Creating Infrastructure Support for Investigator Initiated Research

Karen A. Hartman, MSN, CHRC
Administrator – Research Compliance, Mayo Clinic
HCCA Research Compliance Conference
June 6, 2017

Objectives for this session

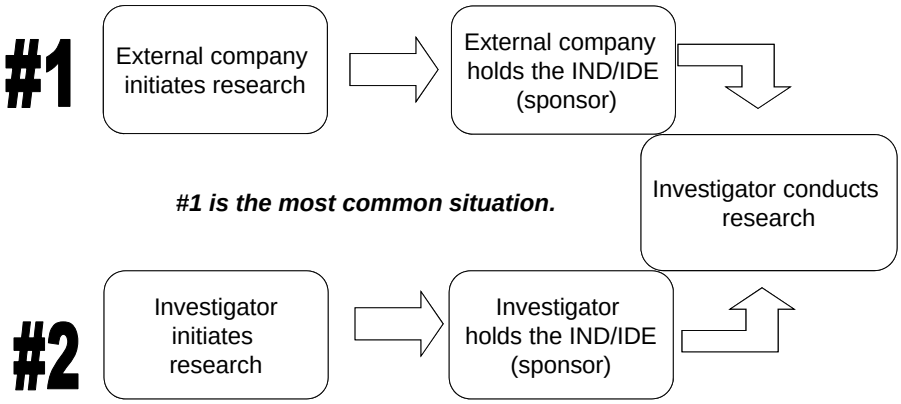
- Discuss support activities for investigator initiated FDA regulated research, including tools and templates
- Describe model of support at Mayo Clinic
- Share best practices and lessons learned

What is Investigator Initiated FDA Regulated Research

Examples

- Novel drug (IND- investigational new drug) or device (IDE- investigational device exemption)
- Marketed drug being researched for a non-approved indication (new route, new patient population, new dose, etc.)
- Marketed/cleared device being researched for a new indication
- Conducting research on the use of a product as a drug or device

Two main paths for IND or IDE research



#1 is the most common situation.

#2 presents higher risk for the Institution and the Investigator.

What is a Sponsor-Investigator?

Investigator conducts the clinical investigation and is responsible to obtain IRB approvals, follow the study protocol, maintain control of investigational product, ensure quality records are complete, file required reports, and oversee the study team.

Regulatory Study Sponsor initiates the investigation and is responsible to obtain FDA approval of the IDE/IND, monitor the collection of quality data, maintain specific records, file required reports, and control distribution of investigational product.

Sponsor-Investigator must meet the responsibilities of both the sponsor and the investigator to ensure the protection of human subjects participating in a clinical investigation.

Creating infrastructure support…..

- Identification of all Sponsor-Investigators
  - Survey
  - Query IRB system
- Benchmarking w/other institutions who offer similar support
- Creation of Templates, Forms, Database, Educational Modules, Training of Staff

Feasible

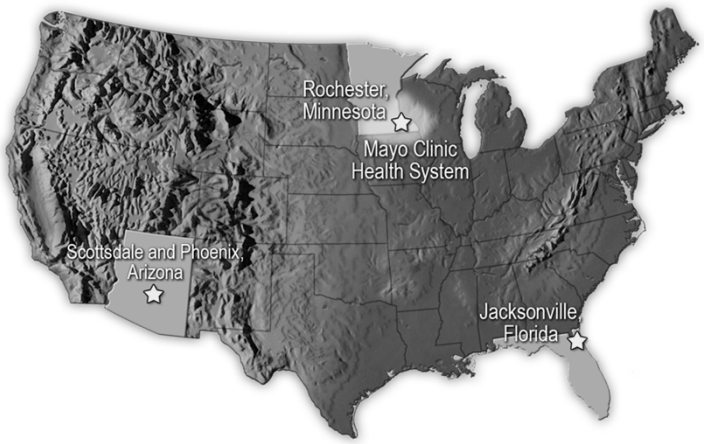
- Hire "great staff"
- Communicate
  - relevant presentations, newsletters, emails
- Build Trust
  - perceptive about customer environment and needs
  - "creating the culture of compliance"

