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**PAGE: 1 of 7**

**SECTION: RESEARCH**

**AREA: SPONSORED RESEARCH ADMINISTRATION**

**SUBJECT: REVIEW AND APPROVAL OF UAMS CLINICAL RESEARCH**

## **PURPOSE**

The purpose of this policy is to establish the review and approval process for UAMS clinical research and to provide an accurate and consistent mechanism to track study expenditures and payments received from sponsors in order to ensure that procedures required by the study protocol are charged appropriately.

## **SCOPE**

This policy applies to all persons conducting or involved in clinical research that involves any of the following:

- (a) UAMS faculty, staff or students;
- (b) UAMS owned assets (e.g. facilities, equipment and property);
- (c) Clinical services provided by UAMS; or
- (d) Research grants, contracts or agreements awarded to or subject to the control of UAMS.

The policy does not apply to research administered through the Biomedical Research Foundation at the Central Arkansas Veteran's Healthcare Administration. Except for [Appendix A](#), the policy does not apply to the Arkansas Children's Hospital Research Institute.

## **ABBREVIATIONS AND DEFINITIONS**

### **Abbreviations**

1. **FDA:** United States Food and Drug Administration
2. **GCP:** Good Clinical Practices
3. **ICH:** International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
4. **IDE:** Investigational Device Exemption
5. **IND:** Investigational New Drug (Application)
6. **IRB:** Institutional Review Board
7. **RSC:** Research Support Center
8. **SOP:** Standard Operating Procedure
9. **UAMS:** University of Arkansas for Medical Sciences

## Definitions:

1. **Research** is defined as any systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
2. **Human subject** is defined as an individual who becomes a participant in research.
3. **Principal Investigator** is defined as the person responsible for the conduct of the study. A clinical research study is often conducted by a team of individuals at an investigative site. In this case, the investigator is the responsible leader of the team and may be called the principal investigator (PI).
4. **Clinical research** is defined as any investigation involving human subjects that meets the definition of research. A **clinical trial** is an investigation involving human subjects that is carried out to discover or verify the safety and/or effectiveness of a diagnostic or preventative test/procedure, treatment, treatment regimen, or other intervention on the course, outcome, or other aspect of a medical condition or disease process. The treatment may be a drug, a multiple drug regimen, a device, a biological, radiation therapy, surgery, or any other intervention or procedure.
5. **UAMS Clinical Research** is clinical research that involves any of the following:
  - (a) UAMS faculty, staff or students;
  - (b) UAMS owned assets (e.g. facilities, equipment and property);
  - (c) Clinical services provided by UAMS; or
  - (d) Research grants, contracts or agreements awarded to or subject to the control of UAMS.
6. **Clinical Research where the IND or IDE is held by the industry sponsor** are clinical research studies that are conducted under an IND application or IDE, regulated by the FDA, funded by a pharmaceutical, biological, or device manufacturer, and subject to formal external monitoring by the sponsor or a designee (e.g., a Contract Research Organizational or Site Management Organization). The industry sponsor accepts the role of “sponsorship” as defined by FDA or International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines.
7. **Clinical Research where the IND or IDE is held by UAMS** is clinical research involving human subjects that may be funded in part or whole by a pharmaceutical, device, or biological manufacturer but does not meet other criteria for “industry sponsorship.” The manufacturer does not accept the role of “sponsorship” as defined by FDA or International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines.
8. **Clinical Research initiated by the investigator or where there is no IND** is research involving human subjects that is conducted by an individual or group of investigators; may be funded by industry, federal or private granting agencies, UAMS departmental or institutional funds, or self-funded; and for which the investigator and institution may bear responsibility for “sponsorship obligations”.
9. **Phase I Clinical Studies** are defined by the FDA as the initial introduction of an investigational new drug into humans. The studies are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness. During Phase I, sufficient information about the drug’s pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid,

Phase II studies. The total number of subjects included in a Phase I study varies with the drug, but is generally in the range of twenty to eighty.

