-institutional trial are being paid for the same participation
- Payments to research subjects are made elsewhere in comparable situations (decided upon by HRAC)

CAVHS Payment Procedure

- Substantiate that proposed payments are reasonable and commensurate with contribution of subject
- State the terms of the subject participation agreement and the amount in the consent form
- Substantiate that payments are fair and appropriate and that they do not constitute undue pressure on the veteran subject to volunteer for the research study

VA R& D Committee and the HRAC shall review all payment of subjects (in excess of reimbursement for travel) in light of the above concerns.

BILLING OF THE RESEARCH SUBJECT

Primary investigators are required to follow the policies and procedures of the institution when billing research and clinical costs. At UAMS, the PI is to follow the policy “Billing for Research Procedures” (Appendix Q). All efforts should be made to assure that research
subjects are billed in a correct and ethical manner. Consent forms should clearly differentiate what costs the subject will be responsible for and what costs the study will pay.
EDUCATIONAL POLICIES AND RESOURCES

INVESTIGATORS AND STUDY STAFF

It is the policy of the HRAC that all investigators desiring to engage in research using human subjects must familiarize themselves with policies and procedures and related federal regulations. Investigators should maintain an on-going relationship with the HRAC to gain assistance in following policies and procedures during the conduct of their studies. This will help assure that both investigators and the HRAC remain in compliance with all state and federal regulations regarding research involving human subjects.

Research staff other than the PI, e.g. sub-investigators, coordinators, data managers, should complete competency-based training applicable to their research responsibilities and the protection of human subjects.
HRAC AUTHORITY IN NON-COMPLIANCE ISSUES

When the HRAC is notified of events for which review is necessary by the convened HRAC, the HRAC chair or designated Chair will bring the issue to the attention of the HRAC for appropriate action.

If the HRAC is notified of events that indicate potential regulatory noncompliance, the committee will attempt to provide assistance through written contingencies to assist them with achieving compliance without the imposition of sanctions. However, in cases where investigator cooperation does not occur, and when it is determined that the safety or welfare of subjects or the integrity of the institution are or have been placed at risk, sanctions may be imposed.

The HRAC has the regulatory authority to:
- Increase the frequency of continuing review
- Appoint a subcommittee of appropriate qualified HRAC members to investigate alleged noncompliance issues and advise the convened HRAC
- Suspend study approval until compliance is achieved
- Terminate individual research protocols
- Report specific noncompliance activities of the investigator to governmental entities.

The HRAC also has the regulatory authority to recommend additional sanctions to the Vice Chancellor for Academic Affairs and Sponsored Research. These sanctions include:
- Research privilege probation
- Suspension of research privileges
- Termination of research privileges
- Embargo of publications.

The principal investigator will be notified in writing if a subcommittee is required to investigate noncompliance issues. The results of the subcommittee will be communicated in writing to the Investigator within 30 days following completion of the review. These communications will either notify the investigator that
- The research may continue
- That the research may continue after contingencies are completed
- That the research may not continue due to placement of sanctions

The HRAC is required to report to the Vice-Chancellor for Academic Affairs and Sponsored Research, institutional officials, sponsoring agencies, the Office for Human Research Protections (OHRP) and grants management officers any suspension or termination of research protocols. If the protocol involves drugs or devices, the HRAC is also required to notify the Food and Drug Administration (FDA).

If the protocol involves the Veterans Administration, HRAC will also notify the VA R & D Committee and the Office for Research Compliance and Assurance (ORCA).
The HRAC is also required to report to these agencies any unanticipated problems involving risks to subjects or others, and serious or continuing noncompliance as determined by the HRAC (45 CFR Part 46.103(b) (5)).

**STUDY CLOSURE**

Study closure is a voluntary process and carries no punitive implications. Closure is not reported to institutional officials or to the department or agency head. Closure typically applies in the following situations:

- At the completion of the study (i.e. new enrollment is closed and all data collection and analysis are completed);
- If the investigator chooses to close the study (e.g. the study has not met its enrollment goal, but the investigator does not plan to enroll new subjects, collect additional data from enrolled subjects, or perform any additional data analysis);
- The investigator leaves the institution and does not intend to transfer responsibility for the study to another investigator.

The investigator must request study closure. The HRAC office must be notified when a study is completed. This notification should be sent when all participants have completed treatment and follow-up phases of the study and analysis is completed to the point that the participant’s records will no longer be needed. The Investigator must complete the **Study Closure Form** (Appendix L) that addresses the following:

- Protocol title and record number
- Name of PI
- Number of subjects enrolled
- Number of subjects completing study
- Any publications that have resulted from data collected during the study
- Any adverse events that have not been previously reported

The HRAC office must be notified within 90 days of closure of the study. If no subjects have been enrolled in the previous five years and all data collection is complete, the investigator should close the study. Studies that are not closed properly by the PI may be terminated.

For studies classified as “exempt”, the HRAC office needs only notification that the study has been closed.

**Reopening of a closed study**

An investigator may reopen a closed study within one year of that closure with a written request to the HRAC and updated information. After one year of closure, a protocol must be resubmitted.
SUSPENSION

Suspension is a non-permanent interruption of research activities. Suspension may occur for the following reasons:

- Unexpected and serious adverse effects that significantly increase risks relative to benefits
- Evidence that an investigator failed to adequately protect participants in a research study
- Willful or repeated failure to comply with federal regulations, state laws, or institutional rules that govern human research activities
- Proven research fraud or scientific misconduct
- At the request of institutional officials who have been charged with responsibility for oversight of research involving human subjects (e.g. the Chancellor or the Vice Chancellor for Academic Affairs and Sponsored Research)
- At the request of the study sponsor, the FDA, the Office for Human Research Protections, or other duly authorized regulatory or governmental department or agency head
- Any other reason deemed necessary by a simple majority vote of the convened HRAC (a quorum must be present)
- The HRAC or the investigator decides that new enrollment and risk-bearing activities should be interrupted pending an investigation into any problem or alleged problem with a particular study
- The continuing review application has not received final approval within 12 months after the last review (or less than 12 months if the study was designated for review at more frequent intervals). This suspension occurs automatically if more than 12 months have passed since the last approval was granted. This is the only situation for which suspension is automatic (i.e. without any action on the part of the committee). It is the responsibility of the investigator to monitor approval dates to ensure that HRAC approval for each study is up to date.

Any study may be suspended by majority vote of the HRAC members. In contrast to a study that has been terminated, a study that is suspended may be reopened without resubmission as a new protocol with a new consent form. If discontinuation of study-related therapy might result in increased risk of significant harm to an individual or a group of study subjects, the HRAC reserves the right to permit continued therapy with an investigational drug, device, or biologic for subjects who are already enrolled in a treatment study. Enrollment of new subjects generally will not be permitted. However, at the request of the investigator, the HRAC Chair or a designee may permit enrollment into a suspended study if and only if there is no alternative therapy for a life-threatening condition.

At the time the study is suspended, the HRAC will establish a unique and specific plan that, if completed by the PI, will lead to re-review of the study resulting in a decision as to whether to continue or end the suspension or to terminate the study. An audit of the investigator and his/her studies may be undertaken. As a minimum, the unique and specific plan will include a set of questions or conditions that must be addressed completely by the investigator and a
specified time period during which the investigator must provide a written response. The HRAC may not end the suspension for CRR delinquency until the requested information is provided by the investigator and is reviewed and approved by the committee.

If an emergency occurs, institutional officials, the HRAC Chair, or an appropriately appointed designee may suspend a study until the next regularly scheduled meeting of the HRAC. Alternatively, the Chair may convene an emergency meeting of the full committee to consider suspension of a study before the next regularly scheduled meeting. In the event that an emergency suspension is considered, the Chair must notify the PI and appropriate institutional officials (e.g. the Chancellor, the Vice Chancellor for Academic Affairs and Sponsored Research, the Director of the ORSP, direct supervisors of the PI, and the appropriate department of agency head). The full committee at the next scheduled meeting must review all emergency suspensions.

TERMINATION

Termination is a non-voluntary process that results in permanent discontinuation of all study-related activities. In contrast to a study that has been voluntary closed, a study that has been terminated may not be reopened without submission and approval of a new protocol. Termination may occur for the following reasons:

- Unexpected and serious adverse effects that significantly increase risks relative to benefits
- Evidence that an investigator failed to adequately protect participants in a research study
- Willful or repeated failure to comply with federal regulations, state laws, or institutional rules that govern human research activities
- Proven research fraud or scientific misconduct
- At the request of institutional officials who have been charged with responsibility for oversight of research involving human subjects (e.g. the Chancellor or the Vice Chancellor for Academic Affairs and Sponsored Research)
- At the request of the study sponsor, the Federal Drug Administration, Office for Human Research Protections, or other duly authorized regulatory or governmental department or agency head
- The investigator leaves the institution and fails to request closure of the study or fails to reassign the investigator’s responsibilities and duties to another qualified investigator
- Any other reason deemed necessary by a simple majority vote of the convened HRAC (a quorum must be present)

A research study that is terminated by the HRAC will be reported to the study sponsor, institutional officials, and to the appropriate department or agency head. Disciplinary action or sanctions may be appropriate. Decisions will be made on a case-by-case basis. At the HRAC level, appropriate sanctions might include a request for further information, an audit of ongoing clinical research activities, or suspension of all ongoing research conducted by the same investigator or group of investigators until all research activities are shown to be free of
similar problems. The investigator will be reminded that if a study is terminated, no further enrollment or data collection is permitted.

If discontinuation of study-related therapy might result in increased risk of significant harm to an individual or a group of study subjects, the HRAC reserves the right to permit continued therapy with an investigational drug, device, or biologic for subjects who are already enrolled in a treatment study. Enrollment of new subjects will not be permitted.

Institutional officials have the right to terminate any research activity without review by or approval of the HRAC. Institutional review is broader in scope and may result in termination for reasons other than those listed above.

**APPEALS PROCEDURES FOR HRAC ACTIONS**

Investigators must try to resolve concerns about HRAC decisions regarding their research protocols by discussing their concerns with the Chair of the HRAC, the Vice Chancellor for Academic Affairs and Sponsored Research, or the Research Compliance Office.

The PI can appeal any action of the HRAC, including actions on exempt, expedited, and fully convened HRAC protocols. Investigators wishing to appeal HRAC decisions should address a formal letter requesting an appeal to the Vice Chancellor for Academic Affairs and Sponsored Research. The formal letter requesting an appeal should:

- Identify the project
- Identify the HRAC action in question
- Describe any steps taken to resolve the concern, and
- List the reason for appealing the HRAC decision.

Upon receipt of the letter, the Vice Chancellor for Academic Affairs and Sponsored Research will review the HRAC decision in question and receive additional information from other relevant sources.
HRAC RECORDS

The HRAC office maintains the following records:

1. A current list of HRAC membership and qualifications.
2. Agenda and minutes of meetings, including information regarding member attendance, discussions held, decisions made, and voting results.
3. All materials submitted to the committee for initial and continued review of each study including: IRB applications, protocols, submitted and final consent forms, serious adverse event and death reports, proposed amendments, progress reports, correspondence generated between the committee and the investigators, and, where applicable, correspondence from sponsoring agencies.

All records are retained electronically following the inactivation or closure of a project.
OFFICE OF RESEARCH COMPLIANCE

The Office of Research Compliance (ORC) and was established to help researchers and the University as a whole, to achieve and maintain compliance with federal regulations governing research. The Office of Research Compliance is a division of Academic Affairs and Sponsored Research, but is independent of the HRAC. This Division is responsible for the development and administration of compliance programs required by federal and state agencies and programs in order to conduct research at UAMS, CAVHS, and ACH.