Challenging

Mayo Clinic

Support for Investigator Initiated Research

Mayo Clinic
Locations



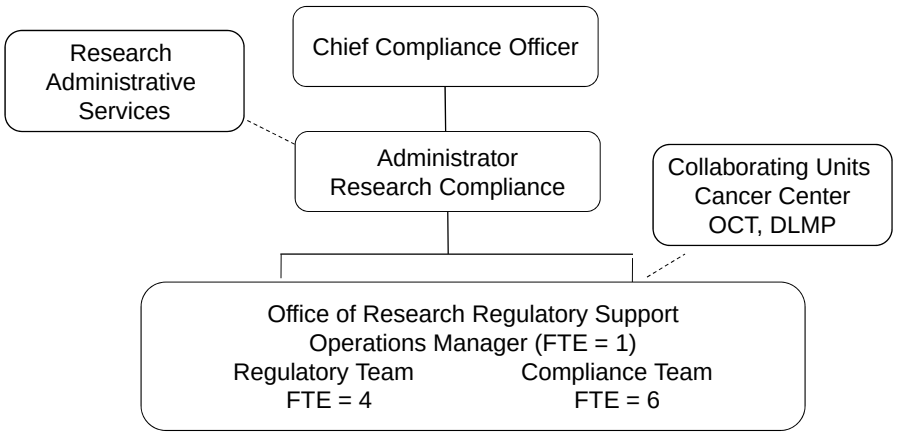
Office of Research Regulatory Support

- Goal is to ensure compliance and integrity in research
- Support the protection of human subjects in research by ensuring compliance with Federal, State, and Institutional guidelines
- Staff work in partnership with Mayo Clinic Office for Human Research Protection, the Institutional Review Board (IRB), Research Administration, and the research community

Office of Research Regulatory Support

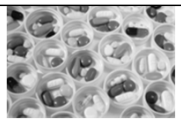
- Centralized resource for information, expertise, and support related to the conduct of clinical research from a regulatory and compliance perspective
  - Investigator-initiated Investigational New Drug (INDs) or Investigational Device Exemption (IDEs) submissions
  - ClinicalTrials.gov support
  - Regulatory questions
  - Proactive Review Program

