The Role of the Clinical Research Coordinator

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Clinical Research Coordinator

- Point person that keeps study together
  - Local protocol expert
  - Person PI counts on
  - Resources for clarification when unsure
    - PI
    - Nurses
    - Sponsor
      - Monitor
      - Medical Director
    - OHSU resources
      - OCTRI
      - OHSU Research Integrity Office
      - RDA offices
    - Other experienced coordinators

Clinical Research Coordinator

What makes a good research coordinator?

Research Coordinator Qualities

- Strong personal ethics
- Clinical competency
- Organized & detail oriented
- Operational knowledge of:
  - Research process
  - Institutional infrastructure
- People skills
- Patience & flexibility
- Problem solver

Required Research Coordinator Training

- Before starting study, get trained
- Know what study related activities you can perform
  - Research Assistant/Associate Scope of Practice
  - http://www.octri.org/octri/public/common/getdocpublic.aspx?docid=017FE84D-7C7D-452F-9B56-FDFE1657812D
- Required training based upon the activities conducted in the study
  - Clinical Research Coordinator Required Training Checklist
  - http://www.octri.org/octri/public/common/getdocpublic.aspx?docid=648678D7-6613-44A3-B5EF-121E0AE1E8CD

Project Assessment

- Is the study suitable for you?*
  - Investigator-initiated vs. industry driven trial
  - Quality of experience with sponsor / ask colleagues
  - Proposed study have scientific merit
  - Potential benefit > risk
  - Suitable for your area of research
  - Other departments/services meet protocol demands
  - Consider enrollment barriers/ recruitment strategies
  - Consider subject compliance problems

*If the PI designed the study, these considerations should be integrated into the study design

Project Assessment, cont.

- Is your unit suitable for the study sponsor?*
  - Industry sponsors send suitability questionnaire:
    - Subject population
      - Proposed enrollment goal, enrollment period
      - Number of pts. seen per year with disease
      - Competing study
    - Dedicated, experienced coordinator
    - Services (procedures, equipment)
    - Is there adequate space to:
      - House study coordinator & binders (regulatory & CRF)
      - Store study supplies
      - Monitor study activities

*Industry initiated studies only

Sponsor Preferences

- High ethical standards & integrity
- Site qualified by PI/coordinator training & experience.
- Knowledge of therapeutic area
- Access to population → referral system
- Understanding of FDA, ICH, GCP (ICH E6)
- Efficient IRB
- Good record keeping w/ source docs
- Research Pharmacy

Decision Made to Participate (Industry)

- Prestudy Visit: To assess appropriateness of site
  - Plan ½ day (schedule meeting room)
  - Schedule PI & sometimes sub-investigators
  - Talk with coordinator about experience/time
  - Schedule pharmacy visit
  - Schedule laboratory visit
  - Visit clinical area (clinic, inpatient, ICU)
  - View coordinator work & study storage space
  - Complete site information questionnaire

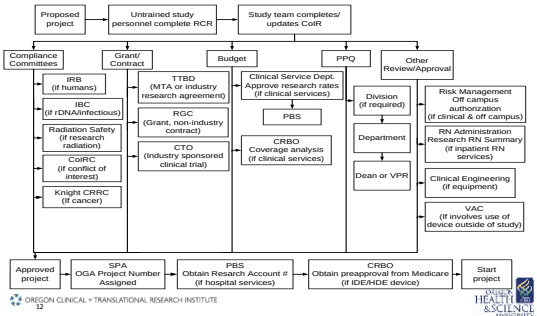
Decision Made to Participate (Industry, cont.)

- Once it's decided to take part, ask for these documents (in electronic form, if possible):
  - Protocol
  - Investigational Drug Brochure: Contains all research results
  - Copy of the case report form (even if draft)
    - Use to develop budget
    - Use to build coordinator checklist or study Standard Operating Procedure (SOP)
  - Sample consent
  - Draft contract: Send to Clinical Trials Office (CTO) - Contracting

Decision Made to Participate (Industry, cont.)