The conducting of audits of research protocols is a component of the Office of Research Compliance. These audits will include random audits and “for cause” audits. The HRAC may request the Office of Research Compliance to conduct an audit based on an investigator’s protocol activities (large numbers of active protocols, subject enrollment, reported protocol deviations and/or serious adverse events). Audit findings will be reported to the investigator and the Vice-Chancellor for Academic Affairs and Sponsored Research.
REFERENCES

Ethical Principles and Codes

Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research
Guidelines for Good Clinical Practice
International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)
ICH Considerations for Clinical Trials
National Bioethics Advisory Commission
Nuremberg Code
World Medical Association Declaration of Helsinki

Federal Regulatory & Advisory Guidelines

Code of Federal Regulations
Department of Veterans Affairs M3-Part I
FDA Information and Regulations
Investigational Devices 21 CFR 812 – U.S. FDA
Investigational Drugs 21 CFR 312 and 314 – U.S. FDA
NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects
Protecting Human Research Subjects: Institutional Review Board Guidebook (NIH/OPRR)
Protection of Human Subjects 21 CFR 50 – U.S. FDA
Protection of Human Humans 38 CFR 16 – U.S. FDA
Protection of Human Subjects 45 CFR 46 – U.S. FDA

Federal Regulatory Agencies

National Institutes of Health
Office of Biotechnology Activities
Office for Research and Compliance
Office of Human Research Protections
U.S. Food and Drug Administration

Local References

HRAC Investigators Handbook for Human Studies
Multiple Project Assurance – UAMS HRAC
UAMS Faculty Handbook

Accreditation References

VA Human Research Protection Accreditation Program Accreditation Standards, NCQA, Version 1.0 August 16, 2001
APPENDIX A: GLOSSARY

Accrual
The process of getting subjects into a trial or the number of subjects in a trial or planned to be in a trial.

Assent
A child's affirmative agreement to participate in research. Mere failure to object should not be construed as assent [45 CFR 46.405 (b)].

Arm
Any of the treatment groups in a randomized trial.

Audit
A comparison of Raw Data and associated records with the interim or Final Study Report in order to determine whether the Raw Data have been accurately reported, to determine whether testing was carried out in accordance with the protocol and Standard Operating procedures (SOP), to obtain additional information not provided in the Final Study Report, and to establish whether practices were employed in the development of data that would impair their validity.

Benefit
A valued or desired outcome; an advantage.

Blind
Used with respect to a randomized trial, a randomized trial is blind if the subject is not told which arm of the trial he or she is on.

Certificate of Confidentiality
Where data are being collected from subjects about sensitive issues (such as illegal behavior, alcohol or drug use, or sexual practices), researches can obtain an advance grant of confidentiality from the Public Health Service that will provide protection against involuntary disclosure of the research subject’s identity and the subject’s participation in the study, even against a subpoena for research data.

Children
Persons who have not attained the legal age for consent to treatment procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted [45 CFR 46.402 (a)].
**Clinical Trials**

Any form of planned experiment, which involves subjects and is designed to elucidate the most appropriate treatment of future subjects with a given medical condition. The essential characteristic of a clinical trial is that the results based on a limited sample of subjects are used to make inferences about how treatment should be conducted in the general population of subjects who will require treatment in the future.

**Cognitively Impaired Individuals**

Those persons having a psychiatric or developmental disorder that affects cognitive or emotional functions to the extent that the capacity for judgment and reason is significantly diminished.

**Compassionate Use**

Use of an investigational drug for treatment of an individual subject for a single use or a single course of treatment that is not covered by an existing IRB approved protocol.

**Compliance**

Action in accordance with a request or institution.

**Double Blind**

Used with respect to a randomized trial, a randomized trial is Double Blind is neither the subject or the subject's investigator or physician are told which Arm of the study he or she is on. The purpose is to prevent any bias in treatment or reporting of results from being introduced.

**Economically Disadvantaged Individuals**

Those persons who struggle to provide basic necessities for themselves and their families or communities. The use of financial incentives for research participation is a special issue with economically disadvantaged persons.

**Educationally Disadvantaged Individuals**

Those persons who may have educational deficits, learning disabilities, or cultural backgrounds that limit communication with a researcher.

**Elderly Subjects**

Persons over the age of 65 years of age.

**Emancipated Minor**

A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by a virtue of assuming adult responsibilities, such as self-support, marriage or procreation.
Emergency Use

Use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which is not sufficient time to obtain IRB approval (21 CFR 50.27).

Experimental Group

The Arm of a randomized trial that gets the new or “experimental” treatment. In some randomized trials, both of the treatments are standard treatments.

Federal Wide Assurance (FWA)

Document, which formalizes an institution’s commitment to protect human, subjects and is required by any institution that participates in Federally supported human subject research.

Guardian

An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care [45 CFR 46.402 (3)].

Human Subject

A living individual about whom a profession or student investigator conducting research obtains data through intervention or interaction with the individual or collects identifiable private information 45 CFR 46.102(f). An individual who is or becomes a participant in research, either as a recipient of a test article or as a control 21 CFR 56.102(e).

Informed Consent

The process of ongoing explanations to help a subject make educated decisions about whether to begin or continue participating in a research protocol or procedure.

Informed Consent Document

A written summary of the research protocol (including its purpose, treatment procedures and schedule, potential risks and benefits, alternative to participation, etc) and explanation of the rights of a research subject. Designed to begin the informed consent process.

Inspection

Officially conducted audit by relevant authorities at the site of investigation and/or at the sponsor site to verify adherence to regulations.

Institutional Review Board

Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects [21 CFR 56.102(g)].
Investigation Device Exemption (IDE)
The process by which the FDA permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations of that device.

Investigational New Drug Application (IND)
The process by which new drugs or biologics, including the new use of an approved drug, are registered with the FDA for administration to human subjects. An IND number is assigned by the FDA to the drug or biologic for use in tracking.

Investigator (Principal investigator)
An individual who conducts an investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

Investigator/Sponsor
A term defined in the FDA regulations as an individual with responsibility for initiating and conducting a research study.

In vitro fertilization
Any fertilization of the human ova that occurs outside the body of a human female.

Life-Threatening
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.

Mature Minor
Someone who has not reached adulthood (as defined by state law) but who may be treated as an adult for certain purposes (e.g., consenting to medical care). Note that a mature minor is not necessarily an emancipated minor.

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. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of routine physical examination.

Multicenter
Refers to a study that is being done at several hospitals or institutions simultaneously.

**NonSignificant Risk (NSR) Device**
A device that does not meet the definition of a significant risk device.

**Permission**
The agreement of parent(s) or guardian to the participation of their child or ward in research [45 CFR 46.402 (c)].

**Placebo**
An inert substance, such as a sugar pill.

**Pregnancy**
The period of time from the confirmation of implantation until the expulsion or extraction of the fetus.

**Prisoner**
Any person who is sentenced to a penal institution under a criminal or civil statute as well as individuals detained in other facilities by virtue of statutes or commitment procedures, which provide alternatives to criminal prosecution or incarceration in a penal institution [45 CFR 46.303(c)].

**Protocol**
A document, which states the rationale, objectives and statistical design and methodology of the trial, with the conditions under which it, is to be performed and managed.

**Protocol Deviation**
An unplanned or unforeseen change in an ongoing study that is not covered under an approved HRAC protocol.

**Protocol Violation**
An unplanned or unforeseen change in an ongoing study that is not covered under an approved HRAC protocol. Usually represents a more serious non-compliance problem than a protocol deviation and is noted after the fact or based on a technical error resulting in the protocol or standard operating procedure not being followed.

**Randomized Trial**
A clinical trial with at least two arms, in which the decision as to which arm a new subject is assigned, is made by change, for instance, by the flip of a coin or by using a computer to select randomly.

**Research**
A systematic investigation developed to develop or contribute to general knowledge.
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."

Significant Risk (SR) Device

A device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is an impact; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject (21 CFR Part 812)

Sponsor

Any person or entity that takes responsibility for and initiates a research study. The sponsor may be an individual, pharmaceutical company, device manufacturer, governmental agency, academic institution, private organization, or other organization.

Standard

A broad description of performance expectation.

Standard Operating Procedure

A written set of methods or steps to be followed for the uniform performance of a function or activity.

Vulnerable Subjects

Individuals whose willingness to volunteer in a research study may be unduly influenced or coerced and individuals with limited autonomy. These individuals may include, but are not limited to, children, prisoners, pregnant women, mentally disabled, or economically or educationally disadvantaged persons.
APPENDIX B: ABBREVIATIONS

Arkansas Area Health Education Centers ........................................ AHEC
Arkansas Cancer Research Center ................................................ ACRC
Arkansas Children’s Hospital .................................................... ACH
Arkansas Children’s Hospital Research Institute .......................... ACHRI
Arkansas State Health Department ............................................ ASHD
Arkansas State Hospital .............................................................. ASH
Automated Research Information Administration ......................... ARIA
Case Reporting Forms .............................................................. CRF
Central Arkansas Veterans Healthcare System .............................. CAVHS
Code of Federal Regulations ...................................................... CFR
Food and Drug Administration ................................................ FDA
Federal Wide Assurance ............................................................ FWA
General Clinical Research Center ............................................. GCRC
Good Clinical Practice ............................................................. GCP
Health and Human Services ..................................................... HHS
Health Insurance Portability and Accountability Act of 1996 .......... HIPAA
Human Research Advisory Board .............................................. HRAC
Institutional Review Board ....................................................... IRB
International Code of Harmonics ............................................... IHP
Investigational New Drug ......................................................... IND
Multiple Project Assurance ....................................................... MPA
National Institutes of Health ..................................................... NIH
Office for Health Research Protections ..................................... OHRP
Office of Research and Sponsored Programs ............................ ORSP
Office of Research Compliance and Assurance ......................... ORCA
Principal Investigator .............................................................. PI
Protocol Review and Monitoring Committee ............................... PRMC
University of Arkansas for Medical Sciences .............................. UAMS
UAMS Biosafety Committee ..................................................... UBC
VA Research and Development ................................................. VA R/D
APPENDIX C: DECISION TREES FOR DETERMINATION OF TYPE OF RESEARCH

Chart 1. Definition of Human Subjects at Section 46.102(f)

Chart 2. Exemption at Section 46.101(b)(4) regarding research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens.

Chart 3. Waiver or Alteration of Informed Consent under Section 46.116(d)

Chart 4. Expedited Review under Category 8
Human Subject Regulations Decision Charts

The Office for Protection from Research Risks (OPRR) provides the following graphic aids to clarify portions of the Department of Health and Human Services (DHHS) human subject regulations at Title 45 Code of Federal Regulations Part 46 (45 CFR 46). These portions of the regulations are the subjects of frequent inquiries to OPRR.

- **Chart 1: Definition of Human Subject at Section 46.102(f)**

  Is the definition of “human subject” at Section 46.102(f) met in this research activity?

  Is there an intervention or an interaction with a living person that would not be occurring or would be occurring in some other fashion, but for this research?

  - Yes
  - No

  Will identifiable private data/information be obtained for this research in a form associable\(^1\) with the individual?

  - Yes
  - 45 CFR Part 46 does not apply

  Human subjects involved. Follow 45 CFR 46 or Meet criteria for exemptions (See Chart 2)

\(^1\)That is, the identity of the subject is or may readily be ascertained or associated with information.
OPRR 10/01/98

- **Chart 2: Exemption at Section 46.101(b)(4)** regarding research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens.