ORRS Organizational Structure



ORRS Services and Support

IND Applications



Clinicaltrials.gov oversight

FDA Audit Support

IDE Applications

Proactive Review Program

Study File Mgmt

ORRS Services and Support

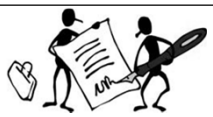
For Cause Audits

Study Initiation Visit

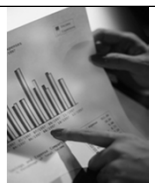
Consults/Education

Protocol Deviations Review

Consenting Process Observations

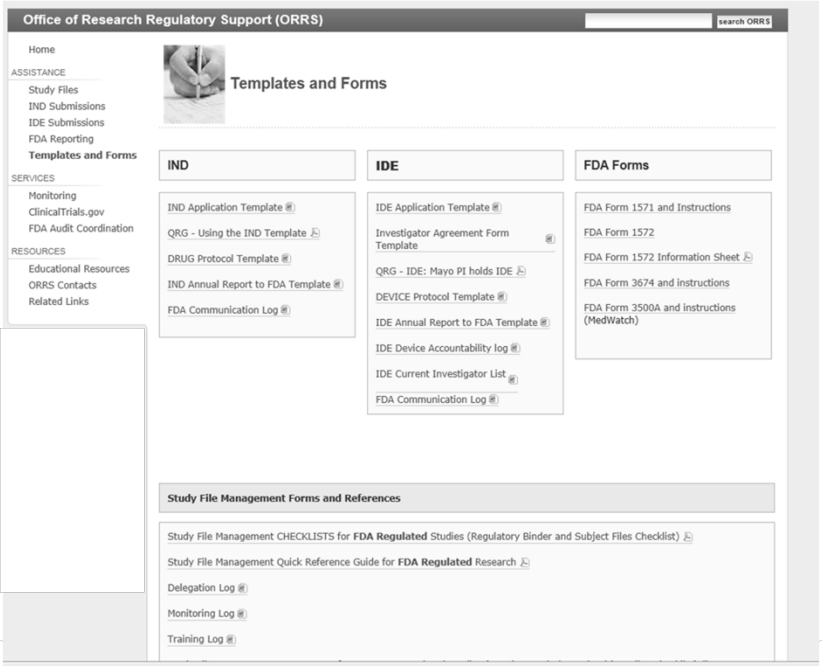


Tracking Trends



Assistance for IND/IDE applications

- Consultation
- Templates and Quick Reference Guides
- Communication and correspondence with FDA as needed
- Pre-IND or IDE meeting assistance
- Maintenance:
  - Annual Report reminders
  - Safety reporting assistance



Proactive Review Program & Monitoring

- Risk based approach for proactive reviews, includes all Mayo research studies
  - Risk assessment (protocol and study team members) used to select studies for review
- Encompasses sponsor-investigator monitoring
  - Frequency determined by protocol and other factors (S-I and team experience, risk of product, etc.)
- Work with PI/team for process improvements based on findings (quality activities)

Proactive Review Program & Monitoring

- Regulatory documents/binder review
- Eligibility determinations
- Informed Consent – document and process
- Protocol adherence – are we doing what we said we would do?
- Other assessments of targeted areas

Reviews of Consenting Process

- Randomly select studies and conduct an observation of the consenting process
  - Ask permission of potential participants
  - Partner with the Research Subject Advocate in conducting these reviews
  - Feedback provided to study team after the consenting session
  - Surveys of participants

Education and Consults

- Provide resources for study teams and serve as educators for orientation program and other training sessions
- Provide required training module for sponsor-investigators as per IRB policy
  - Offered on-line
  - Also review educational components “just in time” during initial meetings regarding the planned IND or IDE

Education and Consults

- Work with CRC Education Group for quarterly “Compliance Corner” Training
  - Identify topics based on identified areas of improvements from proactive reviews, monitoring and for-cause audits
- Communication of findings (general) through presentations to department and other educational initiatives

Education and Consults

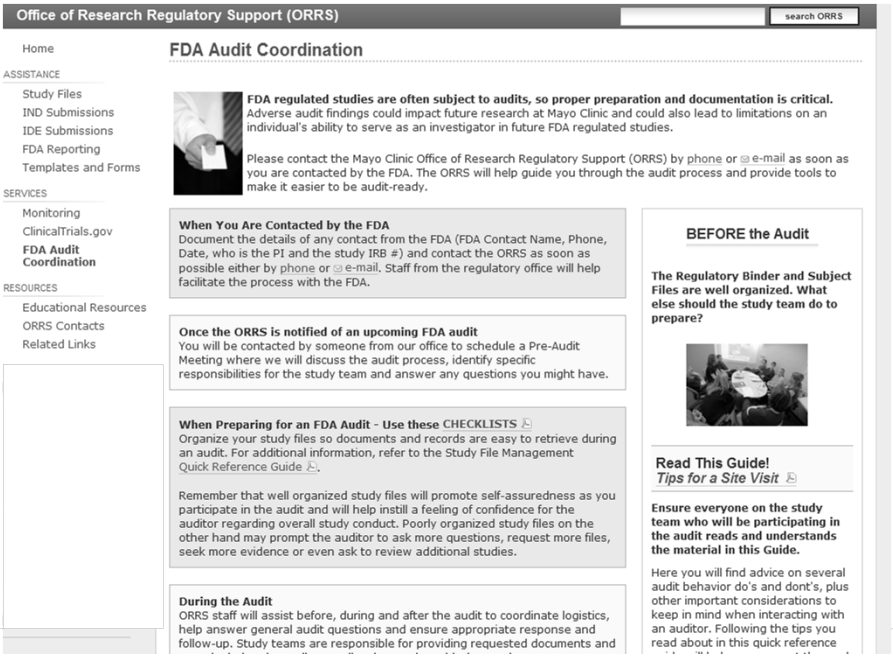
- Building a culture of compliance and trusting environment promotes calls for help and advice versus fear
- Assist study teams with questions about protocol deviations/violations, reporting requirements and creating processes for compliance within their study team activities

