UAMS

UNIVERSITY OF ARKANSAS
FOR MEDICAL SCIENCES

Presented by: Office of the Vice Chancellor for Research

Date: January 7, 2014

Agenda

- **Updates & Timely Information from Research Support**

Office of the VCR
RSC
IRB
IACUC
TRI
UAMS Library
BioVentures
Cost/Grants Accounting
COI
ORSP
ORC
DLAM
OGSP
ACHRI/Core Facilities
Biomedical Informatics

Concept Development Project

Mildred Randolph, DVM, Director, DLAM

- **Want to do Biomedical Research using Animals?**
  - The Concept Development Project in the Division of Laboratory Animal Medicine (DLAM) can help!

Concept Development Project

Mildred Randolph, DVM, Director, DLAM

- **Concept Development's Goal**
  - To assist investigators who are new to animal-based research
  - To encourage IACUC (Institutional Animal Care and Use Committee) submissions
  - To remove barriers for pilot data collection and facilitate grant submissions

Concept Development Project

Mildred Randolph, DVM, Director, DLAM

- **Concept Development**
  - The Concept Development idea is intended to provide intensive one-on-one assistance to researchers who might not otherwise have the *time or experience* needed to do animal-based research

Concept Development Project

Mildred Randolph, DVM, Director, DLAM

- **The Concept Development Model**
  - DLAM will literally “hold your hand” through the following:
    - Animal model/species selection
    - Veterinary issues
    - DEA issues
    - Animal handling
    - Data collection
    - IACUC submittal process

Concept Development Project

Mildred Randolph, DVM, Director, DLAM

- **The Concept Development Model (cont.)**
  - Investigator's Responsibility
    - Develop a research idea/question
    - Do preliminary literature searches to determine feasibility
    - Strategically plan the project with DLAM
    - Gather pilot data for grant proposal submission

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

Rebecca Nickleson, MSHS, CRA
Assistant Director, Research & Sponsored Programs

- **Research & Sponsored Programs**
  - Goal of ORSP proposal review is to ensure adherence with application guidelines and federal, state, funding agency, and campus guidelines.
  - ORSP grants administrators need time to provide a thorough review of each application.
  - Investigators need time to correct applications based on ORSP review.
  - ORSP workflow efficiency and effectiveness are reduced when proposals are not submitted in a timely fashion.

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

Rebecca Nickleson, MSHS, CRA
Assistant Director, Research & Sponsored Programs

- **Initial draft grant applications must be entered into ARIA** (or any subsequent grants management system) and signed by the Principal Investigator *seven (7) business days* prior to the published application deadline.

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

Rebecca Nickleson, MSHS, CRA
Assistant Director, Research & Sponsored Programs

- **Final grant applications**
  - Must be received by ORSP 48 hours (2 business days) before the published application deadline. If the final proposal is not received by ORSP by the 48 hour deadline, it will not be submitted.
- **Final Proposal**
  - A grant application that has been reviewed and approved by the Principal Investigator's sub-department, department, college, and ORSP with all requested corrections made.

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

Rebecca Nickleson, MSHS, CRA
Assistant Director, Research & Sponsored Programs

- **Exception**
  - An exception to this policy will only be made based on prior approval from both the Director of ORSP and the Vice Chancellor for Research.

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

Rebecca Nickleson, MSHS, CRA
Assistant Director, Research & Sponsored Programs

- Sub-departments, Departments and Colleges/Divisions must set **and enforce** their own internal deadlines for grant applications.
  - These deadlines will allow Sub-department, Department and College/Division Administrators to have ample time to provide their own review of grant applications before signing off.

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

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Assistant Director, Research & Sponsored Programs

- Under most circumstances, ORSP will provide a review of the draft proposal within 24 hours of Department approval. In times of heavy proposal volume, review may take up to 48 hours.

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

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Assistant Director, Research & Sponsored Programs

Example Timeline Based on a Monday Deadline

Proposal Entered in ARIA and Signed by PI	Department Approval	ORSP Provides Review of Draft Proposal	Final Due to ORSP	Proposal Due Date
Thursday – 5 pm	Monday – 5 pm	Wednesday – 5 pm	Thursday – 5 pm	Monday – 5 pm

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

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Assistant Director, Research & Sponsored Programs

Organization	Director	Asst. Dir.	Grants Admin.	System & Software	Other	Total Staff	Deadline for Final Application
UAMS	1	1	2	0	0	4	2 Business Days
Princeton	1	1	11	3	0	16	5 Business Days
Boston U.	1 (AVP)	2 Assoc. 1 Assist.	17	6	3 (Contract Admin)	30	5 Business Days

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

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Assistant Director, Research & Sponsored Programs