*Is the research exempt in accordance with Section 46.101(b)(4)?*  
The regulations at 45 CFR Part 46 do not apply if the criteria for exemption under Section 46.101(b)(4) are met.

```
Will this research use solely existing\textsuperscript{1} data or specimens?  
\begin{tabular}{ll}
Yes & No \end{tabular}

\begin{tabular}{ll}
Are those data or specimens publicly available? & \\
Yes & No \end{tabular}

\begin{tabular}{ll}
Will information be recorded by the investigator in such a way that it can be linked to the subject? & \\
No & Yes \end{tabular}

\begin{tabular}{ll}
\textit{This research is exempt from 45 CFR} & \\
This exemption does not apply. This research may be eligible for IRB waiver of informed consent (Section 46.116(d)). See Chart \end{tabular}
```

\textsuperscript{1}“Existing” means collected (i.e., on the shelf) prior to the research for a purpose other than the proposed research. It includes data or specimens collected in research and non-research activities.
Chart 3: Waiver or Alteration of Informed Consent under Section 46.116(d).

Can the Institutional Review Board employ Section 46.116(d) to waive informed consent or alter informed consent elements?

1. Will the research in its entirety involve greater than "minimal risk" (Section 46.116(d))?
   - No
   - Yes

2. Is it practicable to conduct the research without the waiver/alteration?
   - No
   - Yes

   No waiver or alteration.

3. Will waiving/altering informed consent adversely affect subjects' rights and welfare?
   - No
   - Yes

   No waiver or alteration.

4. Will pertinent information be provided to subjects later, if appropriate?
   - Yes
   - No

   Waiver or alteration possible, if IRB documents those 4 findings and approves the waiver or alteration.

   No waiver or alteration.

OPRR February, 1998
Web posting: 1998/12/28
Chart 4: Expedited Review Procedure, Category 8

Is the research eligible for expedited review under Category 8 of the Expedited Review List? (Section 46.110(b)(1))

If the research involving “human subjects” (defined at Section 46.110(f)) is not exempt (detailed at Section 46.110(b)) from 45 CFR Part 46, the Institutional Review Board may be able to use the expedited review procedure authorized at Section 46.110(b)(1). Category 8 on the Expedited Review List (46 Federal Register 8392) issued by the Department of Health and Human Services is the category most useful in considering research using data or specimens that exist prior to the research.

1 “Existing” means collected (i.e., on the shelf) prior to the research for a purpose other than the proposed research. It includes data or specimens collected in research and non-research activities.

OPRR April, 1996
APPENDIX D. HUMAN RESEARCH ADVISORY COMMITTEE (HRAC)
INFORMED CONSENT AND PROTOCOL CHECKLIST

Answer each of the following questions by checking the appropriate response:

I. Information Regarding the Application

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is there a complete protocol? (Includes Background, References, Rationale, Methods, and Data Analysis sections; or the entire Research Plan of an application for extramural support) Are there any protocol amendments or revisions included?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>Is there a one-page summary?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Does the protocol document adequate scientific background for the proposed study?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Is the study design rational and well described?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Are recruitment procedures appropriate and well described?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Is there an investigator brochure? (only with an industry-sponsored study)</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Is the HRAC Research Protocol Form completed correctly?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Have all the parts of the Report of Individual Review of Proposal for Project Involving Human Subjects Form been completed correctly?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Has the Drug/Device Form been completed correctly?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>If the study is being done at the CAVHS or UAMS, have the drug forms been completed correctly?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>If the study is initiated by an investigator on our campus, does the study involve an institution other than UAMS, ACH, the VA, the Health Dept., the State Hospital, CARTI, or ACHRI? If yes, is there evidence that the study was reviewed by an IRB at the other site? Was the approval letter from the other IRB included? If yes, is there evidence that there is a Multiple Project Assurance (MPA) or Federal Wide Assurance for the other site?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Did an investigator at another institution initiate the study? If so, where is the primary study site?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
</tbody>
</table>

II. Information Regarding the Format of the Consent Form

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is a written consent form required? How many?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Is the consent form written in second person (except the last paragraph) at a level that a person with eighth-grade education can understand?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Have all consent form pages been numbered and dates?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Are the protocol title, institution names(s) and sponsoring agency shown on each page of the consent form?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Does the consent form indicate the number of subjects that will be included in the study, both locally and at all sites? If more than one consent form is required, the number of local subjects is identical on all consent forms.</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>---</td>
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<td>----</td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td>Has the age group for the subjects been stated in the consent form?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Does the consent form identify the PI as the contact person for questions related to the research?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Are both day and night telephone numbers, including area codes, for the PI presented on the consent form? <em>(Specific phone numbers are required, not the switchboard; these numbers may reach the PI or listed co-investigators, but not fellows on call)</em></td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Does the last paragraph of the consent form state: &quot;I have read the above statement and have been able to ask questions and express concerns, which have been satisfactorily responded to by the investigator. I understand the purpose of the study as well as the potential benefits and risks that are involved. I hereby give my informed and free consent to be a participant in the study. I have been given a copy of this consent form&quot;?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Does the consent form have signature lines and dates for the subject, a witness, the investigator, parent permission (if subjects are ≤ 18 years of age;), child assent, and person obtaining consent?</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>On NIH multi-center clinical trial protocols (POG, SWOG, GOG, or RTOG), does the local consent form have substantive modifications on risks or alternative procedures when compared to the sample consent? If yes, has the investigator provided justification for the modification?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>12</td>
<td>Does the consent form address the inclusion or exclusion of women, pregnant women, minorities and children as research subjects in this study? If not addressed, was the omission justified? If yes, was the selection process appropriate?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>13</td>
<td>Is the consent form consistent with the protocol, including all revisions and amendments?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
### III. Information on Consent Form Regarding the Background and Purpose of the Study

<table>
<thead>
<tr>
<th></th>
<th>Does the Consent Form indicate that the study involves research?</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td>Is the purpose of the research clearly stated?</td>
<td></td>
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<tr>
<td>3</td>
<td>Is the study designed to determine the safety of a drug or device?</td>
<td></td>
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<td></td>
<td>If yes, is the safety aspect clearly stated?</td>
<td></td>
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<tr>
<td>4</td>
<td>Is the study designed to determine the effectiveness of a drug or device?</td>
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<td></td>
<td>If yes, is the effectiveness aspect clearly stated?</td>
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<tr>
<td>5</td>
<td>If it is a treatment study, does the consent form indicate how the experimental procedures differ from the current standard of care?</td>
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</tbody>
</table>

### IV. Information on Consent Form Regarding the Study Procedures

<table>
<thead>
<tr>
<th></th>
<th>Does the consent form clearly describe all procedures that subjects will follow?</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td>Are all experimental procedures clearly identified as experimental?</td>
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</tbody>
</table>

### V. Information on Consent Form Regarding Duration of Participation

<table>
<thead>
<tr>
<th></th>
<th>Does the consent form clearly state the amount of time each subject will be actively involved in the study (i.e., scheduled for visits or contact for treatment and/or evaluation)?</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
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<tr>
<td>2</td>
<td>Will patient data be collected after the subject's active involvement? If Yes, is the duration of this data collection discussed in the consent form?</td>
<td></td>
<td></td>
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<tr>
<td>3</td>
<td>Will subject data be stored and made available for future studies? If yes, has this been stated on the consent?</td>
<td></td>
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<tr>
<td>4</td>
<td>Will subject specimens be stored and made available for future studies? If yes, has this been adequately described on the consent form together with information regarding the rationale for storing the samples?</td>
<td></td>
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<tr>
<td>5</td>
<td>Does the consent form indicate that the investigator or sponsor may terminate the study at any time without subject consent?</td>
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</tbody>
</table>
## VI. Information on Consent Form Regarding Costs/Compensation

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
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<tbody>
<tr>
<td>1</td>
<td></td>
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<tr>
<td></td>
<td>Will the subjects or their third party payer be responsible for additional costs (e.g., travel, child care, meals, medication, treatment, per diem, etc.) as a result of participating in the research?</td>
<td>☐️</td>
<td>☐️</td>
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<tr>
<td></td>
<td>If there are no additional costs, has this been stated in the consent?</td>
<td>☐️</td>
<td>☐️</td>
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<tr>
<td></td>
<td>If additional costs may occur, is the following statement included in the text: &quot;You understand that you may be personally responsible for all or part of the costs associated with this procedure. You have had the opportunity to discuss the costs with your physician and the institution, and all your questions have been answered to your satisfaction&quot;.</td>
<td>☐️</td>
<td>☐️</td>
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<td>2</td>
<td></td>
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<tr>
<td></td>
<td>Has the sponsor offered to pay for treatment of injury resulting from the study?</td>
<td>☐️</td>
<td>☐️</td>
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<td></td>
<td>Is this disclosed in the consent form?</td>
<td>☐️</td>
<td>☐️</td>
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<td></td>
<td>Is there a letter from the sponsor indicating it will pay for this treatment?</td>
<td>☐️</td>
<td>☐️</td>
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<tr>
<td>3</td>
<td></td>
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<tr>
<td></td>
<td>Is the following mandatory statement included in the consent: &quot;In the event of complications, injury or illness requiring emergency medical treatment resulting from your participation in this study, appropriate acute medical care will be provided at no cost to you. However, the Principal Investigator and this institution have made no provision to reimburse you for the cost of medical care beyond emergency medical treatment or to pay for any lost wages, pain and suffering, hospitalization, or other expenses you may incur as a result of any such complication, injury or illness. If you develop a medical problem related to the study or have any question concerning the study please contact [insert the P1’s name and day and night phone numbers]&quot; (This paragraph may be omitted from the consent form of survey studies, when no physical measurements or treatments are performed on subjects)</td>
<td>☐️</td>
<td>☐️</td>
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<td>4</td>
<td></td>
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<tr>
<td></td>
<td>In addition to reimbursement of costs, will the subject receive incentives (payment, gift certificates, etc.) for participating?</td>
<td>☐️</td>
<td>☐️</td>
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<tr>
<td></td>
<td>If yes, has the payment been fairly prorated if the subject leaves the study before the end?</td>
<td>☐️</td>
<td>☐️</td>
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<tr>
<td></td>
<td>Are the incentives coercive for the population being studied?</td>
<td>☐️</td>
<td>☐️</td>
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</tbody>
</table>

## VI. Information on Consent Form Regarding Voluntary Participation

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
<td></td>
<td>Does the consent form indicate that subject participation is voluntary, both in terms of initial agreement to participate and withdrawal anytime during the study?</td>
<td>☐️</td>
<td>☐️</td>
</tr>
</tbody>
</table>
**VII. Information on Consent Form Regarding Risks and Discomforts**