10. **Phase II Clinical Studies** include the early controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug for a particular indication or indications in patients with the disease or condition. Phase II studies are typically well-controlled, closely monitored, and conducted in a relatively small number of patients (usually involving several hundred people if feasible).
11. **Phase III Clinical Studies** are expanded controlled or uncontrolled trials performed after preliminary evidence from Phase II trials suggests that a drug is effective. The purpose of these studies is to gather additional information about effectiveness and safety that is needed to evaluate the overall risk-benefit relationship of a drug. Phase III studies typically involve several hundred to several thousand people.
12. **Phase IV Clinical Studies** are studies done on an approved drug or device for the approved indication. These studies can be required by the FDA or can be initiated to study some particular parameter of the drug or device.
13. **Device** is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory that:
  - (a) Is recognized in the official National Formulary, the United States Pharmacopeia or any supplement to them
  - (b) Is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease in humans or animals
  - (c) Is intended to affect the structure or any function of the body of humans or animals
  - (d) Does not achieve any of its primary purposes through a chemical action within or on the body of humans or animals, and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes.

Exempt device – a device that meets the requirements of 21 CFR 812.2(c)

Non-significant risk device – a device that does not meet the specifications for a significant risk device.

Significant risk device – an investigational device that:

- (a) Is intended as an implant and presents a potential for serious risk to the healthy, safety, or welfare of a subject;
- (b) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- (c) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a serious risk to the health, safety, or welfare of a subject; or
- (d) Otherwise presents a potential for serious risk to the health safety, or welfare of a subject.

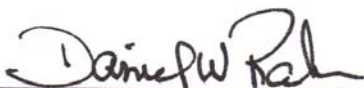
## **POLICY**

1. All UAMS clinical research must be reviewed and approved by the Research Support Center (“RSC”). The RSC shall facilitate the review process by assisting the Principal Investigator in preparing and finalizing required documents.
2. No UAMS clinical research may be submitted to the IRB prior to CRIMSON approval or specific, limited authorization from the UAMS RSC.
3. No clinical research may be conducted without funding for all direct costs associated with the project. Funding may be internal or external. External funding sources for clinical research must provide indirect costs.
4. UAMS, through RSC, will be the Sponsor, as defined by the FDA, and hold the IND or IDE for all UAMS investigator-initiated studies which require an IND or IDE in accordance with Administrative Guide policies 12.1.10 and 12.1.11. RSC will have the authority to require changes to the protocol and/or any other study documents as needed to meet UAMS’ obligations as Sponsor.
5. The RSC will only approve studies after first assuring that:
  - (a) the protocol is complete, proper in form, consistent with applicable regulations and appropriate for consideration by the IRB;
  - (b) the informed consent is complete, in appropriate form, consistent with applicable regulations, the protocol, any applicable clinical trial agreement or notice of grant award, and appropriate for review by the IRB;
  - (c) there is a coverage analysis for insurance/federal payor (Medicare, Medicaid, etc.) for the services to be provided in a clinical trial;
  - (d) there are sufficient funds and resources to cover all direct and indirect costs of the study;
  - (e) the budget prepared by the principal investigator is accurate, is in accordance with UAMS billing policies and is sufficient to cover all costs of the trial;
  - (f) the regulatory requirements applicable to the clinical trial are appropriately developed;
  - (g) studies involving an investigational device conducted by an investigator who is a faculty member, student, or employee of UAMS will be evaluated under the procedures outlined in Appendix A for determination of risk.
  - (h) any clinical trial agreement or other sponsor agreement for the clinical trial is consistent with University and UAMS policies, applicable state and federal law and appropriate to address all issues described in this policy; and
  - (i) the clinical trial is appropriately established and prepared to be in compliance with all applicable Federal and State laws to include all Medicare, Medicaid and other federal programs’ billing regulations.

## **PROCEDURE**

1. Review of clinical research by the RSC is initiated by the electronic submission of the following:
  - (a) ARIA CRIMSON submission form,
  - (b) the study protocol, which will set forth the types and frequency of tests, procedures, and services that are associated with the clinical research,

