Starting a new clinical study
Process overview and discussion

Research Support Services | September 10, 2018

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Learning Objectives

- Review process for activating a new clinical study at UC Irvine

- Understand roles and responsibilities of different central offices

- Know where to go for help and guidance

- Question & answer session

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Term overview

- Sponsor-initiated clinical study
  - UC Irvine is activated as one site on an industry-authored protocol
  - Competitive activation and time sensitivity
  - High complexity, high financial risk/reward

- Investigator-initiated clinical study
  - Generally, authored by researchers at UCI or another academic institution
  - External funding, when present, is subject to sponsor's peer review
  - UCI Scientific Review evaluates non-peer-reviewed studies

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Term overview (continued)

- Institutional Review Board
  - Committee review of clinical studies for risks/benefits to human volunteers (subjects), in relation to benefits to scientific knowledge
  - Review may be conducted by UC Irvine Human Research Protections (HRP) or by an external single IRB (sIRB)
  - External sIRB approval must be registered with UCI HRP

- Coverage Analysis
  - Identifies appropriate payer for all items/services in a protocol schedule of events (SOE), whether patient/insurance, or research funding

- Contract/Grant
  - Mechanism to pay UC Irvine for work performed
  - Terms/conditions negotiated by Sponsored Projects Administration (SPA) or Applied Innovation (AI), subject to UC policies

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Term overview (continued)

- Clinical Study
  - A research study involving human subjects that is intended to add to medical knowledge.
    - Observational/data collection study: assesses biomedical or health outcomes; subjects are not assigned to a specific intervention/treatment
    - Interventional study: assigns subjects to intervention and/or control groups to evaluate the effects of the interventions on biomedical or health outcomes

- Clinical Trial (FDA)
  - Assigns subjects to intervention and/or control groups per an FDA Investigational New Drug (IND) or Device Exemption (IDE) filing

- Clinical Trial (NIH-funded)
  - Assigns subjects to intervention and/or control groups to evaluate the effects of those interventions on biomedical or behavioral outcomes

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Process Overview (general)

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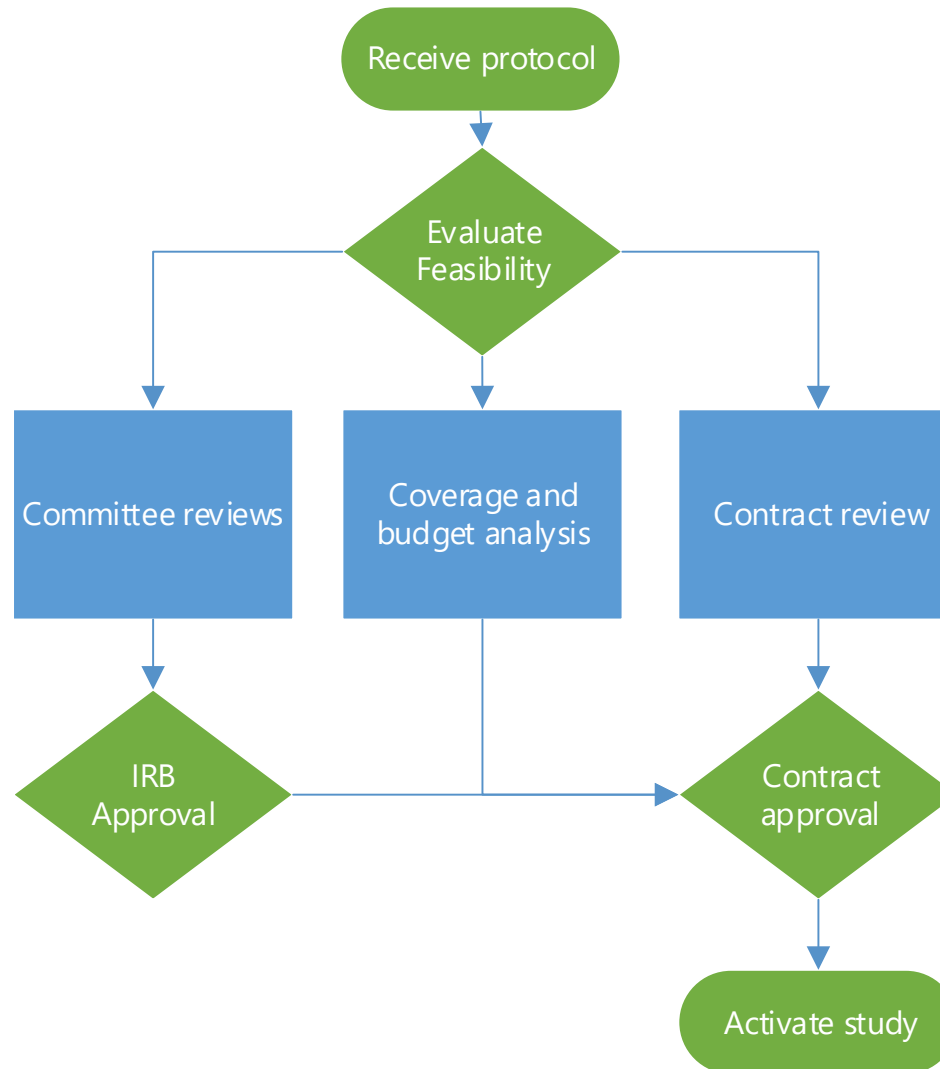
Sponsor-initiated clinical studies: process overview