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Does the consent form identify the risks and possible adverse effects in appropriate detail?</td>
<td></td>
<td></td>
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<tr>
<td>2</td>
<td>If appropriate, does the consent form discuss unforeseeable risks to the fetus?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3</td>
<td>Have the risks associated with the research, as distinguished from the risks of therapies the subjects would receive if not participating in the research, been clearly identified?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td>Are the risks minimized to the extent possible given the nature of the research and the subjects' underlying medical condition(s)?</td>
<td></td>
<td></td>
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<tr>
<td>5</td>
<td>Are the probable benefits to be derived from the research appropriately described in the consent form? (Benefits do not include compensation)</td>
<td></td>
<td></td>
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<tr>
<td>6</td>
<td>Are the risks reasonable in relation to subject benefits, if any, and in relation to the importance of the knowledge to be gained?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>7</td>
<td>If ionizing radiation is to be used, does it present increased radiation exposure over the current standard of care? If radiation exposure is increased by the procedure, is this disclosed in the consent form using language that the subject can understand? If radiation exposure is increased by the procedure, has it been approved by the appropriate Radiation Safety Committee (i.e., is an approval letter attached)?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>8</td>
<td>Is a device being evaluated in the study? If yes, has the device been approved by the FDA for the proposed use? If investigational, has the IDE number of the device been listed on the Drug/Device Form? Is the device considered a significant risk? Have the device, its status and its associated risks been described adequately in the consent form?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Will the study identify any portion of the subject's genotype? If yes, has genetic linkage and its risks been explained in the consent form?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Will tissue samples or specimens be collected and stored for later gene identification? If yes, have the subjects been specifically informed of this use of their specimens and the associated risks?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Does this study involve research in gene therapy or gene product therapy? If yes, is the material from human origin? If the study involves gene therapy or gene product therapy, have the risks been adequately described in the consent form?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>No</td>
<td>N/A</td>
</tr>
<tr>
<td>---</td>
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</tr>
</tbody>
</table>
| 12 | Does the study involve vulnerable groups (prisoners, elderly, pediatrics, UAMS)  
If yes, is adequate information provided and appropriate consent required? | ☐ | ☐ | ☐ |
| 13 | Will the subject be tested for HIV?  
If yes, does the consent form indicate that they will be tested and that both the subject and the Department of Health will be notified if the test is positive?  
If yes, does the consent form indicate that subjects testing positive will be given information about opportunities for counseling? | ☐ | ☐ | ☐ |
| 14 | Does the study involve a Psychological/Psychiatric/Mental Disorder or Thought Impairment? | ☐ | ☐ | ☐ |
| 15 | If the study involves children (≤18 years of age), classify it as I-IV. | ☐ | ☐ | ☐ |

### VIII. Benefits

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Are the benefits described in the consent form reasonable?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>Is the possibility of no personal benefits stated?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### IX. New Findings

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the following statement included in the consent: “Significant new findings developed during the course of the research that may relate to your willingness to continue participation will be provided to you”? (This may not be applicable)</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### X. Alternative Treatments

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>If this is a treatment study, are the alternatives to the research procedures adequately discussed in the consent form?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>Is the alternative of no treatment discussed?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
### XI. Confidentiality

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Does the consent form discuss subject confidentiality, indicating that the subject will not be identified in any reports of the study with the exception of possible reviews by the institution, FDA, sponsor or designee, OHRP, and HRAC?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2</td>
<td>Is the following mandatory statement included in the consent: &quot;If you have any questions about your rights as a research subject or concerning a research-related injury, you can call the Human Research Advisory Committee representative at phone number (501) 686-5667.&quot;?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>3</td>
<td>Does the consent form indicate that the subject has not waived any legal right to which he/she is otherwise entitled by signing this form?</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
**HRAC OFFICE CHECKLIST**

Please check each submitted application for the following items. If any of the items is missing, return the application to the investigator as soon as possible.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is there a complete protocol (consisting of Background including References, Rationale for the study, Methods and Data analysis)?</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2</td>
<td>Are any sponsor-submitted protocol amendments or revisions included?</td>
<td></td>
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</tr>
<tr>
<td>3</td>
<td>Is there an investigator brochure? (There will be an investigator brochure only with investigational drug or device studies sponsored by a drug/device company.)</td>
<td></td>
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<tr>
<td>4</td>
<td>Have all parts of the Human Research Advisory Committee Research Protocol Form, including a summary, been completed?</td>
<td></td>
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<tr>
<td>5</td>
<td>Have all parts of the Report of Individual Review of Proposal for Project Involving Human Subjects Form been completed?</td>
<td></td>
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<tr>
<td>6</td>
<td>Has the Drug/Device Form been completed?</td>
<td></td>
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<tr>
<td>7</td>
<td>If the study is being done at the CAVHS, have the CAVHS drug forms been attached?</td>
<td></td>
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<tr>
<td>8</td>
<td>If the study is being done at the ACH, is the ACH signoff letter attached?</td>
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<td>9</td>
<td>Has the PI. attached a simplified CV, or is one on file?</td>
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<tr>
<td>10</td>
<td>On NIH multi-center clinical trial protocols (POG, SWOG, GOG, RTOG or UARK), is the sample consent form enclosed in the full sets?</td>
<td></td>
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</tbody>
</table>
APPENDIX E: REQUEST FOR PHARMACY COST IMPACT UAMS HOSPITAL AND CLINICS FORM

Link to Request For Pharmacy Cost Impact UAMS Hospital and Clinics Form
REQUEST FOR PHARMACY COST IMPACT UAMS HOSPITAL AND CLINICS

Project Title:  

Study Sponsor:  

Principal Investigator:  

Contact Person/Phone:  

1. Estimated number of subjects from UAMS to be enrolled  
2. Estimated duration of the study (yrs/mos)  
3. Randomization procedure (if randomization required)  
4. List all drugs to be given as part of this protocol. *May use additional page if additional space is needed.*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
<th>Duration</th>
<th>Sponsor Provided (Y/N)</th>
<th>Standard of Care (Y/N)</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

5. Will the drugs be administered as an: Inpatient [ ] Outpatient [ ]  
6. If as an outpatient, estimate the total number of prescriptions that will be dispensed for each subject. If as an inpatient, estimate the total number of doses each subject will receive.  
7. Estimate the number of site visits involving the pharmacist  
8. Anticipated study close-out date  

Pharmacy Cost Impact:  

<table>
<thead>
<tr>
<th>Dispensing Fee</th>
<th>$ per dispensing action</th>
<th>$ per subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empty Vial storage</td>
<td>$ per year fee</td>
<td>$</td>
</tr>
<tr>
<td>Drug/Supply Cost</td>
<td>$ per subject</td>
<td></td>
</tr>
</tbody>
</table>

Total cost per subject: $  

Complexity level: Low [ ] Moderate [ ] High [ ]  

Administrative/Start-Up Fee $  

Director, Pharmacy  

Signature (or designee)  

Date:  

I hereby agree to reimburse Pharmacy Service the above noted expenses:  

Investigator:  

Date:  

APPENDIX E: REQUEST FOR PHARMACY COST IMPACT UAMS HOSPITAL AND CLINICS FORM
APPENDIX F: VA R & D SUBMISSION FORM

Request To Review Research Proposal/Project CAVHS #598 (4 pages)
Request for Pharmacy Cost Impact
Request for Cost Impact CAVHS Clinical Services
Investigational Drug Information Record VA Form 10-9012

Individual investigators are responsible for ensuring that all of their research activities are approved by the CAVHS R&D before they begin the project. Projects reviewed by the CAVHS R&D committee must have received all applicable sub-committee reviews before they can be approved as a CAVHS R&D project. Investigators and their staff are responsible for adhering to all applicable regulations regarding the proper use and handling of hazardous materials (i.e., radioactive materials), animal welfare, human subject protections and laboratory fire and safety rules. In particular, investigators conducting protocols with human subjects must also have received credit for training in the mandatory instruction on human subject protections.
REQUEST TO REVIEW RESEARCH PROPOSAL/PROJECT AND INSTRUCTIONS
CAVHS #598, LITTLE ROCK, AR

GENERAL INFORMATION

R&D Committee approval is required for all research performed using VA patients or VA facilities. A final R&D approval to perform research will NOT be granted until all other subcommittee approvals (e.g., IRB, animal, radiation safety, biohazard) are received.

Please submit, with this form, all documents needed by the R&D Committee and the Animal and Human Studies Subcommittees to completely review your proposal. If this is the first research proposal submitted at this Medical Center, also submit an Investigator Data Sheet (Page 18 - VA Form 10-5368) and a Personal Data form.

The R&D Committee meets on the last Tuesday of each month. All proposals received in good order in the Research Office (151/LR) at least 14 working days before each month's scheduled meeting of the R&D Committee will be considered at that meeting. Any proposals returned for obvious omissions or proposals turned in after the deadline will be held until the next meeting. They will not be considered for expedited review.

If you are submitting the same or a similar proposal simultaneously to more than one agency, please complete a separate "Request to Review" form for each agency.

It is NOT necessary to type entries on this form. However, if handwritten, please print or write legibly.

INSTRUCTIONS

Item 1. For approval by the R&D Committee, the PI must have either 1) a salaried VA appointment, or 2) a WOC appointment and be physically located at this VA Medical Center. It is expected that the PI will have faculty status, or its equivalent. Exceptions will be considered by the R&D Committee on an individual basis.

Items 2-5, Item 8 and Item 10. Self-explanatory.

Item 6. Enter 02 if another Investigator will be the direct recipient of the funds or is the initiator of the proposal. Otherwise, enter 01.

Item 7. If type of Submission is Renewal, enter in 7a) the number of the project being renewed, i.e., the VA Project Number. If you do not know the number, call the Research Office at 501-257-4857. Also, indicate in 7b) whether the title has changed. A title change is permissible ONLY if there is NOT a change in funding source (see Item 11). If the funding source is different, the project is New. If you are resubmitting a proposal that has been approved by the R&D Committee within 1 year, check New and if animal or human use is involved, indicate in Item 19 whether or not there has been a change in protocol or consent form.

Item 9. Do NOT enter a Co-Principal Investigator if the project is not funded. All Co-Principal Investigators must have a VA appointment and must be designated a Co-Principal Investigator on
the submitted proposal or, as noted in Item 1 above, have an appointment at another VAMC. Do NOT enter Co-Investigators, collaborators, technicians, etc. (Note: Co-Principal Investigators have equal access to allotted funds.)

**Item 11.** Funding Source. Check who will be funding the study, and specify the name of the funding agency.

**Item 12.** Funding Administration. Check who will administer the funds.

**Item 13.** Check "Yes" only if the major reason for the research proposal is to study the particular entity.

**Item 14.** Please enter only key words that are MeSH terms. If possible, at least one of the key words should identify the disease, the disorder, or the organ being studied. A booklet containing all MeSH terms is available for your use in the Research Administration Official use.

**Item 15.** If Animal Subjects (Item 18) is "Yes," enter every species and strain of animal that will be used.

**Item 16.** If this study will utilize any hospital clinical service, you must complete a "Request for Cost Impact" sheet and have it signed off by the appropriate service chief before submission to the R&D Committee.

**Item 17.** Please include an abstract of the proposed work (<500 words) organized under the following headings: OBJECTIVES, RESEARCH PLAN, METHODS, and, CLINICAL RELEVANCE. The abstract may be submitted typed single-spaced, or sent by e-mail to earnestdiane@exchange.uams.edu, or on an IBM-compatible 3.5" diskette. If the latter, save the abstract single-spaced and label the disk with the filename and the word processor used. In both instances, do NOT format (underline, italicize, right justify) and do NOT use subscripts, superscripts, Greek letters, or symbols. Use +/- for ±.