For Cause Audits

- Conducted when allegations of suspected or actual noncompliance with federal regulations, state laws, Mayo policies, and/or IRB requirements
- May be referred by IRB, Compliance Office, Participants, Staff, Whistleblower Complaints
- Targeted or full study audit
- Reports and findings are sent back through IRB committee for determination of non-compliance (serious and/or continuing if applicable)

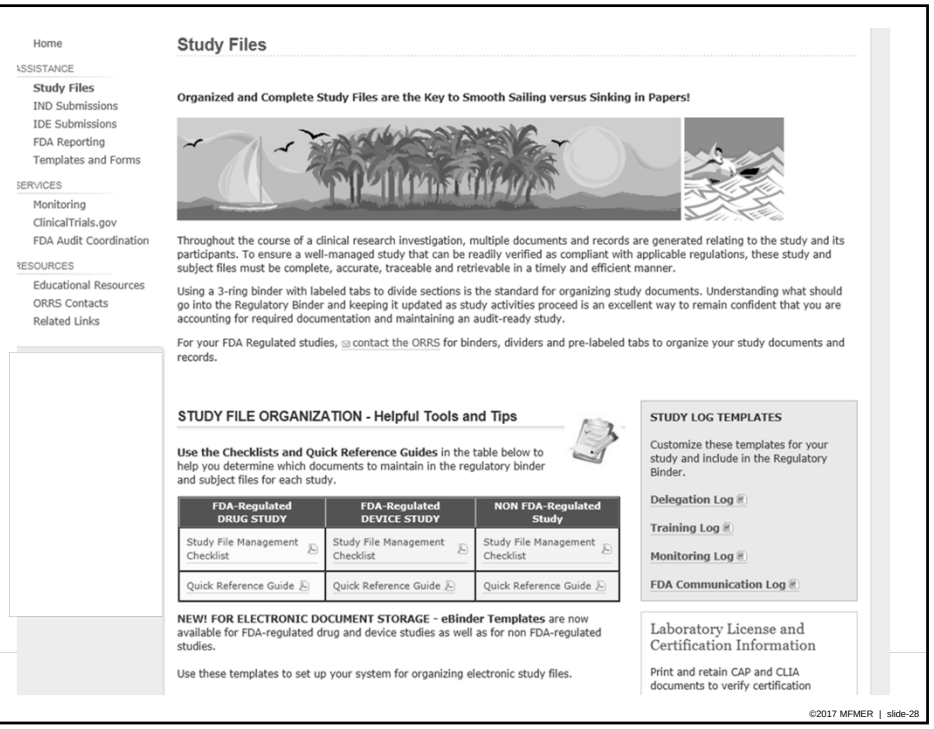
FDA Inspections – Centralized Coordination

- Pre audit meetings with PI/research team
- Notification of areas involved
- Just in time training to prepare for upcoming audit
- Assistance provided to study teams during the audit from first phone call through written response (if needed)



Study File Management Resources

- Resources for study teams
  - Checklists for FDA and non-FDA regulated study file management
  - Quick Reference guides
  - On-line module and in-person workshop
  - eBinder for ease of maintenance
- Assistance for questions as well as providing tabs to study teams to assist them in organizing study regulatory documents



Regulatory Binder Checklist for FDA-Regulated Studies

Directions: Refer to the Study File Management Guidelines Quick Reference Guide for detailed information about each section. Please review the Study File Management for Clinical Research Policy and Procedure for additional details and information.