- Ask sponsor for express mail acct. number
- Collect sponsor regulatory documentation (prior to site initiation, helpful links at OCTRI Study Start-up website):
  - Form FDA 1572
  - Protocol signature page
  - Investigators' CVs, licenses
  - Lab: certifications (CLIA, CAP) & normal ranges
  - IRB membership roster
  - IRB minutes if PI IRB member showing recusal
  - Financial disclosure for investigators

Preaward Process



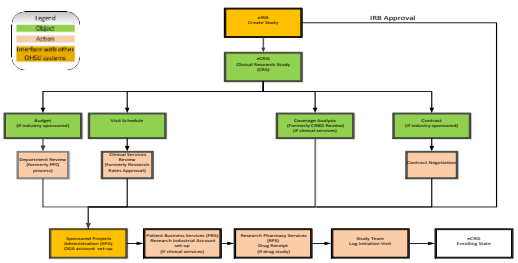
Electronic Clinical Research Information System (eCRIS)

- An institution-wide computer application for the budgeting, financial management, contracting, and study management, including subject tracking, regulatory reporting and document management, of OHSU clinical research studies
- Vendor: Huron/ClickCommerce (same as eIRB)
- Interfaces: eIRB, OGA, and Epic
- eCRIS information
  - www.ohsu.edu/crms
  - ecrissupport@ohsu.edu

Electronic Clinical Research Information System (eCRIS) cont.

eCRIS Adoption Schedule	Date
Big Brain training available to all users	June
Mandatory 4 Hr Classroom Training Available*	22-Jul-13
Phase 1 Go Live: Campus Wide Optional Use	22-Jul-13
Phase 2 Go Live: Invoicing Available	4-Nov-13
All new studies submitted to IRB require eCRIS/Knight Go Live	29-Jan-14
Phase 3 Go Live: Additional Functionality	Summer-14
All existing studies migrated to eCRIS	14-Jul-14

eCRIS Preaward



Budget Development

- Determine standard of care vs. research-related procedures
- Create cost based budget
- Remember applicable fees/costs (automatically populated in eCRIS for industry studies)
  - pharmacy (for drug studies)
  - IRB review fees (required for industry studies)
  - Radiology start-up fee (industry studies, $100)
  - archiving costs
- Develop based on funding type
  - Non-industry: follow grant instructions (salary cap, allowable expenses, etc.)
  - Industry:
    - Negotiate
    - Enter negotiated terms in eCRIS
- Use appropriate indirect cost rate (IDC)
  - Federal: modified total direct cost (MTDC): Change annually
    - Clinical Trial: 32% MTDC
    - Research: 54% MTDC
  - Industry clinical trial:
    - 25% total cost (TC)
    - May be additional Department or Division Assessment: Separate line item, do not include in IDC
    - eCRIS: Automatically included in budgets (IDC and DA)

Industry Budgets

- Charge for start-up costs
  - Budget development & negotiation
  - Regulatory document preparation & submission
  - IRB document preparation & submission
- Review and negotiate payment terms
- Negotiate at least neutral budget (5-10% cushion optimal)
- Add ~10% inflation per year of the study to healthsystem prices

Budget Development Training

- Clinical Trial Financial Training: Research Administration Training & Education (RATE): http://www.ohsu.edu/xd/research/administration/rate.cfm
- 2 classes (Preaward and Postaward)

Contracts (industry sponsored)

- Negotiated by Clinical Trials Office (CTO) Contracting
- Contract analyst assigned by department
- As soon as decide to participate in study, send to Contract Analyst via eCRIS:
  - Contract in Word format
  - Contact information for sponsor
- Inform CTO of:
  - Involvement of VA, if any
  - Subcontracts, if any
- Contracts tracked and stored in eCRIS
- Contract signatures
  - Documents legally binding OHSU can only be signed by an OHSU official with designated signature authority. For industry sponsored clinical trials:
    - Darlene Kitterman
    - Jaci Brown
  - PI signature acknowledging terms