- **What happens when proposals miss the 48 deadline?**
  - ORSP does not have time to complete a thorough review which leads to:
    - Grants.Gov errors that must be corrected before moving forward
    - Funding agency errors that must be corrected and the proposal re-submitted
    - The window for PI review is shortened or goes away completely (NIH only)

UAMS Administrative Policy 16.1.14 Grant Submission & Deadlines

Rebecca Nickleson, MSHS, CRA
Assistant Director, Research & Sponsored Programs

- If you have a **true emergency* situation**
  - Contact your ORSP administrator
    - We are here to provide support
    - We understand difficulties that arise
    - NIH accepts late applications in extenuating circumstances

***Lack of time management does not constitute a true emergency.**

CMS' New Rule for Clinical Trials
Subtitle: They're making a list… checking it twice…

Tom Wells, MD, MBA
Director, Research Support Center

- Clinical Trial Registration
- Reasons to Register Clinical Trials & Report Results
- Registered Trials
- Center for Medicare and Medicaid Services
- Requirements
- "Desirable Characteristics
- New Rule
- Who Must Register Trials?
- Investigator Initiated Trials
- Investigator Initiated Studies
- Last Minute Update…The Latest from CMS
- Questions

Clinical Trial Registration

- Registration of clinical trials grew out of several well publicized cases where unfavorable data were not disclosed to the FDA in NDA submissions
- FDA Amendments Act (FDAAA) passed in 2007 requires registration of most clinical trials
- ICMJE will not publish studies if the trials are not registered in an approved database

Reasons to Register Clinical Trials and Report Results

- Human Subject Protections
  - Allows potential participants to find studies
  - Assists ethical review boards and others to determine appropriateness of studies being reviewed (e.g., harms, benefits, redundancy)
  - Promote fulfillment of ethical responsibility to human volunteers – research contributes to medical knowledge
- Research Integrity
  - Facilitates tracking of protocol changes
  - Increases transparency of research enterprise
- Evidence Based Medicine
  - Facilitates tracking of studies and outcome measures
  - Allows for more complete identification of relevant studies
- Allocation of Resources
  - Promotes more efficient allocation of resources

Deborah A. Zarin, MD, October 2009

Registered Trials

- Trials are registered on ClinicalTrials.gov
- Each trial receives an NCT number
  - NLM Clinical Trials database assigns numbers
  - All numbers are preceded by "NCT"
  - Followed by an 8-digit number
- Failure to register or update trials that fall under the requirements of FDAAA may result in penalties (up to $10,000 per day)

Center for Medicare and Medicaid Services

- CMS allows most routine costs of a clinical trial to be billed to Medicare for "qualifying clinical trials" (note: there are exceptions)
- "Qualified" means that a trial meets conditions established by CMS to allow billing for covered services and procedures
- "Not qualified" = billing not allowed
- Trials receiving Medicare coverage for routine costs must meet certain conditions

Requirements

- Trials receiving Medicare coverage for routine costs must meet three requirements:
  1. Purpose of the trial must be the evaluation of an item or service that falls within a Medicare benefit category
  2. Must have a therapeutic intent
  3. Trials of therapeutic interventions must enroll patients with diagnosed disease rather than healthy volunteers; trials of diagnostic tests may enroll healthy subjects as controls

“Desirable Characteristics”

- Meeting the three requirements is insufficient to qualify a clinical trial for Medicare coverage of routine costs.
- Seven desirable characteristics should also be present (note: many of these must be determined by the investigator)
- “Deemed Trials”: special category automatically qualified to receive Medicare coverage for routine costs

New Rule

- Effective January 1, 2014, it is mandatory to report a clinical trial number (NCT) on claims submitted to Medicare for payment of routine costs for qualifying clinical trials
- Voluntary reporting has been in effect since January 18, 2008

Who must register trials?

- The sponsor is responsible
  - Industry
  - Cooperative group
  - Investigator-initiated
- When should you register?
  - FDAAA: up to 21 days after enrollment of the first subject
  - ICMJE: before enrollment of the first subject

Investigator initiated trials

- If a trial is a Medicare qualifying clinical trial and you wish to bill patients for any costs of the trial, it must be registered (e.g. if you compare the effectiveness of standard of two drugs to treat any condition and the trial meets the requirements and desirable characteristics for a qualifying trial, and you intend to bill subjects for costs related to the study), you need an NCT number

Investigator initiated studies

- When to register:
  - To meet FDAAA or ICJME provisions
  - If registration is not needed for these reasons then only if the trial meets both of the following:
    - Meets criteria for a qualifying trial
    - The trial includes any service or procedure cost is billable to Medicare on an individual subject/patient bill
  - If all costs are covered by a grant and nothing is billed to a subject, registration is not required