1. Sponsor designs a clinical study
    a. Sponsor provides a disclosure agreement (NDA/CDA) allowing UCI to review the clinical protocol and study documents

2. Study team assesses study documents for feasibility

3. Parallel processes ensure timely study activation
    a. HRP Approval/sIRB registration
    b. Coverage and Budget Analysis
    c. Contract negotiation

4. Upon approval, UC Irvine is activated as a study site and begins screening/enrolling subjects

5. UC Irvine is closed to enrollment, finishes subject assessments, and closes study

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Investigator-initiated studies: process overview

1. Researchers design a clinical study
   a. UCI Principal Investigator (PI) designs study
      1. For external funding, sponsor conducts peer-review and issues an award to UCI
      2. For internal funding, UCI Scientific Review approves protocol and Chair approves financial commitments
   b. An external PI designs the study, applies for funding and selects UCI to participate as a site

2. Parallel processes ensure timely study activation
   a. IRB/Ancillary Committee submissions
   b. Coverage Analysis/Budgeting submissions
   c. Contract/grant negotiation

3. Upon approval, UC Irvine begins screening/enrolling subjects

4. UC Irvine is closed to enrollment, finishes subject assessments, and closes study

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Disclosure agreements and feasibility
Is the study a good fit for UC Irvine?

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Steps to Conduct Feasibility Review

1. If sponsor-initiated, UC Irvine completes disclosure agreement (CDA/NDA)
   a. Only SPA/AI Officers may sign CDA/NDAs

2. Departmental feasibility
   a. Does the department have sufficient patients that meet the criteria, and bandwidth to recruit/engage them?
   b. Which team members will conduct the study?
   c. What are the clinical throughput and skill requirements?

3. Institutional feasibility
   a. Ancillary units: does UC Irvine have the necessary capabilities?
   b. Budget overview: Can the sponsor cover standard fees?

Discussion: Feasibility Assessment

- How does your department assess a clinical protocol?

- How does your department engage support units to evaluate feasibility?
  - Investigational Drug Service
  - Radiology Research Services
  - Experimental Tissue Resource
  - Institute for Clinical and Translational Sciences

- What opportunities and challenges have you encountered?

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IRB and Ancillary Committee reviews
Is the study a good fit for UC Irvine subjects?

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Steps to Secure Institutional Review Board Approval

1. PI greenlights the IRB application process

2. Study team selects appropriate Review Board
   a. sIRB: when UC Irvine defers to an external IRB's approval, we must work with the IRB Reliance Administrator to register that approval with HRP
   b. UCI HRP: Can review all clinical studies; specializes in UCI investigator-initiated studies

3. Study team initiates IRB application or sIRB registration

Resource: sIRB Reliances Chart

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Steps to Secure Ancillary Committee Approvals

- Do the study activities require approval from Ancillary Committees? Some common committees include:
  - **Institutional Biosafety Committee (IBC)**: Analysis of human materials in a non-clinical area; recombinant DNA.
  - **Human Stem Cell Research Oversight (hSCRO)**: Research involving human stem cells
  - **Radiation Safety Committee (RSC)**: Research exposing subjects to radiation not considered conventional care
  - **Protocol Review and Monitoring Committee (PRMC)**: cancer-related studies
  - Other committees

Resource: list of Committees and domains

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Discussion: Committee Reviews

- How do you select UCI IRB or sIRB review?

- How do you identify applicable ancillary committees?

- What opportunities and challenges have you encountered?

Coverage Analysis/Budgeting
What are the costs of conducting the study?