**Item 18.** For any item marked "yes", you must describe and also submit an application to the appropriate committee.
REQUEST TO REVIEW RESEARCH PROPOSAL/PROJECT
CAVHS #598 Little Rock, AR

<table>
<thead>
<tr>
<th>1. Principal Investigator:</th>
<th>Last</th>
<th>First</th>
<th>MI</th>
<th>Degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. SSN:</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>3. Telephone</td>
<td></td>
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</tr>
<tr>
<td>Pager</td>
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</tr>
<tr>
<td>4. Mail Code:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. VA Appointment (Check one):</td>
<td>Full-Time</td>
<td>Part-Time (HRS/WK)</td>
<td>WOC</td>
<td>Consultant</td>
</tr>
<tr>
<td>6. Status of PI in Proposal:</td>
<td></td>
<td>(01 = Awardee or initiator; 02 = Not Awardee; i.e., Participant in VA Co-Op Study) (Enter Code)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Type of Submission:</td>
<td>New</td>
<td>Renewal of Active Project (Check one)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(If Renewal, complete a and b):</td>
<td>a) Enter 4-digit number of active project:</td>
<td>b) Has title changed?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>8. Project Title:</td>
<td>(142 characters maximum)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Co-Principal Investigators: (Enter only if study is funded. Must have a VA appointment and must be designated a Co-PI in application)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Last name</td>
<td>First name</td>
<td>MI</td>
<td>degree</td>
<td>(Social Security Number)</td>
</tr>
<tr>
<td>Last name</td>
<td>First name,</td>
<td>MI</td>
<td>degree</td>
<td>(Social Security Number)</td>
</tr>
<tr>
<td>10. Anticipated Starting Date:</td>
<td></td>
<td></td>
<td></td>
<td>(mm/dd/yy)</td>
</tr>
<tr>
<td>11. Funding Source:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIH</td>
<td>(name institute)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA (identify Research Svc)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pharmaceutical Co. (name company)</td>
<td></td>
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<tr>
<td>Other (specify)</td>
<td></td>
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<tr>
<td>12. Funding Administration:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VA</td>
<td>Biomedical Research Foundation</td>
<td>UAMS</td>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>13. Project Focus: (Mark each item)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agent Orange</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>Yes</td>
<td>No</td>
<td>Prisoner of War</td>
<td>Yes</td>
</tr>
</tbody>
</table>
14. Keywords: (Minimum 3, maximum 6. Use MeSH terms only. Enter one term per line)

<table>
<thead>
<tr>
<th>1)</th>
<th>3)</th>
<th>5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2)</td>
<td>4)</td>
<td>6)</td>
</tr>
</tbody>
</table>

15. Animal Subjects: (Species and, if applicable, strain. Enter one species per line)

<table>
<thead>
<tr>
<th>1)</th>
<th>3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2)</td>
<td>4)</td>
</tr>
</tbody>
</table>

16. Cost Impact: If this study utilizes any hospital clinical service, you must complete a "Request for Cost Impact" sheet and have it signed off by the appropriate service chief before submission to the Research & Development Committee.

17. Abstract: (Submit on separate sheet or on floppy disk; see instructions)

18. Project Uses:

<table>
<thead>
<tr>
<th>Human Use:</th>
<th>Date Submitted to the Institutional Review Board</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Animal Use:</th>
<th>Date Submitted to Animal Care &amp; Use Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Investigational Drugs:</th>
<th>(Note: Any drug used for investigational purposes is considered 'investigational' and you must complete a Form VA 10-9012).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Investigational Device:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radioisotopes:</th>
<th>Date submitted to Radiation Safety Committee:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemicals and Biohazards:</th>
<th>(State isotope &amp; chemical form, e.g., ³H-glucose, ¹²⁵I-insulin, etc.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

(If 'yes', please enclose form. See instructions.)
19. Investigator's Statement:

"The information above is true to the best of my knowledge. For any items in #18 checked "yes", I will obtain the appropriate subcommittee approvals and will not begin this study until I have received approvals from the Research & Development Committee, and from all other appropriate committees."

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signature</td>
<td>Date</td>
<td>Time</td>
</tr>
</tbody>
</table>

20. Institutional Approvals:

<table>
<thead>
<tr>
<th>Service Chief</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signature</td>
<td>Date</td>
<td>Time</td>
</tr>
</tbody>
</table>

Note: If this is your First Research Proposal submitted at this Medical Center, please also submit an Investigator Data Sheet (Page 18) and a Personal Data Form. These can be obtained from the Research Administration Office. The same applies to co-principal investigators who have not submitted these forms.

Revision: May 1999
# INVESTIGATIONAL DRUG INFORMATION RECORD

<table>
<thead>
<tr>
<th>1. TITLE OF STUDY</th>
<th>6. SOURCE OF DRUG (If other than manufacturer or sponsor)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>2. RESPONSIBLE INVESTIGATOR (Individual who signed Form FD-1573)</td>
<td>7. THERAPEUTIC CLASSIFICATION AND EXPECTED THERAPEUTIC EFFECT(S)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>3. PRINCIPAL INVESTIGATOR (If different than responsible investigator)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>4. ALL DESIGNATIONS FOR DRUG (Generic and chemical, code, trade-names, other designations)</td>
<td>8. DOSAGE FORMS AND STRENGTHS</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>5. MANUFACTURER OR OTHER SPONSOR</td>
<td>9A. IS THIS DRUG A CONTROLLED SUBSTANCE?</td>
</tr>
<tr>
<td></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>10. STABILITY AND STORAGE REQUIREMENTS</td>
<td>9B. CLASSIFICATION</td>
</tr>
<tr>
<td>A. PRIOR TO MIXING, STORAGE SHOULD BE (Check applicable box(es))</td>
<td></td>
</tr>
<tr>
<td>[ ] AT ROOM TEMPERATURE</td>
<td>[ ] IN REFRIGERATOR</td>
</tr>
<tr>
<td>B. AFTER MIXING, DRUG REMAINS STABLE IN REFRIGERATOR FOR (Check appropriate box and enter quantity)</td>
<td></td>
</tr>
<tr>
<td>[ ] ______ MINUTES</td>
<td>[ ] ______ HOURS</td>
</tr>
<tr>
<td>11. DRUG ADMINISTRATION PROCEDURES</td>
<td>12. DRUG ADMINISTERED BY (Also complete Item 12B)</td>
</tr>
<tr>
<td>A. ROUTES OF ADMINISTRATION (Check appropriate box(es))</td>
<td>B. ADMINISTRATION DIRECTIONS</td>
</tr>
<tr>
<td>[ ] ORSPL</td>
<td>[ ] INFUSION</td>
</tr>
<tr>
<td>12A. DRUG ADMINISTERED BY</td>
<td>12B. ROUTE</td>
</tr>
<tr>
<td>[ ] A. PHYSICIAN ONLY</td>
<td>[ ] B. PROFESSIONAL NURSE</td>
</tr>
<tr>
<td>14. KNOWN SIDE EFFECTS AND TOXICITIES</td>
<td>15A. DOUBLE BLIND?</td>
</tr>
<tr>
<td>[ ] YES</td>
<td>[ ] NO (If “Yes,” complete Items 15B and 15C)</td>
</tr>
<tr>
<td>15C. TELEPHONE NUMBERS</td>
<td></td>
</tr>
<tr>
<td>DAYTIME</td>
<td>EVENING</td>
</tr>
<tr>
<td>16. SPECIAL PRECAUTIONS (Include drug interactions (synergisms, antagonisms), contraindications, etc.)</td>
<td></td>
</tr>
<tr>
<td>17. ANTIDOTE</td>
<td></td>
</tr>
<tr>
<td>18. STATUS (Check one)</td>
<td></td>
</tr>
<tr>
<td>[ ] INVESTIGATIONAL</td>
<td>[ ] PHASE II</td>
</tr>
<tr>
<td>[ ] PHASE I</td>
<td>[ ] PHASE III</td>
</tr>
<tr>
<td>19. NAMES OF AUTHORIZED PRESCRIBERS</td>
<td></td>
</tr>
<tr>
<td>A.</td>
<td>B.</td>
</tr>
<tr>
<td>C.</td>
<td>D.</td>
</tr>
<tr>
<td>20. SIGNATURE OF RESPONSIBLE OR PRINCIPAL INVESTIGATOR</td>
<td>22. PATIENT IDENTIFICATION (I.D. plate or given name – last, first, middle)</td>
</tr>
<tr>
<td>DATE</td>
<td></td>
</tr>
<tr>
<td>21. APPROVED BY</td>
<td></td>
</tr>
<tr>
<td>A. SUBCOMMITTEE ON HUMAN STUDIES</td>
<td></td>
</tr>
<tr>
<td>21A. SIGNATURE OF CHAIRPERSON</td>
<td>21B. SIGNATURE OF CHAIRPERSON</td>
</tr>
<tr>
<td>DATE</td>
<td></td>
</tr>
<tr>
<td>B. RESEARCH AND DEVELOPMENT COMMITTEE</td>
<td></td>
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</tbody>
</table>

APPENDIX F: VA R & D SUBMISSION FORMS
REQUEST FOR PHARMACY COST IMPACT  
Central Arkansas Veterans Healthcare System

<table>
<thead>
<tr>
<th>Project Title:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator:</td>
<td></td>
</tr>
<tr>
<td>Contact Person/Phone:</td>
<td></td>
</tr>
</tbody>
</table>

1. Estimated number of subjects from the VA to be enrolled: #

2. List all drugs to be given as part of this protocol including any adjuvant drug therapies such as aspirin, Tylenol, etc. *May use additional page if protocol calls for more than 10 drugs.*

<table>
<thead>
<tr>
<th>A. Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Schedule</th>
<th>Duration</th>
<th>Sponsor Provided (Y/N)</th>
<th>For Office Use Only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

3. Will the drugs be administered as an:  
   - Inpatient [ ]  
   - Outpatient [ ]

4. If as an outpatient, estimate the total number of prescriptions that will be written for each subject.
   If as an inpatient, estimate the total number of doses each subject will receive: #

5. Is this protocol considered "the standard of care"?  
   - Yes [ ]  
   - No [ ]

Signature of Principal Investigator:  
Date:  

For Office Use Only:  

**Pharmacy Cost Impact:**

| Dispensing Fee | $ per dispensing action | $ per subject | Drug/Supply Cost | $ per subject | Total: $ per subject | Administrative Fee | $  
|----------------|------------------------|---------------|------------------|---------------|-----------------------|-------------------|-----
|                |                        |               |                  |               |                       | Chief, Pharmacy Service | Date: |

Signature (or designee)
REQUEST FOR COST IMPACT
CENTRAL ARKANSAS VETERANS HEALTHCARE SYSTEM (CAVHS)
CLINICAL SERVICES

The attached research protocol utilizes one or more of the following hospital clinical services. The R&D Committee has decided that it is the responsibility of the Principal Investigator to obtain the cost impact from the Chiefs of the services involved. THIS FORM MUST BE COMPLETED AND SIGNED BY THE APPROPRIATE SERVICE CHIEF(s) BEFORE SUBMISSION TO THE RESEARCH & DEVELOPMENT COMMITTEE FOR APPROVAL.

STUDY IS:

<p>| | | |</p>
<table>
<thead>
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<tbody>
<tr>
<td></td>
<td>Cardiology Section</td>
<td>Pharmacy Service</td>
</tr>
<tr>
<td></td>
<td>Nuclear Medicine Service</td>
<td>Radiology Service</td>
</tr>
<tr>
<td></td>
<td>*Laboratory (analysis)</td>
<td>Other (specify)</td>
</tr>
<tr>
<td></td>
<td>Laboratory (blood draw)</td>
<td>Ophthalmology</td>
</tr>
</tbody>
</table>

Principal Investigator and Project Title:

*If laboratory studies are to be done:

1) Type and number of laboratory tests per patient beyond usual patient care:

2) Estimated number of patients:
   a. Cost to be reimbursed to laboratory (please confer with Chief, Laboratory Service):

   I have reviewed the attached protocol and find that:
   a) There is no cost impact on our service; or
   b) There is cost impact on our service and it is as follows:

   SERVICE CHIEF
   Date

   I have reviewed the attached protocol and find that:
   a) There is no cost impact on our service; or
   b) There is cost impact on our service and it is as follows:

   SERVICE CHIEF
   Date

   NO CLINICAL COST IMPACT INVOLVED: ☐

   Principal Investigator Signature and Date: ________________________________

   APPENDIX F: VA R & D SUBMISSION FORMS
APPENDIX G: ACHRI SUBMISSION INFORMATION

To access the Arkansas Children’s Hospital Research Institute forms, select AWARD FORMS

ACHRI Grant Submissions should use the following forms:

- Grant Proposal Submission Form
- ACHRI Checklist Page
- Conflict of Interest Disclosure Form

Industry Sponsored/Clinical Trials/Pharmaceutical studies should use the following forms:

- ACHRI Clinical Trial Submission Form
- ACHRI Checklist Page
- Conflict of Interest Disclosure Form
- Research Price Study Summary Sheet

For more information or assistance with submission of federal forms or from a foundation, please contact the Grants Administrator at 501-364-3581.