Obtain Accounts

- Receive Oracle Grants Accounting (OGA) alias number after IRB approval obtained and contract executed or grant received
- If hospital services must be charged to research account:
  - Requires eCRIS Clinical Services Review
    - Can be submitted as soon as study procedures entered into eCRIS (don't have to have finished sponsor negotiation if industry)
    - Approval from all OHSU departments providing clinical services for study
      - Cost center can provide the service
      - The service listed is the appropriate service
    - Research/industrial account:
      - Requested automatically from PBS when OGA account is set-up
      - Used to order clinical services that should be charged to the OGA account

Medicare Start-up Issues

- Some devices require prior approval from Medicare prior to enrolling Medicare beneficiaries
  - Category A devices for "life-threatening conditions"
  - Category B devices
  - Humanitarian Use Devices (HUD/HDE): Also require patient specific approval
- Approval obtained after IRB approval and contract execution
- Contact: Melanie Hawkins, Director, Clinical Research Billing Compliance Office (CRBO)

Clinical Trial Registration

- ClinicalTrials.gov
- Required for all studies of health outcomes with interventions
- Prior to enrollment of first patient
- Responsibility of IND holder or party running study (if no IND)
- Updates required
- Penalty:
  - Probably will not be able to publish
  - Federal regulation for IND studies
- OHSU Guidance on IRB website: http://www.ohsu.edu/xd/about/services/integrity/policies/upload/icjme_guidance.doc
- If investigator initiated study and in eCRIS, eCRIS can produce xml document to upload to ClinicalTrials.gov

Prestudy Administration Help

- Investigator Support & Integration Services (ISIS)
  - All sponsorship (industry, federal, other)
  - Services:
    - Proposed Project Questionnaire (PPQ)
    - Budgets
    - IRB submission (OHSU, VA)
    - Account set-up (research rates/industrial account)
    - Clinicaltrials.gov registration
    - Regulatory consultation
    - INDs/IDEs
    - GCP Monitoring
    - DSMPs/DSMBs
  - Fees:
    - Industry sponsored: $5,000 + 25% IDC charged to sponsor
    - Non-industry sponsored
      - Free: Junior investigators/first human subjects study
      - Fee schedule for funded investigators
  - Contact: Bridget Adams, 4-5077

Study Document Definitions

- Source Documents: Location where information is first recorded including original documents, data and records. Contains all information contained in original records and certified copies of results, observations or other facets required for the reconstruction and evaluation of the study.
  - Usually = medical records
  - OHSU clinical information = Epic (OHSU's Integrated Health Record)
- Data Collection Form: Form to facilitate the collection of data for entry into a database.
- Case Report Forms (CRFs): Data collection forms for clinical trials. Contains pertinent information collected on each subject during a clinical trial, as outlined in the study protocol.
- Abstraction: The process of translating information in a health record to data in a data collection form/CRF.
- Coding: The process by which data are converted into variables and categories of variables using numbers, so that the data can be entered into computers for analysis.

Create Study Documents

- Source documentation
  - May need if not existing clinical data element/form
- Screening Log
  - All subjects consented (at minimum)
  - If do not enter study, list reason
  - If enter study, assigned ID and enrollment date
  - eCRIS subjects tab = screening log
- Study data collection forms
  - Create CRFs (if PI initiated): OCTRI /BMIP can assist with and provide software for CRF creation and electronic data collection for free
  - Each subject will have assigned CRF (identified by unique identifier) into which subject data entered

Create Study Documents (cont.)