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Steps to Secure Coverage Analysis

1. Study team identifies if activities occur in any UC Irvine Health facility

2. Coverage analysis identifies all Health System items/services under a clinical protocol and the appropriate payer for each
    a. Patient/Insurance
    b. Research funding (internal/external)

3. PI accepts contents of Coverage Analysis

4. Coverage analysis is used throughout the study to safeguard patients' charges and uphold UCI's commitments in the Informed Consent Form (ICF)

Resource: Coverage Analysis Request Form

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Steps to Secure Budget Analysis

1. The budgeter identifies all expenses in an internal budget
   a. Standard startup/maintenance/closeout fees
   b. Study team time & effort
   c. Data management time & effort
   d. Ancillary unit costs (from Feasibility Analysis)
   e. UC Irvine Health costs (from Coverage Analysis)
   f. Departmental overhead
   g. University overhead

2. The budgeter compares expenses against proposed payments in the sponsor budget

3. The budgeter negotiates and accepts sponsor payments to recover all costs

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Discussion: Coverage Analysis/Budgeting Reviews

- How does your department approach internal budgeting? Do you use a standard fee schedule?

- How does your department conduct budget negotiations? How do you engage and leverage the PI to remove barriers?

- What opportunities and challenges have you encountered?

Contract/Grant Negotiation
What are the terms of conducting the study?

Steps to Secure Contract Approval

1. Study team requests contract review from SPA/AI Officers
   a. SPA/AI Officers use the Kuali Research (KR) document routing system to review study documents
   b. Study team must upload protocol, contract/budget drafts, and notify assigned Clinical Trial Officer
   c. Depending on the study type, either SPA or AI will review

2. Once budget is final, Analyst uploads in KR and routes for approvals
   a. PI and Chair approve department commitments
   b. Dean's delegate matches budget to coverage analysis
   c. SPA/AI Officers send final compiled agreement for PI signature

Resources: Kuali Research main page
Contract Officer departmental assignments

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Discussion: Contract Reviews

- How does your department request contract review, coverage analysis/budget review, and IRB review? If the duties are separated, how do you coordinate with your colleagues?

- How do you analyze the protocol to determine whether SPA/AI officers will handle, and the correct overhead rate to use?

Protocol amendments
What documentation must be updated throughout the study?

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Steps to track protocol amendments

When the study sponsor provides an updated protocol reflecting changed items/services, study teams must:

1. Submit amended protocols for UCI HRP review (local IRB only);

2. Request coverage analysis modification;

3. Negotiate budget changes with the sponsor;

4. Submit revised budget and amendment request to SPA/AI officers

Discussion: Protocol Amendments

- How does your department coordinate protocol amendments to ensure that documentation is updated throughout the life of the study?

- What opportunities and challenges have you encountered?

Points of Contact

- UCI Human Research Protections: IRB@research.uci.edu

- UCI IRB Reliance Administrator: IRBReliance@uci.edu

- Coverage Analysis: coverageanalysis@uci.edu

- Budgeting
  - Departmental Administrative/Financial Officers
  - Mark Bourbonnais, Director, Contracts & Grants, School of Medicine, mbourbon@uci.edu

- Contract negotiation
  - Tam Tran, Assistant Director, Sponsored Projects Administration, tamkt@uci.edu
  - Angie Karchmer, Industry Contracts Officer, Applied Innovation, akarchmer@uci.edu

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Training Resources

- ## Clinical Research 101 training: UC Learning Center

Day 1	Day 2
September 18th (11am-12:30pm)	September 20th (2pm-3:30 pm)
October 16th (11am-12:30pm)	October 18th (2pm-3:30 pm)
November 15th (2pm-3:30 pm)	November 20th (11am-12:30pm)
December 18th (11am-12:30pm)	December 20th (2pm-3:30 pm)

http://uclc.uci.edu

- ## CITI online training
  - ### Human Research Protections (HRP), Good Clinical Practice (GCP), Clinical Research Coordinator (CRC)

    https://www.research.uci.edu/compliance/human-research-protections/researchers/training-and-education.html

- ## ACRP online training
  - ### Ethics and Human Subjects Protections, Good Clinical Practice (GCP), Clinical Research Coordinator (CRC)

    http://www.icts.uci.edu/crc/acrp.pdf

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Wrap-up Discussion

- What content areas interest you for further training?

- What questions do you have for us?

- Contact us: School of Medicine Research Support Services, somrss@uci.edu

Thank you for attending!