Investigator initiated trials

- Types of studies that do not need to be registered to meet CMS billing requirements:
  - Observational studies (retrospective chart reviews, surveys, etc.)
  - Studies not involving any procedures or services that are billed to patients/subjects
  - Studies that include potentially billable services and procedures but all costs are covered by a grant and Medicare is not billed for any services or procedures

Last Minute Update…the latest from CMS

- People or institutions that do not have the capacity to report the NCT number may enter "99999999" in the appropriate field
- Claims will be processed
- This "grace period" lasts one year
- As of January 1, 2015, everyone must report a NCT number on every bill submitted to Medicare Administrative Contractors (MACs)

Questions

- Trial registration (ClinicalTrials.gov):
  - Tracy Gatlin — Office: 686-6803
- Medicare Coverage:
  - Mtonya Hunter-Lewis — Office: 686-8184
  - Barbara Adams — Office: 686-8187
- Complaints:
  - Tom Wells — Office: 603-1638
  - President of the U.S. — Office: 202-456-6213


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"HERE—THE ROYAL SAFETY COUNCIL SAID YOU HAVE TO WEAR THIS."

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **CRS Program**
  - Provides essential training in key areas for individuals involved in, or interested in learning more about, research at UAMS

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **Earn CRS Status**
  - 20 Required hours
  - 6 Elective Hours
  - CRS Exam

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **Training/Education**
  - CITI Human Subject Protection Training
  - Essentials of Quality Human Subject Research
    - CLARA/IRB Review
    - Informed Consent
    - Record Keeping & Regulatory Binders
  - Advanced Research Ethics
  - Adverse Event Reporting
  - Developing a Research Protocol
  - Writing Standard Operating Procedures

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **Training/Education**
  - Responsible Conduct of Research
  - Information Quality
  - Research Billing
  - ClinicalTrails.Gov Overview
  - Webinars
    - AAHRPP
    - Barnett
    - PRIM&R
    - Huron

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **Maintain CRS Status**
  - 6 elective hours
  - CITI Human Subject Protection Training

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- No charge for participation
- 1-2 years to complete
- Annual ceremony

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **To Register**
  - Full Name
  - Email
  - Department
  - Supervisor
  - Slot Number
  - SAP (if applicable)

ctvirgil@uams.edu

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Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **IMPORTANCE**

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **Contact Information**

  Charnise Virgil

  Office of Research Compliance

  ctvirgil@uams.edu

  501.526.6879

http://www.uams.edu/ice/CRSProgram.htm

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Certified Research Specialist (CRS) Program

Charnise Virgil, Research Compliance

- **Questions?**

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

- What Are They?
- How Do I Get One?
- Warning Letter Elements
- Most Common Citations
- Mass General Warning Letter Citations
- FDA 1572 – Investigator's Agreement – Drugs
- NSR Device Investigator's Agreement
- SR Device Investigator's Agreement
- Questions – Contacts
- Links

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

What is a Warning Letter?

- Contains documented violations that FDA uncovered during inspections or investigations of regulated entities
- Notifies responsible individual or firm of activities FDA considers in violation of the Federal Food, Drug, and Cosmetic Act (the Act)
- Only issued for violations of regulatory significance, (i.e., may lead to enforcement action)
- One of FDA's principal means of achieving prompt voluntary compliance with the Act
- Considered to be informal and advisory – does not commit FDA to take enforcement action

Warning Letters

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How Do I Get One?

- FDA shows up at your door; does NOT have to give advance notice
- Issues a 482 – Notice of inspection presented upon arrival
- Issues a 483 – What they discovered during the inspection
- Issues an EIR – Establishment Inspection Record after which time FDA determines issuance of “Untitled” or Warning Letter
- Warning Letter – 15 business days to respond with Correction Action Plan
- NIDPOE - Notice of Initiation of Disqualification Proceedings and Opportunity to Explain
- NOOH – Notice of Opportunity for Hearing
- Disqualification – Can be for a period of months, years, or permanent

Warning Letters

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Warning Letter Elements

- "WARNING LETTER" will be noticeably at the top
- Addressed to the highest known official in the firm; sent via overnight delivery
- Dates of inspection, description of violated condition, practice, or product along with a citation of the law/regulation section violated
- Acknowledgements of corrections promised during the inspection or provided in a written response
- Request for a response (usually within 15 working days) and instructions on how to respond
- Warning statement that failure to achieve prompt correction may result in enforcement action without further notice
- Identification of Agency official issuing the letter

Warning Letters

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Most Common Citations

- You failed to conduct the studies according to the investigational plan [21 CFR 312.60 or 21 CFR 812.100 and 812.110(b)]
- You failed to obtain informed consent of subjects involved in research in accordance with the provisions of 21 CFR Part 50 [21 CFR 312.60 or 21 CFR 812.140(a)(3)]
- You failed to maintain adequate and accurate records for disposition of the investigational drug [21 CFR 312.62(a)]
- You failed to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation [21 CFR 312.62(b) or 21 CFR 812.140(a)(3)]
- You failed to assure that an Institutional Review Board (IRB) complying with applicable regulatory requirements was responsible for the continuing review and approval of a clinical study [21 CFR 312.66]

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Warning Letters

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Massachusetts General Hospital Warning Ltr.