- Study specific pre-printed physician order(s)
  - Must use paper order (downtime form) to direct charges to research/industrial accounts
  - Downtime form research templates available, required to be uploaded in eCRIS to be reviewed by department when submit for clinical services review
    - Pharmacy
    - Laboratory
    - Radiology
- Create pocket cards for personnel
- Log for specimens
  - Subject info, date/time collected
  - Date shipped to sponsor, central laboratory, or collaborator
- Study visit flow charts
- Subject schedules: subject specific and all subjects, spreadsheet and calendar formats available in eCRIS
- Create ID cards for subjects

Handling & Shipping Specimens

- Safe shipping certification required per FAA regulations (49 CFR 172.700-704)
- OHSU Clinical Lab shipping services:
  - OHSU lab personnel IATA certified
  - Process & ship specimens for nominal fee
- Coordinator shipping specimens:
  - Must complete Infectious Substances & Diagnostic Specimen shipping training: http://ozone.ohsu.edu/ehrs/mh/pages/bio/infsub.shtml
    - Before shipping
    - Renew training every 2 years
  - Contact Debra Brickey, 4-0655 with questions

Portland Arial Tram: Transporting Research Material

- Carts
  - 2 lockable wheels
  - Non-marking wheels
  - No dimension > 48 inches
- Specimens
  - Sealed plastic bag
  - EHRS issued outer container
- Medications: Container packaged by pharmacy

Site Initiation (Industry only)

- Performed by Sponsor's monitor
- Schedule Site Initiation occurs after:
  - IRB protocol & consent approved
  - Contract fully executed
  - Study drug/device on site: Drug/device sent after IRB approval & contract fully executed
- To make sure site is ready to begin enrolling subjects
  - All supplies on site
  - Facilities ready
  - Final training and all questions answered

Site Initiation (Industry only, cont.)

- Participants: schedule date/time/room
  - PI
  - Sub-investigators
  - Study coordinator
  - Pharmacist
  - Laboratory
  - Home care
  - Other as needed (radiologist, pathologist, etc.)

Site Initiation (Industry only, cont.)

- Conducted by site monitor/Clinical Research Associate (CRA)
- Review:
  - Protocol
    - PI responsibilities
    - Delegation of duties – complete signature log
  - Drug / device / study product accountability
  - Specimen processing, storage/shipping
  - Randomization
  - Data management (CRF, e-entry, IVRS)
  - Address any final questions, tweak forms

Staff Education

- In-service staff – Remember sign-in sheet
  - Investigators
  - Residents
  - Pharmacy
  - Laboratory
  - Nursing – inpatient/outpatient (MD orders, etc.)
    - Contact Deborah Eldredge for assistance with training inpatient nursing staff
  - Clinical nurse coordinators/CNS/NP/PA
  - Office staff

Recruitment

- **National Data from NIH**
  - Only 4% of the US population participate in clinical trials
  - 85% of trials are delayed due to low enrollment
  - 30% of trial sites fail to enroll any participants
- **OHSU Data[1]**
  - More than 30% of clinical studies at OHSU enroll only $\leq$ 1 participant
  - Cost of non-enrollment to OHSU of ~$1 million per year
  - Non-enrollment across all funding sources and departments

[1]Kitterman D, Cheng, SK, Dilts DM, Orwoll E. The Prevalence and Economic Impact of Low Enrolling Clinical Studies At An Academic Medical Center. Academic Medicine, November, 2011.

Recruitment Strategy

- Web sites
  - OHSU Study Opportunities Website: Indicate on IRQ
  - ResearchMatch.org: Indicate on IRQ
    - Feasibility
    - Recruitment
  - Craig's list, etc.
- Identify potential subject in OHSU Healthsystem: Contact OCTRI BMIP
  - Reports can be built in Epic to identify patients in healthsystem as they enter the healthsystem
  - Epic queries can be run to screen medical records
  - Cohort discovery tool can provide counts of subjects
- Community partners (the Vancouver Clinic, Kaiser, etc.)
- Newspapers – may realize poor results, costly
- Television/radio – better results (contact University New & Publications)
- Direct mail
- Health fairs
- Local support group meetings
- Investigator's meeting (industry) – see what others doing
- Flyers

Obtaining Informed Consent

Who obtains informed consent?