IRB number _____ **PI name** _____

Study title _____

Checklist completed by _____ **Date:** _____

PI initials indicating that checklist is complete _____ **Date:** _____

Note: If you are using a Regulatory Binder provided by the sponsor, review the binder to ensure that documents listed in the checklist below are included, but be aware additional documents may be required by sponsor.

Regulatory Binder Checklist					
A. Study Documents				**Check one**	
Tab or eFolder Label			**Documents to include in binder**	**Yes**	**NA***
1.	Protocol Templates available on ORRS web site.		Include current and all previously IRB approved versions, amendments and/or modifications		
2.	Informed Consent Form		Include current and all previously IRB approved versions (unsigned)		
3.	Drug Study	Investigator's Brochure	Include all versions. Alternatively, may include a product/package insert here if there is no IB.		
	Device Study	Investigational Device Information	Summary document describing the device under study.		

Oversight of ClinicalTrials.gov process

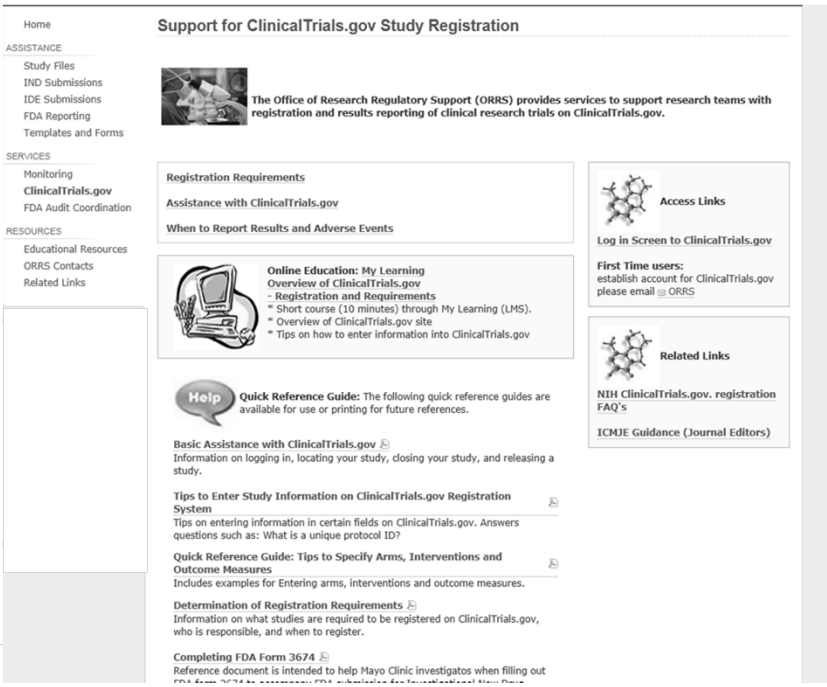
- Protocol Registration System (PRS) administrator part of the ORRS team
- Resources for study teams
  - Quick Reference guides
  - On-line module
  - Classroom training
- Assistance for questions on registration process
- Results reporting assistance (direct entry and support for study teams)

Identifying Applicable Clinical Trials

- Triggers from responses to questions in IRB application once IRB approval is received
- Able to map a subset of the data required in the Clinicaltrials.gov record to our IRB application system. Data is automatically entered in record for study team to complete
- Email sent to PI/SC to finish the registration of the study if they have an account, or to set up account to complete the registration (through system and PRS administrator)

Results Reporting

- Based on number of trials and efficiency gained with dedicated position, have one FTE for this role (split this between two staff along with other responsibilities)
- Identification of studies needing results posting through our internal system and PRS system
- Senior Regulatory Specialist works with PI and study team to gather information and data, then directly enters results
- Why - savings of Investigator (physician) time