- You failed to ensure that the investigation was conducted according to the signed investigator statement, the investigational plan, and the applicable regulations, and to protect the rights, safety, and welfare of subjects under your care. [21 CFR § 312.60]
- You failed to administer the drug only to subjects under the investigator's personal supervision or under the supervision of a subinvestigator responsible to the investigator. [21 CFR § 312.61]
- You failed to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation [21 CFR 312.62(b)]
- You failed to obtain informed consent of subjects involved in research in accordance with the provisions of 21 CFR Part 50 [21 CFR 312.60]

Issued to Massachusetts General Hospital - 29 November 2013

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

FDA 1572 – Investigator's Agreement - Drugs

- I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects
- I agree to personally conduct or supervise the described investigation(s)
- I agree to inform any patients or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR 50 and institutional review board (IRB) review and approval in 21 CFR 56 are met
- I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) ion accordance with 21 CFR 312.64. I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

FDA Form 1572 (cont.)

- I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed abut their obligations in meeting the above commitments
- I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68
- I will ensure that an IRB that complies with the requirements of 21 CFR 50 will be responsible for the initial and continuing review and approval of the clinical investigation
- I agree to comply with all the other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR 312

Warning Letters

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NSR Device Investigator's Agreement

- I agree to maintain the following Investigator Records
  - Informed consent
  - Adverse events (expected and unexpected)
  - Deviations from the clinical protocol
- Investigator Reports
- I agree to report to the Sponsor within 5 working days, if there is withdrawal of IRB approval
- I agree to report any enrollment into the study or activities performed without informed consent
- I agree to supply other reports as requested by the Sponsor, IRB, or FDA

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

SR Device Investigator's Agreement

- I agree to maintain accurate, complete, and a current records related to my participation in the investigation. These records shall be maintained throughout the investigation and for two years after the completion of the investigation, provided the sponsor then releases them for disposal. These records include the following:

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

SR Device Investigator's Agreement (cont.)

- Complete records of each subject's case history and device exposure, to include:
  - Informed consent documents
  - Relevant observations, including records of Serious Adverse Events, Unanticipated Risks to subjects and others, information and data on subjects' initial condition as well as condition during and after completion of investigation (e.g., information on medical history and diagnostic test results)
  - Records of subject investigational device exposure, including date/time of each use as well as therapy

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

SR Device Investigator's Agreement (cont.)

- Investigational Study Protocol, including dates and reasons for deviations, as well as documentation of appropriate reporting of deviations
- Other sponsor-required documentation or records as identified in the investigational plan or official correspondence
- Other documentation or records required by FDA

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

SR Device Investigator's Agreement (cont.)

- I agree to obtain written informed consent before including any individual in this investigation. I agree to maintain the following Investigator Records
- I agree that no consent shall be obtained prior to IRB and/or FDA approval (as applicable).
- I agree to report withdrawal of IRB approval of any part of the study to the sponsor, within five working days.
- I agree to submit progress reports at regular intervals and no less than yearly, to the sponsor and the reviewing IRB

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

SR Device Investigator's Agreement (cont.)

- I agree to deviate or modify from the investigational plan only in the case of emergency protection of the life or physical well being of the subject. I will notify the sponsor and IRB no later than 5 working days after the deviation/modification occurred. Non-emergency deviations or modifications require prior approval from the sponsor, IRB, and (if applicable) FDA. I agree to maintain the following Investigator Records
- I agree to report the use of an investigational device without the informed consent from the appropriate individual, to both the sponsor and reviewing IRB within five working days.

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

- **Questions?**
- **Contacts**
  - Carole Hamon, Regulatory Affairs Manager, HamonCaroleA@UAMS.edu; 526-7437
  - Amy Jo Jenkins, Monitoring Manager AJJenkins@UAMS.edu; 686-5939

Warning Letters

Carole Hamon, Assoc. Director, Regulatory Affairs Mgr., Research Support Center

- **Links**
  - **Warning Letters**
    http://www.fda.gov/iceci/enforcementactions/warningletters/default.htm
  - **Disqualification Proceedings**
    http://www.fda.gov/ICECI/EnforcementActions/ucm321308.htm

Next RESIN

- **Next RESIN**
  - **February 4, 2014 @ 12:00 p.m.**
  - Location - **Walton Auditorium**, Winthrop P. Rockefeller Cancer Institute, 10th floor
  - All RESIN presentations archived on the UAMS Research website
    - http://www.uams.edu/research/RESIN_Achive.asp