For more information or assistance with submission of forms using funds from a pharmaceutical company, please contact the Legal and Human Protections Administrator at 501-364-3571.
APPENDIX H: REQUIRED ELEMENTS OF INFORMED CONSENT DOCUMENTS AND THE CAVHS TEMPLATE

The Informed Consent Document

Consent forms must be written so that they meet the HRAC specifications regarding content and form. This appendix is the investigator’s guide to the creation of an appropriate consent form.

Sponsors may provide model consent forms for assisting investigators in construction of the consent forms to be used by each investigator. These forms are helpful guides. However, there are required elements for inclusion in every written informed consent form that are described in the following checklist. These must be included in a written informed consent form unless the HRAC determines otherwise.

In most instances, Consent Forms for studies to be conducted at the VA must be submitted on the VA template.

All other consents must include a header or footer with the following information:
Protocol Title
Institutional Name(s)
Sponsoring Agency
Page Number and Date of Consent Submission or Revision
Grant Title: If the study involves a grant application, the name of the grant must be included on the first page of the informed consent document.

For CAVHS patients, please use the VA Consent Form 10-1086. An interactive version of this form can be found at:
http://pws.prser.ven/vanjchs_reserch/forms/VA_form_consent_10-1086.doc
### INVESTIGATOR’S CHECKLIST FOR INFORMED CONSENT

<table>
<thead>
<tr>
<th>Consent Form Element</th>
<th>Element Include</th>
</tr>
</thead>
<tbody>
<tr>
<td>The consent form is written in the second person, using a standard-size type font (12 pt)</td>
<td>YES NO</td>
</tr>
<tr>
<td>Language is not greater than 8th grade reading level</td>
<td>YES NO</td>
</tr>
<tr>
<td>The last paragraph should be in the first person, stating:</td>
<td>YES NO</td>
</tr>
<tr>
<td>I have read the above statement and have been able to ask questions and express concerns, which have been satisfactorily responded to by the investigator. I understand the purpose of the study as well as the potential benefits and risks that are involved. I hereby give my informed and free consent to be a participant in this study. I have been given a copy of this consent form.</td>
<td>YES NO</td>
</tr>
<tr>
<td>The following is a mandatory paragraph</td>
<td>YES NO</td>
</tr>
<tr>
<td>In the event of complications, injury or illness requiring emergency medical treatment resulting from participation in this study, appropriate acute medical care will be provided at no cost to you. However, the Principal Investigator and this institution have made no provision to reimburse you for the cost of medical care beyond emergency medical treatment or to pay for any lost wages, pain and suffering, hospitalization, or other expenses you may incur as the result of any such complication, injury, or illness. If you develop a medical problem related to the study or have any question concerning the study, please contact [insert the Principal Investigator’s name and phone numbers]. (This paragraph may be omitted from the consent forms of survey studies or when no physical measurements or treatments are performed on subjects).</td>
<td>YES NO</td>
</tr>
<tr>
<td>The following is a mandatory paragraph</td>
<td>YES NO</td>
</tr>
<tr>
<td>If you have any questions about your rights as a research subject or concerning a research related injury, you can call the Institutional Review Board representative at phone number (501) 686-5667.</td>
<td>YES NO</td>
</tr>
<tr>
<td>A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental (i.e., in medical research, those procedures which deviate from standard, accepted practice). If the purpose of the research cannot be fully revealed to subjects, describe exactly what subjects will be told, the justification for any deception of subjects, and plans to debrief subjects after their participation in the research.</td>
<td>YES NO</td>
</tr>
<tr>
<td>The Principal Investigator(s) name(s) and affiliation(s).</td>
<td>YES NO</td>
</tr>
<tr>
<td>A description of any reasonably foreseeable risks or discomforts (both physical and mental) that could reasonably be anticipated. Also describe 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.</td>
<td>YES NO</td>
</tr>
<tr>
<td>Description</td>
<td>Yes</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------</td>
<td>-----</td>
</tr>
<tr>
<td>A description of any benefits to the subject or to others which may</td>
<td></td>
</tr>
<tr>
<td>reasonably be expected from the research. If no direct benefits due to</td>
<td></td>
</tr>
<tr>
<td>participation are foreseen, it is appropriate to state this.</td>
<td></td>
</tr>
<tr>
<td>Any costs or payments to the subjects that may result from participation</td>
<td></td>
</tr>
<tr>
<td>in the research. If there are no costs or payments, this should be stated</td>
<td></td>
</tr>
<tr>
<td>as well.</td>
<td></td>
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<tr>
<td>A statement that participation is voluntary, refusal to participate will</td>
<td></td>
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<tr>
<td>involve no penalty or loss of benefits to which the subject is otherwise</td>
<td></td>
</tr>
<tr>
<td>entitled, and the subject may discontinue participation at any time</td>
<td></td>
</tr>
<tr>
<td>without penalty or loss of benefits to which the subject is otherwise</td>
<td></td>
</tr>
<tr>
<td>entitled. If the participant has been promised financial compensation,</td>
<td></td>
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<tr>
<td>but chooses to withdraw, state that a pro-rated portion of the fee will be</td>
<td></td>
</tr>
<tr>
<td>paid up to the point of withdrawal.</td>
<td></td>
</tr>
<tr>
<td>The approximate number of subjects to be studied; if the study if a</td>
<td></td>
</tr>
<tr>
<td>multi-center one, include the number in the whole study and the</td>
<td></td>
</tr>
<tr>
<td>number at this site.</td>
<td></td>
</tr>
<tr>
<td>A statement that significant new findings developed during the course of</td>
<td></td>
</tr>
<tr>
<td>the research which may relate to the subject's willingness to</td>
<td></td>
</tr>
<tr>
<td>continue participation will be provided to the subject.</td>
<td></td>
</tr>
<tr>
<td>If ionizing radiation is to be used in procedures such as chest x-ray,</td>
<td></td>
</tr>
<tr>
<td>please illustrate the amount in lay terms, (e.g., flying from New York</td>
<td></td>
</tr>
<tr>
<td>to Denver at 30,000 feet). This information is available from the Radiation</td>
<td></td>
</tr>
<tr>
<td>Safety Office.</td>
<td></td>
</tr>
<tr>
<td>If there is a device involved, please state if it has or has not been</td>
<td></td>
</tr>
<tr>
<td>approved by the FDA and if it is a significant or non-significant risk.</td>
<td></td>
</tr>
<tr>
<td>Is the amount of time each subject is expected to be involved with the</td>
<td></td>
</tr>
<tr>
<td>project clearly defined?</td>
<td></td>
</tr>
<tr>
<td>If the Principal Investigator is not on staff, are the names of the</td>
<td></td>
</tr>
<tr>
<td>responsible staff of the institution listed in the consent form? House</td>
<td></td>
</tr>
<tr>
<td>Officers are not considered staff</td>
<td></td>
</tr>
<tr>
<td>The consequences of a subject's decision to withdraw from the research and</td>
<td></td>
</tr>
<tr>
<td>procedures for orderly termination of participation by the research.</td>
<td></td>
</tr>
<tr>
<td>A disclosure of appropriate alternative procedures or courses of</td>
<td></td>
</tr>
<tr>
<td>treatment, if any that might be advantageous to the subject.</td>
<td></td>
</tr>
<tr>
<td>A statement describing the extent, if any, to which confidentiality of</td>
<td></td>
</tr>
<tr>
<td>records identifying the subject will be maintained which should include</td>
<td></td>
</tr>
<tr>
<td>how records will be kept confidential, (e.g., locked cabinet, erasing of</td>
<td></td>
</tr>
<tr>
<td>tapes, etc.). If audiotaping is to occur, indicate whom will hear the</td>
<td></td>
</tr>
<tr>
<td>tapes, where they will be stored, and how and when they will be disposed.</td>
<td></td>
</tr>
<tr>
<td>If videotaping is to occur, indicate to whom the tapes are to be shown and</td>
<td></td>
</tr>
<tr>
<td>where they will be stored.</td>
<td></td>
</tr>
<tr>
<td>A statement that all records will be confidential with the</td>
<td></td>
</tr>
<tr>
<td>exception of a possible review by OHRP, FDA (for drug/device studies),</td>
<td></td>
</tr>
<tr>
<td>ORCA (for VA studies), sponsoring agency,</td>
<td></td>
</tr>
<tr>
<td>Institutional Officials and HRAC</td>
<td></td>
</tr>
<tr>
<td><strong>An explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of research-related injury to the subject. Include the name and both daytime and after-hours telephone numbers of the P1 (and primary physician in appropriate) so the subject will know whom to contact regarding the research.</strong></td>
<td>Yes</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>The consent form must state that the subject has not waived any legal rights to which he or she is legally entitled to by signing the form.</strong></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>If the study involves drugs or procedures not paid for by the study, the following paragraph should be added:</strong> You understand that you may be personally responsible for all or part of the costs associated with this procedure. You have had the opportunity to discuss the costs with the physician and the institution, and all your questions have been answered to your satisfaction.</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>A statement must be added regarding subject notification of any test that is positive for AIDS and advising of available counseling.</strong></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## APPENDIX I: COGNITIVE IMPAIRMENT DETERMINATION ALGORITHHM

**Human Research Advisory Committee**

**Decision Tree for Informed Consent**

**Involving Patients with a Mental Disorder or Thought Impairment**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does patient have a court-appointed guardian?</td>
<td>Court approval must be obtained under Arkansas law</td>
<td>The special rules for mental disorders and thought impairments do not apply</td>
</tr>
<tr>
<td>Does patient have a &quot;mental disorder&quot; or &quot;thought impairment&quot;?</td>
<td></td>
<td>Consent for the patient's participation must be obtained from another person authorized to grant consent under Arkansas law</td>
</tr>
<tr>
<td>Is the patient &quot;competent to make rational, informed decisions concerning his medical treatment and understand the nature of the research and the right to withdraw from the study at any time&quot;?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the research study involve more than &quot;minimal risk&quot;?</td>
<td>Patient may participate in Research study without second opinion or consent</td>
<td></td>
</tr>
<tr>
<td>After a full review by a qualified physician or licensed psychologist not involved in the research, is it the opinion of the second physician or psychologist that the patient is competent to make informed decisions concerning his or her medical treatment, and, if so, is the second opinion and the factors supporting it fully documented in the patient record?</td>
<td>Patient may participate in the research study</td>
<td>Patient may not participate in the research study</td>
</tr>
</tbody>
</table>

*If a patient alternates between periods of mental competence and incompetence:* The investigator should obtain consent from the patient as provided and ask permission from the patient to obtain consent and upon the judgment of a relative or other person who could otherwise grant legal consent for treatment in event patient becomes incapable of continuing to make informed consent decisions in the future. **If a patient asks to withdraw from a research study at any time, the research study must terminate,** even if the investigator does not believe the patient to be competent to make informed decisions and even if a second Opinion or third party consent has been obtained.
APPENDIX J: NON-ENGLISH SPEAKING CONSENT INFORMATION AND SHORT FORM

Subjects who do not speak English should be presented with a consent document written in a language understandable to them. An oral presentation of informed consent information in conjunction with a short form written consent document (stating that the element of consent have been presented orally) may be used if the HRAC has approved the foreign language version of the short form document. A witness to the oral presentation is required, and the subject must be given copies of the short form document and the summary. The HRAC approved English version of the informed consent document may serve as the summary.