Reportable Events or Protocol Deviations Review Process

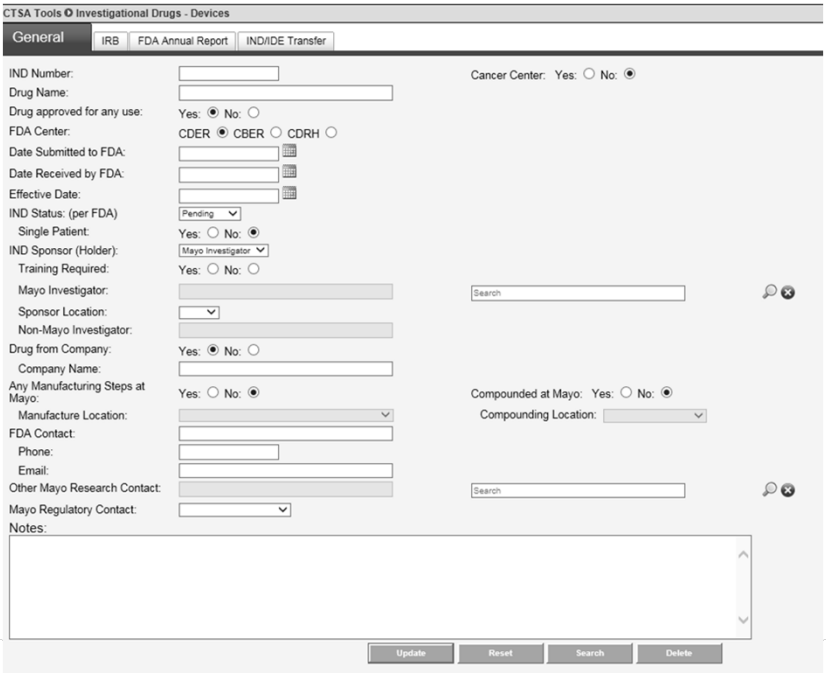
- Review submissions timely to provide additional direction to study team; key when a potential PHI disclosure in research
- Deviations happen in research: determinations as to whether need to be reported immediately or at time of continuing review w/study team
  - More tips and training have been added to assist study teams to make this decision
- Leads to awareness of non-compliance in an expedited fashion

Study Initiation Visits

- Typically 2-4 hours spent with study team to review overall study and plans for success
  - S-I attends, often for subset of the meeting
- Typical topics covered include: recruitment plans, consent process, study file management, eligibility checklists, AE reporting and study documentation requirements
- Includes documented protocol training for team members and review of delegation log
- Review of sponsor-investigator responsibilities

Other Key Components

- Tracking all Mayo Clinic sponsor-investigator INDs or IDEs
  - Database to maintain pertinent information
  - Notification to sponsor-investigators when annual reports due to FDA
    - Email reminder sent with annual report template for S-I to complete
  - Ability to run reports



Best Practices to consider for Investigator Initiated Research

Points for Consideration

- What is your organization's goal for research?
- Volume of investigator initiated research
- Size and support needed
  - Can support activities be incorporated within another office/team?
- Consider phased in approach
  - What are the critical aspects to provide initially and what can be added next phase

Key Areas of Support

- Protocol development and writing
- Regulatory writing/documentation and submissions to agency
- Monitoring for participant protections and quality
- Tools and templates, IT system needs
- Education and Training – formal and just in time
- Funding (projects/research and infrastructure support)

Lessons Learned – Tips to create support

- Set the tone and culture of the group
  - Supportive and not punitive
  - What is the focus? How will findings be received?
- Identify how much FTE will be needed. What services are you planning to provide? Can you implement a phased in approach?
- Determine early what activities are “out of scope”

More Tips and Lessons Learned

- Consider how you will identify depts. in your institution with investigator initiated activities
  - Survey, work with your IRB, department chairs, research administration, etc.
  - Once identified – how will you address and identify infrastructure support needed?
- Identify key groups to partner with for quality results and improved compliance
  - Research administration, education, study coordinator groups, departments, etc.

Conclusion

- Consider the following key points when implementing infrastructure and support
  - Importance of setting the right tone and creating a culture of compliance
  - Invest resources to provide services
  - Track findings from audits and monitoring activities with overall goal to improve the research and sustain quality efforts
  - Provide targeted education and training

Thanks for Your Time and Attention!

Contact Information:

Karen Hartman
(507) 538-5238
hartman.karen@mayo.edu