Obtaining Informed Consent (cont.)

- Process depends on:
  - Complexity of study
  - Urgency of medical condition
  - Involvement of vulnerable populations
    - Children
    - Mentally impaired
    - Elderly
    - Prisoners
    - Students, employees
    - Terminally ill or comatose

Obtain Informed Consent (cont.)

- Attempt to establish trust
  - Essential to remain unbiased, neutral, non-coercive
  - Not ideal to be clinician & researcher/research staff
- Discuss study specifics
  - Purpose: why subject fits
  - Procedures: visits, tests, specimens
  - Risks, benefits with alternatives
  - Any cost(s), liability to participants
  - Handling of PHI
  - Participation voluntary

Obtain Informed Consent (cont.)

- Answer questions
  - Questions that immediately arise
  - Questions that arise after subject/family has had time alone to discuss participation
  - Obtain signed informed consent after
    - Study explained thoroughly
    - All questions answered

Obtain Informed Consent (cont.)

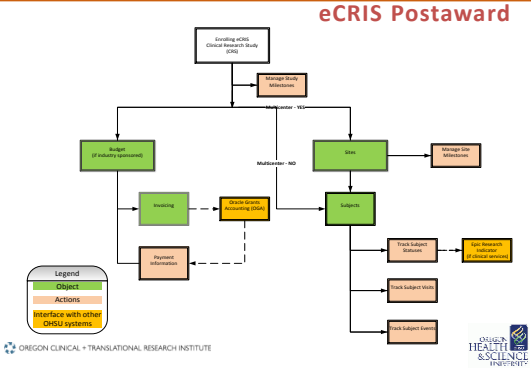
- Dated/signed note that subject has agreed to participate
  - Date study entry / consent signed
  - Protocol number
  - Subject study ID number
  - Investigational product being studied
  - Diagnosis or indication under treatment
  - Discussed study, all questions answered
  - Copy of consent given

Obtain Informed Consent (cont.)

➔NEVER➔

perform any study-related procedures before signed informed consent has been obtained

eCRIS Postaward



Documentation Requirements

- If subject receives OHSU clinical services (even if not "OHSU patient"):
  - Informed consent form must be scanned into IHR
  - Obtain an medical record number for subject (MRN)
  - If not in eCRIS or requires scheduling prior to subject consent, create research indicator in Epic:
    - After subject signs informed consent
    - Before scheduling visit if clinical services at first visit
    - Research Subject Status Change form to CRBO@ohsu.edu
  - All clinical information generated for a research subject that could at any time be used to make clinical decisions must be documented in the IHR (includes all clinical services)
- If the study involves inpatient nursing staff, an Inpatient Research Nursing Communication Order containing the Study Nursing Summary Form must be placed in Epic immediately following admission of the subject.

Subject Encounter Documentation

- Dated/signed note for study visit/phone contact: Include Protocol ID, subject ID
- Required notes
  - Consent of subject
  - Study completion or premature withdrawal (with reason)
  - Customizable Epic smartphrase templates available
- Other issues to document
  - Date/time dosing/exposure to study product
  - Document adverse experiences: onset, duration, tx, action, outcome
  - Results of procedures, exams (condition of subject)
  - Labs drawn – results signed by investigator
  - Concomitant medications
  - Document investigational medications on the patient's medication list
- If in eCRIS, must log subject visits as complete

Scheduling Research Subjects

- Healthsystem (non-CTRC)
  - Ambulatory
    - Make sure research visit type utilized if visit for research purposes only (no standard of care), provide scheduler with research account number
    - If includes standard of care, should be regular clinical visit
    - Requires Epic Research Indicator associated with patient
  - Inpatient
    - Complete Medical Admission Request Form
    - Email CRBO@ohsu.edu: Name, MRN, admission date
- CTRC
  - Email octrisch@ohsu.edu
  - Include information in CTRC Guide: Scheduling Participant Visits