If an oral presentation is used, the

- Short form document should be signed by the subject or the subject’s legally authorized representative
- Summary (i.e., the English language informed consent document) should be signed by the person obtaining consent as authorized under the protocol, and
- Short form document and the summary should be signed by the witness

See Next Page for Form Example
SHORT FORM WRITTEN CONSENT DOCUMENT FOR SUBJECTS WHO DO NOT SPEAK ENGLISH

This document must be written in a language understandable to the subject Short Form Written Consent Document

Consent to Participate in Research

You are being asked to participate in a research study.

Before you agree, the investigator must tell you about (I) the purposes, procedures, and duration of the research; (ii) any procedures which are experimental; (iii) any reasonably foreseeable risks, discomforts, and benefits of the research; (iv) any potentially beneficial alternative procedures or treatments; and (v) how confidentiality will be maintained.

Where applicable, the investigator must also tell you about (I) any available compensation or medical treatment if injury occurs; (ii) the possibility of unforeseeable risks; (iii) circumstances when the investigator may halt your participation (iv) any added costs to you; (v) what happens if you decide to stop participating; (vi) when you will be told about new findings which may affect your willingness to participate; and (vii) how many people will be in the study.

If you agree to participate, you must be given a signed copy of this document and a written summary of the research.

You may contact _____________________ at _____________________ any time you have questions about the research.

You may contact _____________________ at _____________________ if you have questions about your rights as a research subject or what to do if you are injured.

Your participation in this research is voluntary, and you will not be penalized or lose benefits if you refuse to participate or decide to stop.

Signing this document means that the research study, including the above information, has been described to you orally, and that you voluntarily agree to participate.

__________________________     _________________
Signature of Subject   Date

__________________________     _________________
Signature of Witness   Date

(OHRP Policy Guidance Information   Non-English Speakers – 11/95)
APPENDIX K: STUDY CLOSURE FORM
UAMS Human Research Advisory Committee
Study Closure Form

It is the responsibility of the Principal Investigator to submit information for study closure when all subjects have completed treatment and follow-up phases of the study and all data analysis has been completed.

I. Investigator and Study Information

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Department/Division</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Address:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title:</th>
<th>HRAC Record Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

II. Study Status Information

<table>
<thead>
<tr>
<th>The status of this Study is:</th>
<th>Completed - all subjects have completed treatment and follow-up activities. Data analysis complete</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>□ Never initiated by investigator.</td>
</tr>
</tbody>
</table>

Is the Study approved by the VA Research and Development Committee?

□ Yes □ No

<table>
<thead>
<tr>
<th>Study Site</th>
<th>Total Subjects Enrolled</th>
<th>Total Number of Discontinued Subjects</th>
<th>Total Number of Subjects who Completed Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>UAMS (University Hospitals and Clinics)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAVHS (All VA facilities)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACH/ACHRI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHEC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State Hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (Attach a list of all participating study sites).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### APPENDIX K: STUDY CLOSURE FORM

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have all Serious and Unexpected Adverse Events from this site and other sites (if multi-center study) been reported to the HRAC?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have all modifications in the protocol or consent form been reported to the HRAC?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have all subjects signed an HRAC approved consent form (if written informed consent required)? <em>(If no, attach an explanation.)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are you including any serious and unexpected Adverse Events or modifications in the protocol or consent form to the HRAC with this Study Closure report? <em>(If yes, attach a copy.)</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Are there any publications or presentations that have resulted from data collected during this study? [ ] Yes [ ] No

If yes, please list below:

The investigator should complete, sign and date this form, and submit it to the HRAC. Upon receipt of this form, the HRAC will review the report and place the protocol on the agenda. The investigator will receive written confirmation of protocol closure by the convened HRAC.

Signature of Principal Investigator: _____________________________________

Date: _____________________________________

Phone: _____________________________________

Time: _____________________________________

Revised 10/1/2001
APPENDIX L: SERIOUS ADVERSE EVENT REPORTING FORM

UAMS Human Research Advisory Committee
Serious Adverse Event / Death Reporting Form

| Reporting requirements for adverse events should include only those reactions associated with the use of a drug or device which are both SERIOUS AND UNANTICIPATED |

Prompt reporting of deaths and serious adverse events to the HRAC is the responsibility of the investigator. Serious adverse events must be reported to the HRAC within seven (7) days of the event.

A death occurring while the subject is on active treatment must be reported within three (3) days of investigator’s notification. A death that occurs during long-term follow up after completion of the experimental (active treatment) portion of an approved study protocol and is not study related should be reported within sixty (60) days of the investigator’s notification.

The investigator should complete, sign and date this form, and submit it to the HRAC. Upon receipt of this form, the HRAC will review the report.

Investigator and Study Information

| Principal Investigator: |
| Institution: |
| Department/Division |
| Address: |
| Project Title |
| HRAC Record Number |

Subject Information

| Subject’s Study ID (If Available) |
| Subject’s Medical Record Number |
| Is the Subject a patient at CAVHS? | Yes | No |
| Where did this event occur? |

Please check one: | Yes | No |
| Is this a report of the death of a research subject: |
| Is this a report of an event involving a research subject that is serious AND UNANTICIPATED? |
| Is this a report of an event involving a research subject that is serious and anticipated? |
**APPENDIX L: SERIOUS ADVERSE EVENT FORM**

**Please check one:**

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did the Serious Adverse Event result in the death of the Subject?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did the adverse event involve the use of an investigational drug?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, was the adverse event related to the drug?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did the adverse event involve the use of an investigational device?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, was the adverse event related to the device?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the risk of this event contained in the current consent form?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Should the consent form and/or protocol be revised as a result of this event?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is the risk of this event contained in the current Investigator’s Brochure?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Will currently enrolled subjects be notified of this event?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Describe the actions that have been taken.** (Check all that apply and explain fully with attachments.)

<table>
<thead>
<tr>
<th>Check If Done</th>
<th>Action</th>
<th>Date Taken</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No further action required</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stop enrollment of new participants</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Halt the Study</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Change data management/coding procedures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Form a committee to review study procedures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Modify Informed Consent Document</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sponsor Notification (A copy of this completed form should be attached to the Sponsor notification letter)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Notification of Pharmacy and Therapeutics Committees at the institution(s) where the study takes place (if a drug was involved)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other (Please specify in attachments)</td>
<td></td>
</tr>
</tbody>
</table>

If the event is **Serious and Unanticipated**, please return this form to the HRAC office with a description of the adverse event. The summary **must** include the following information:

- Was hospitalization required or prolonged?
- Was medical treatment necessary, and an explanation of the extent of treatment
- Does this adverse event present any risk or relate in any way to current and prospective study subjects at this institution?
- Has your institution’s risk management officer been notified?
- Is there any litigation pending from this event?

Signature of Principal Investigator: ________________________________

Date: ________________________________

Phone: ________________________________

Pager: ________________________________

Time: ________________________________

Revised 10/01/2001
APPENDIX M: REPORTING FORMATS FOR PROTOCOL DEVIATIONS, VIOLATIONS

The above events should be reported promptly to the HRAC in written form. The following are guidelines, which may be used to report these events to the HRAC:

a. Include name of protocol and HRAC record number
b. Classify category of event
   1. Protocol deviation
   2. Protocol violation
   3. Research noncompliance issue
   4. Research suspension by sponsor and/or investigator
   5. Potential or actual risk to subject
c. Details of event (include subject study identification if applicable)
d. If the event affects the continuation or the integrity of the study, this should be addressed by the principal investigator.
APPENDIX N: HRAC CONTINUING REVIEW FORM

Link to revised HRAC Continuing Review Form

Link to Directions For Completing the HRAC Continuing Review Form.
This link goes to the UAMS Human Research Advisory Committee (HRAC) website. On this page, select the HRAC forms link. On the HRAC Forms page, under the Continuing Review Report Forms (CRRF) section, select Directions for Completing the HRAC Continuing Review Report Form.
APPENDIX O: RESOURCES LIST OF COMMITTEES AND INSTITUTIONAL CONTACTS

**ARKANSAS CHILDREN'S HOSPITAL (ACH) web site**

<table>
<thead>
<tr>
<th>Service</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Number</td>
<td>(501) 364-1100 (Phone)</td>
</tr>
<tr>
<td>Research Pharmacy</td>
<td>(501) 364-2596 (Phone)</td>
</tr>
<tr>
<td></td>
<td>(501) 364-2595 (Fax)</td>
</tr>
<tr>
<td>Pediatric Clinical Research Unit</td>
<td>(501) 364-2338 (Phone)</td>
</tr>
<tr>
<td>Radiation Safety Committee</td>
<td>(501) 364-3800 (Phone)</td>
</tr>
</tbody>
</table>

**ARKANSAS CHILDREN'S HOSPITAL RESEARCH INSTITUTE (ACHRI) web site**

<table>
<thead>
<tr>
<th>Service</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assistance with IRB Submissions, ARIA, and HIPAA</td>
<td>(501) 364-3571 (phone)</td>
</tr>
<tr>
<td>Clinical Trials (Pharmaceutical/Industry), Confidentiality and Study Agreements</td>
<td>(501) 364-2705 (Fax)</td>
</tr>
<tr>
<td>CUMG Awards</td>
<td>(501) 364-3581 (Phone)</td>
</tr>
<tr>
<td>Federal and Private Grants</td>
<td></td>
</tr>
<tr>
<td>Education Coordinator</td>
<td>(501) 364-2760 (phone)</td>
</tr>
<tr>
<td>Pediatric Clinical Research Unit Coordinator</td>
<td></td>
</tr>
<tr>
<td>Procedure Prices for Research</td>
<td></td>
</tr>
<tr>
<td>Research Coordinator Pool</td>
<td></td>
</tr>
<tr>
<td>Subject Tracking System</td>
<td></td>
</tr>
<tr>
<td>Manuscript Grant Writing/Editing</td>
<td>(501) 364-2469 (Phone)</td>
</tr>
<tr>
<td>Research Accounts</td>
<td>(501) 364-2513 (Phone)</td>
</tr>
<tr>
<td>Research Compliance Officer</td>
<td>(501) 364-2861 (Phone)</td>
</tr>
<tr>
<td>Research Computer Systems</td>
<td>(501) 364-3570 (Phone)</td>
</tr>
</tbody>
</table>

**CENTRAL ARKANSAS VETERANS HEALTHCARE SYSTEM (CAVHS) web site**

<table>
<thead>
<tr>
<th>Service</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Number</td>
<td>(501) 257-1000 (Phone)</td>
</tr>
<tr>
<td>Biomedical Research Foundation</td>
<td>(501) 257-4517 (Phone)</td>
</tr>
<tr>
<td></td>
<td>(501) 257-4623 (Fax)</td>
</tr>
<tr>
<td>Subcommittee for Research Safety</td>
<td>(501) 257-4816 (Phone)</td>
</tr>
<tr>
<td></td>
<td>(501) 257-4821 (Fax)</td>
</tr>
<tr>
<td>Radiation Safety Committee</td>
<td>(501) 257-6108 (Phone)</td>
</tr>
<tr>
<td>Research Compliance Office</td>
<td>(501) 257-5558 (Phone)</td>
</tr>
<tr>
<td></td>
<td>(501) 257-4821 (Fax)</td>
</tr>
<tr>
<td>Research &amp; Development Committee</td>
<td>(501) 257-4816 (Phone)</td>
</tr>
<tr>
<td></td>
<td>(501) 257-4821 (Fax)</td>
</tr>
<tr>
<td>Research Pharmacy</td>
<td>(501) 257-6338 (Phone)</td>
</tr>
<tr>
<td></td>
<td>(501) 257-6339 (Fax)</td>
</tr>
</tbody>
</table>
**University of Arkansas for Medical Sciences (UAMS) web site**