- (c) the study informed consent form, which must delineate financial responsibility for the tests, procedures, and services associated with the clinical research,
  - (d) the study budget which must address all direct and indirect costs, and
  - (e) a copy of any proposed clinical trial agreement or other sponsorship arrangement, if applicable.
2. Studies that do not include clinical services shall be reviewed expeditiously.
  3. A timely, responsive and thorough review is essential. The RSC may be assisted by specialists in various aspects of the review by other departments. The RSC will work to render its decisions to investigators in an expeditious manner, and will work with investigators and sponsors to meet critical deadlines necessary to advance the UAMS' research agenda.
  4. RSC staff shall be available to Principal Investigator(s) to assist in the preparation of a study. Staff will also assist in the preparation of documents.
  5. The review process is expected to be fluid and shall progress simultaneously (in accordance with staff and RSC resources) as necessary predicates are met. Where the protocol is prepared by an external sponsor full review may proceed upon submission of required documents.
  6. The department chair, the Dean, and the Hospital CFO, or respective designee, shall review the budget and acknowledge that sufficient funds are available to cover the direct and indirect costs of the study.
  7. The RSC shall document approval of the study through CRIMSON which will provide notification to the Principal Investigator
  8. The RSC will document the reasons for disapproving the study proposal, and will indicate, where possible, corrective measures to rehabilitate the proposal for possible resubmission.
  9. A Principal Investigator may request reconsideration of any disapproval and submit additional information in support of his/her request. The RSC shall consult with the Vice Chancellor for Research prior to rendering a decision on reconsideration.
  10. The RSC will provide the IRB with documentation of study approval that includes the following items:
    - (a) date and version number of RSC approved protocol,
    - (b) date and version number of RSC approved consent form,
    - (c) for industry sponsored studies, specific acknowledgment that the subject injury language in the consent form does not conflict with the contractual language, and
    - (d) for investigator initiated drug/device studies, RSC Regulatory Analysis Risk Determination letter.
  11. CRIMSON-approved documents will be submitted to ARIA in PDF format. The IRB staff shall compare submissions to ARIA against the CRIMSON-approved documents to identify modifications or changes. Material changes to protocol or informed consent shall be returned to the RSC for review and approval.

Signature: 

Date: February 8, 2012

## Appendix A

1. UAMS is the sponsor for all investigator-initiated clinical research protocols that include an investigational device and are conducted by UAMS faculty, students, or employees.

All such studies will be reviewed by the Risk Determination Committee which will be comprised of three representatives from Quality Assurance, Regulatory, Monitoring groups from the Research Support Center (“RSC”) as well as two faculty members, selected by the Vice Chancellor for Research (“VCR”), who have expertise in the use of medical devices, preferably in an investigational setting. The Risk Determination Committee will serve as UAMS’ (the sponsor’s) method for assigning risk to a device involved in an investigation.

2. A decision will be rendered by the Regulatory Unit of the Research Support Center as to whether a proposed clinical investigation using an investigational device is exempt from the device regulations (21 CFR Part 812) as defined by 21 CFR 812(c) and (d).
3. If the study involves an investigational device and is not exempt, the Risk Determination Committee will meet and determine if the study meets the criteria for a significant risk device (21 CFR 812.3(m)). If the device is not exempt and does not meet the criteria for a significant risk device, it will be declared a non-significant risk device.
4. The Risk Determination Committee may recommend that the study protocol and other relevant information be submitted to the United States Food and Drug Administration (FDA) for a determination.
5. If the investigator disagrees with the risk determination decision rendered by the Risk Determination Committee, including a recommendation by the committee to submit the study to the FDA for review, the investigator may appeal the decision by providing written notice to the VCR within 10 working days after notification of the Risk Determination Committee’s decision.
6. Upon receipt of the appeal, the VCR will convene the Investigational Device Review Committee (IRDC).
7. The IDRC will be composed of the following three members appointed by the VCR:
  - (a) The Director of the Research Support Center.
  - (b) Two faculty members who have expertise in the use of medical devices, preferably in an investigational setting who are not serving as members of the Risk Determination Committee. At least one of the faculty members must be a licensed physician.
  - (c) The VCR may appoint alternate members to serve when committee members are unable to attend a meeting.
8. The IRDC will review the Risk Determination Committee’s decision and advise the VCR. The IDRC will provide the VCR with a written opinion either agreeing with the

decision or providing an alternative determination with appropriate supporting information. The IRDC may develop a SOP describing its processes.

9. In the event that the IDRC is convened because of a disputed risk determination, the VCR will examine the reports from the Risk Determination Committee and the IDRC and render a final decision regarding the status of the investigational device. The VCR may choose to defer making a final decision and may instruct the RSC to request a formal risk determination from the FDA if one had not been previously obtained. If a determination is sought from the FDA, the result is final and may only be appealed further through the FDA.
10. Prior to the convened IRB meeting at which the study protocol is reviewed, the VCR or a designee will provide the sponsor's risk determination to the IRB in the form of a written letter or memorandum. The IRB will make an independent decision concerning risk as required in 21 CFR 812. That decision may not be less restrictive than a formal decision rendered by the FDA if one was obtained.
11. The investigator may begin the investigation only after final approval has been granted by the IRB and, if the investigational device is deemed to be significant risk, final written approval from the FDA. The investigator will be responsible for complying with appropriate sections of 21 CFR 812.