Epic Subject Communication Mechanisms

- Inpatient & Ambulatory
  - Research Indicator
    - Purpose: Shows subject enrolled and information about the study
    - Required for all research subjects receiving OHSU clinical services
    - Visible in the Epic header
    - Created and inactivated by CRBO
  - Research Protocol Patient Problem
    - Purpose: Communicate study specific information to clinical personnel
    - Triggers research specific BPA, shows up on problem list

Epic Subject Communication Mechanisms (cont.)

- Ambulatory only
  - Specialty Comments
    - Purpose: Communicate study specific information to clinical personnel
    - Appears in patient snapshot
- Inpatient only
  - Inpatient Research Nursing Communication Order
    - Purpose: To communicate study related information to inpatient nurses
    - Required for research related admissions to communicate the information contained in the study's Clinical Research Nursing Summary Form, can also be used for other purposes
    - Appears in the nursing Kardex
  - Inpatient Provider Sticky Notes
    - Purpose: To communicate study related information to inpatient providers
    - Provider specific (physician or nursing)

Epic Subject Communication Mechanisms (cont.)

- Special situations
  - MyChart Messages
    - Purpose: To communicate with subjects where it should be documented in Epic
  - Stork Sticky Notes
    - Purpose: To communicate with clinical providers regarding pregnant research subjects
    - Only available in obstetric departments for pregnant patients
  - Epic inbasket notifications
    - Purpose: To alert study personnel of research subject clinical events (such as admissions)
    - Subject must be associated with an Epic Research Indicator

Epic Access & Training

- Training
  - Epic training website: http://ozone.ohsu.edu/ozone/epic/
  - Training dictated by scope of practice and access requirements
  - Access granted after training
  - Epic Research Documentation training: http://ozone.ohsu.edu/ozone/epic/learning/learning.cfm
- Monitor access:
  - Monitors access Epic through OHSU Connect
  - Training document must be emailed to monitor before first access
  - "Epic Access for External Auditors", http://ozone.ohsu.edu/healthsystem/HIS/medrectrx/Epic_Access_for_External_Auditors1212locked.docx

Insurance Issues

- If study involves standard of care clinical procedures
  - Preauthorization
    - Oregon State law requiring coverage of standard or care for clinical trials
    - Laws in other states different, may not cover standard of care in clinical trial
    - Participation in clinical trial must be preauthorized with private insurers if insurer requires preauthorization
  - If subject enrolled in Medicare Advantage Plan services must be billed to traditional Medicare
    - Determination subject insurance is Medicare Advantage made by CRBO when Research Subject Study Status Change form submitted or notified of research indicator from eCRIS
    - Coordinator informed if subject's insurer = Medicare Advantage Plan
    - Coordinator must provide subject with Medicare Advantage Plans and Clinical Trials Information Sheet

Data Collection

- If it is not documented it did not happen
- Always follow research documentation guidelines for paper data collection forms
  - Use black indelible ink pen
  - Single line through incorrect data, Do not obliterate original entry
  - Initial and date corrections and additions
- Assure that all study procedures are completed in timely manner & documented

Data Collection (cont.)

- All data must derive from a source document
  - Except if the data is the source document (i.e., questionnaires) or the data is not clinical information
- Data abstracted from a variety of sources
  - Inpatient and outpatient records
  - Research charts
  - Offsite medical records (with appropriate release of information permission)
- Store CRF & study supplies in locked area

Epic Data

- Research Data Warehouse (RDW)
  - IRB-approved repository of Epic and other data created specifically for research purposes
  - Can interface to other databases (i.e., RedCap) or produce reports
  - Contact: OCTRI BMIP
- Reporting workbench:
  - Reports generating lists of patients using tool within Epic
  - Free
  - Some limitations