<table>
<thead>
<tr>
<th>Organization</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Number</td>
<td>(501) 686-7000 (Phone)</td>
</tr>
<tr>
<td>Animal Research Committee</td>
<td>(501) 686-5347 (Phone)</td>
</tr>
<tr>
<td>Biosafety Committee, Dr. Lee Soderberg</td>
<td>(501) 686-6368 (Phone)</td>
</tr>
<tr>
<td>Biohazards Committee</td>
<td></td>
</tr>
<tr>
<td>DNA Committee</td>
<td></td>
</tr>
<tr>
<td>Dr. Charles Winter, Associate Dean of Research College of Medicine</td>
<td>(501) 686-5347 (Phone) (501) 686-8501 (Fax)</td>
</tr>
<tr>
<td>General Clinical Research Center (GCRC)</td>
<td>(501) 257-5399 (Phone)</td>
</tr>
<tr>
<td>Steven C. Elbein, MD Professor of Medicine, Program Director</td>
<td>(501) 257-5817 (Fax)</td>
</tr>
<tr>
<td>Suzanne Ritter Lumpkin, MS, JD GCRC Administrator</td>
<td>GCRC web site</td>
</tr>
<tr>
<td>Institutional Review Board (IRB)</td>
<td>(501) 686-5667 (Phone)</td>
</tr>
<tr>
<td>Tim Atkinson, Director Research Privacy Officer</td>
<td>(501) 686-7265 (Fax)</td>
</tr>
<tr>
<td>Connie Hendrixson, ARIA/IRB Administrator</td>
<td>501-526-5494</td>
</tr>
<tr>
<td>Office for Clinical Trials</td>
<td>(501) 686-8572 (Phone)</td>
</tr>
<tr>
<td>Dr. Thomas G. Wells, Director</td>
<td>(501) 686-8501 (Fax)</td>
</tr>
<tr>
<td>Julia Washam, R.N. Liaison Specialist</td>
<td></td>
</tr>
<tr>
<td>Office for Research and Sponsored Programs</td>
<td>(501) 686-5502 (Phone) (501) 686-8359 (Fax)</td>
</tr>
<tr>
<td>Tim Atkinson, Director Research Privacy Officer</td>
<td></td>
</tr>
<tr>
<td>Office of Research Compliance</td>
<td>(501) 526-6876 (Phone)</td>
</tr>
<tr>
<td>Danna K. Carver, Director</td>
<td>(501) 526-6272 (Fax)</td>
</tr>
<tr>
<td>Kevin Simmons, UAMS Compliance Educator</td>
<td></td>
</tr>
<tr>
<td>Pharmacy Committee</td>
<td>(501) 686-6220 (Phone)</td>
</tr>
<tr>
<td>Mike Parr, Pharm.D.</td>
<td>(501) 296-1133 (Fax)</td>
</tr>
<tr>
<td>Protocol Review &amp; Monitoring Committee (PRMC)</td>
<td>(501) 686-8274 (Phone) (501) 296-1466 (Fax)</td>
</tr>
<tr>
<td>Angie Smith, LCSW, CRA PRMC Administrator</td>
<td></td>
</tr>
<tr>
<td>Radiation Safety Committee</td>
<td>(501) 686-5299 (Phone)</td>
</tr>
</tbody>
</table>
APPENDIX P: INVESTIGATOR’S STATEMENT REGARDING PROTECTION OF HUMAN SUBJECT

All Investigators must submit this form with new protocols.

**Investigator’s Agreement**

University of Arkansas for Medical Sciences Human Research Advisory Committee

I hereby agree that I will comply with the rules and regulations of the Human Research Advisory Committee, the Food and Drug Administration and the Office of Human Research Protections. If I am conducting research involving VA property or subjects, I also agree to comply with the rules and regulations of the Office for Compliance and Assurance.

By signing this document, I agree to the following:

1. No subjects will be recruited or entered into a protocol until an approval notification is received from the HRAC;
2. Changes or modifications in the research protocol during the period for which HRAC approval has been granted shall not be initiated without prior HRAC review and approval, except where necessary to eliminate immediate hazards to the subjects.
3. Written reports will be submitted to the HRAC as per HRAC policies described in the HRAC Investigators' Handbook for Human Studies regarding any deviation from the protocol and/or consent form, adverse events that are serious, unanticipated, and related to the study, or a death occurring during the study.
4. Continuing Review Report Forms will be submitted within the time limit stated on the forms.
5. If the study involves any funding or resources from outside sources, the Grants Coordinator in the Research Administration Office will be contacted regarding a contract. Subjects cannot be enrolled prior to completion of the contract, unless specified by the institution.
6. No human being will be involved as a research subject unless legally effective informed consent of the subject has been obtained.
7. The HRAC will be notified within 30 days of a change in the principal investigator or the closure of the study.
8. The proposed research protocol will be conducted by me or under my close supervision.
9. The HRAC shall have the authority to suspend or terminate approval of the research project if it is not being conducted in accordance with the HRAC’s decision, conditions, and requirements.

I agree to conduct the research protocol according to the above conditions.

_________________________________   _______________________
Signature           Date
APPENDIX Q: UAMS POLICY AND PROCEDURE FOR BILLING OF RESEARCH SUBJECTS

Policy No.: A.3.05
Section: Administration
Effective: July 1, 2000
Revision:
Subject: Billing for Research Procedures
Source:

**SCOPE:** University of Arkansas for Medical Sciences clinical research, patient registration, hospital and physician billing services.

**PURPOSE:** To ensure that research procedures are billed to the appropriate research study and are not billed to any third party payor.

**POLICY:** Each research study performed at UAMS will be assigned a unique guarantor CPI number and insurance plan code. Patient Business Services will be contacted at the inception of the research study to establish the research CPI number and insurance plan code. The unique CPI number and plan code will be forwarded to Medical College Physician Group (MCPG) via electronic transfer.

Persons registering patients for a research study visit must register the patient under the study's unique CPI number and insurance plan code to ensure that the study rather than the patient or third party payor is billed for the research visit. Standard of care procedures (procedures which would have been performed, regardless of participation in a research study, due to the patient's condition) are to be billed to the patient's third party payor.

Research personnel working with Patient Business Services and MCPG personnel will identify research procedures and ensure that those procedures are not billed to third party payors. Research personnel working with Patient Business Services and MCPG personnel will monitor the research study account and ensure that the research procedures are billed to the appropriate research study.
The following is a list of current contact persons and phone numbers for questions regarding establishing clinical research accounts and billing for clinical research procedures. The list will be updated as necessary.

<table>
<thead>
<tr>
<th>Issue</th>
<th>Contact Person</th>
<th>Phone Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>General questions regarding clinical research studies</td>
<td>Julia Washam</td>
<td>686-8572</td>
</tr>
<tr>
<td>Establishing clinical research study and CPI number and insurance plan code</td>
<td>Saundra Cooper</td>
<td>614-2809</td>
</tr>
<tr>
<td>Registering research patients for a visit in an outpatient clinic</td>
<td>Richard Starks</td>
<td>686-5808</td>
</tr>
<tr>
<td>Registering research patients for a visit in the Emergency Department</td>
<td>Mary Nellums</td>
<td>603-1323</td>
</tr>
<tr>
<td>Registering research patients for a visit in the Hospital (inpatient visit)</td>
<td>Cynthia Asuncion</td>
<td>686-6789</td>
</tr>
<tr>
<td>Registering research patients for a visit to the following ancillary areas: Cath lab, non-invasive lab, neurology lab, renal, and labor and delivery</td>
<td>Cynthia Asuncion</td>
<td>686-6789</td>
</tr>
<tr>
<td>Questions regarding hospital billing for research procedures</td>
<td>Wynndolyn Randall</td>
<td>526-5341</td>
</tr>
<tr>
<td>Questions regarding physician billing for research procedures</td>
<td>Michelle Barton</td>
<td>614-2016</td>
</tr>
<tr>
<td>Registering research patients for a Radiology procedure referred from outside</td>
<td>Odessa Miles</td>
<td>686-8328</td>
</tr>
<tr>
<td>Registering research patients for a Laboratory procedure referred from outside</td>
<td>Doris Torrence</td>
<td>686-6069</td>
</tr>
<tr>
<td>Establishing charges for grants</td>
<td>Cathy Young</td>
<td>682-3052</td>
</tr>
</tbody>
</table>
APPENDIX R: GUIDELINES FOR BLOOD DRAWS IN PEDIATRIC AND ADULT POPULATIONS

Note: For requests greater than the maximum draw, please contact the attending physician for approval of additional amounts for inpatients and the laboratory pathologist for additional amounts for outpatients.

Maximum Allowable Blood Draw Volumes Chart Based on Body Weight in Kilograms (Revised 09/2002)

<table>
<thead>
<tr>
<th>Body Weight In Kg</th>
<th>Maximum Drawn In One Blood Draw</th>
<th>Maximum Drawn In A 30 Day Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Kg</td>
<td>2.5 ml</td>
<td>23 ml</td>
</tr>
<tr>
<td>2 Kg</td>
<td>4.5 ml</td>
<td>23 ml</td>
</tr>
<tr>
<td>3 Kg</td>
<td>6 ml</td>
<td>23 ml</td>
</tr>
<tr>
<td>4 Kg</td>
<td>8 ml</td>
<td>30 ml</td>
</tr>
<tr>
<td>5 Kg</td>
<td>10 ml</td>
<td>40 ml</td>
</tr>
<tr>
<td>6 Kg</td>
<td>12 ml</td>
<td>40 ml</td>
</tr>
<tr>
<td>7 Kg</td>
<td>14 ml</td>
<td>40 ml</td>
</tr>
<tr>
<td>8 Kg</td>
<td>16 ml</td>
<td>60 ml</td>
</tr>
<tr>
<td>9 Kg</td>
<td>18 ml</td>
<td>60 ml</td>
</tr>
<tr>
<td>10 Kg</td>
<td>20 ml</td>
<td>70 ml</td>
</tr>
<tr>
<td>11 thru 15 Kg</td>
<td>22-30 ml</td>
<td>70-100 ml</td>
</tr>
<tr>
<td>16 thru 20 Kg</td>
<td>32-40 ml</td>
<td>130-140 ml</td>
</tr>
<tr>
<td>21 thru 25 Kg</td>
<td>42-50 ml</td>
<td>160-180 ml</td>
</tr>
<tr>
<td>26 thru 30 Kg</td>
<td>52-60 ml</td>
<td>200-220 ml</td>
</tr>
<tr>
<td>31 thru 35 Kg</td>
<td>62-70 ml</td>
<td>240-250 ml</td>
</tr>
<tr>
<td>36 thru 40 Kg</td>
<td>72-80 ml</td>
<td>270-290 ml</td>
</tr>
<tr>
<td>41 thru 45 Kg</td>
<td>82-90 ml</td>
<td>290-330 ml</td>
</tr>
<tr>
<td>46 thru 50 Kg</td>
<td>92-100 ml</td>
<td>330-350 ml</td>
</tr>
<tr>
<td>Greater than 51 Kg</td>
<td>100 ml</td>
<td>350 ml</td>
</tr>
</tbody>
</table>

Reference: 2.2 lb = 1 Kg

This information, for single draw, is similar to that recommended by the Committee on Clinical Investigations at Children’s Hospital in Los Angeles, and also used at Baylor College of Medicine in Dallas, Texas, and at Children’s Hospital and Regional Medical Center Laboratory in Seattle, Washington. The maximum draw volumes for a 30-day period are similar to those recommended by Becan-McBride, Phlebotomy Handbook (5th edition).

Adapted by Paula North, M.D., Ph.D., August 2002, Arkansas Children’s Hospital, Little Rock, Arkansas. Approved by ACH Patient Care Committee September 2002.