Subject Follow-up

- Communicate with subject at regular intervals
  - Assess medical status/study compliance
  - Answer questions re: study protocol
  - Communicate significant changes to PI or SubI
- Provide direction & supervision for primary health care providers
  - Home town physician, care provider
  - Local non-University provider
  - With subject's permission

Regulatory Document Maintenance

- Correspondence (written, phone, and email)
  - Sponsor (if applicable)
  - Subjects
- Lab documentation (if lab used)
  - Lab Director CV
  - Licenses
  - Normal ranges
- FDA 1572s (if IND)
- IRB
  - Member list
  - Approvals
  - Communication
- IDB (if drug)
- Pharmacy records (if not utilizing RPS or post-termination)
- Screening log
- Delegation of authority log
- Safety reports (FDA, NIH, DSMB reports, etc.)
- No financial records in regulatory binder, keep separately
  - Budget
  - Contract
  - Invoices

Monitoring Visits (industry studies)

- Purpose
  - The facilities continue to be acceptable
  - The study protocol or investigational plan is being followed.
  - Changes to the protocol have been approved
  - Accurate, complete, and current records are maintained.
  - Accurate, complete, and timely reported are being made
  - The investigator is fulfilling responsibilities
- Conducted by sponsor employee or contractor (Clinical Research Associate (CRA))
- At intervals specified in the contract
- Length of time dictated by intensity and enrollment
- Monitor must arrange at mutually acceptable time
  - Monitor needs to specify what areas being addressed at visit
  - CRC needs to arrange visit with units involved **in advance**
    - Health Information Management: If accessing EPIC, "EPIC Access for External Auditors" on HIM website, at least 1 week in advance
    - RPS, at least 48 hours, though may be full
    - CTRC
    - Other clinical units and ancillary units if required (radiology, etc.)

VA Monitoring Visits

- Inform Research Assurance Officer when visit is scheduled
- At beginning of visit: Come to R&D Office and sign in
- Call Research Assurance Officer at end of visit
- Meet if serious issues of non-compliance
- Complete & FAX Monitoring Visit Report Form prior to monitor leaving

Financial Management

- Perform or assist with fiscal management
- Review accounts and bills for appropriate charges and rates
- Invoice for payments (if applicable)
- If not in eCRIS:
  - Track study enrollment and visits to assure correct payment
  - Track study payments

Close-out Activities

- IRB notified when
  - Study is closed to enrollment
  - Study is terminated
- Inform RPS when no drug storage/dispensing
- Prepare for termination visit (industry only)
  - Data final
  - Final drug accountability; drug returned to sponsor or destroyed
  - Lab, other study supplies returned to sponsor or destroyed
  - Final report to sponsor (if applicable)
  - Final payment reconciliation
- Store Documents (notify sponsor if off-site if applicable)

Close-out Activities (cont.)

- After final payment and all charges/expenses posted
  - Close OGA account
    - For industry sponsored
      - Residual funds transferred into Project Development Account (PDA)
      - Deficits applied to existing PDA or Department GL
  - Close research/industrial account, if applicable

Self-development

- Maintain affiliation with a professional organization
  - Association of Clinical Research Professionals (ACRP)
  - Society of Clinical Research Associates (SoCRA)
  - Drug Information Association (DIA)
  - Society of Research Administrators (SRA)
  - National Council of University Research Administrators (NCURA)
  - Public Responsibility in Medicine & Research (PRIMR)
- Review research journals
  - Library
  - Applied Clinical Trials
  - Centerwatch

Self-development (Cont.)

- Complete a clinical research certification program
  - ACRP or SoCRA
  - Why
    - Personal development
    - Looks good to sponsors
    - Looks good to employers
    - Assists with promotion in OHSU research ranks
  - 2 yrs experience to sit for exam
  - SoCRA certification exam offered at OHSU annually
- Attend local research conferences and training