



Creating Infrastructure Support for Investigator Initiated Research

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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

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What is Investigator Initiated FDA Regulated Research

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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

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Two main paths for IND or IDE research

#1 External company initiates research → External company holds the IND/IDE (sponsor) → Investigator conducts research

#1 is the most common situation.

#2 Investigator initiates research → Investigator holds the IND/IDE (sponsor)

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

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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.

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Creating infrastructure support.....

<ul style="list-style-type: none">• Identification of all Sponsor-Investigators<ul style="list-style-type: none">• Survey• Query IRB system• Benchmarking w/other institutions who offer similar support• Creation of Templates, Forms, Database, Educational Modules, Training of Staff	<ul style="list-style-type: none">• Hire "great staff"• Communicate<ul style="list-style-type: none">• relevant presentations, newsletters, emails• Build Trust<ul style="list-style-type: none">• perceptive about customer environment and needs• "creating the culture of compliance"
Feasible	Challenging

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Support for Investigator Initiated Research

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Mayo Clinic Locations

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Office of Research Regulatory Support

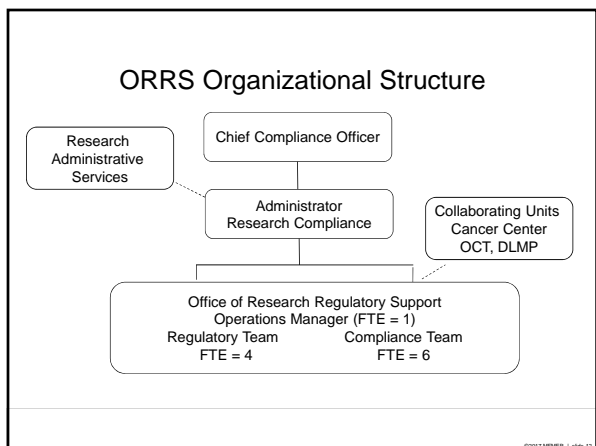
- Goal is to ensure compliance and integrity in research
- Support the protection of human subjects in research by ensuring compliance with Federal, State, and Institutional guidelines
- Staff work in partnership with Mayo Clinic Office for Human Research Protection, the Institutional Review Board (IRB),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

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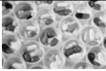





Office of Research Regulatory Support

- 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

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ORRS Services and Support

IND Applications 	Clinicaltrials.gov oversight 	FDA Audit Support 
IDE Applications 	Proactive Review Program 	Study File Mgmt 

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ORRS Services and Support

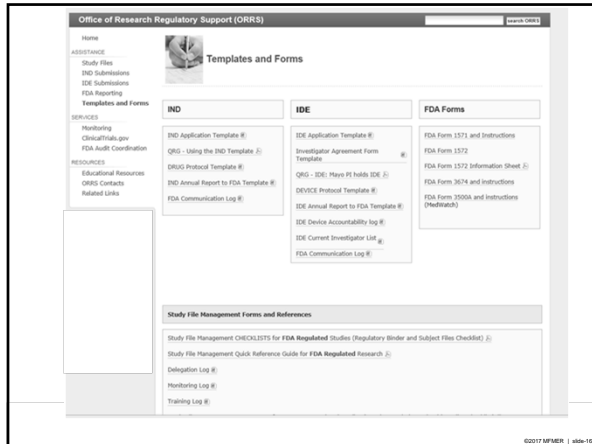
For Cause Audits 	Study Initiation Visit 	Consults/Education 
Protocol Deviations Review 	Consenting Process Observations 	Tracking Trends 

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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

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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

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

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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

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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)

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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)

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The screenshot shows the 'FDA Audit Coordination' page on the ORRS website. The page includes a navigation menu on the left with sections like ASSISTANCE, SERVICES, and RESOURCES. The main content area features several informational boxes: 'FDA regulated studies are often subject to audits...', 'When You Are Contacted by the FDA', 'BEFORE the Audit', 'When Preparing for an FDA Audit - Use these CHECKLISTS', and 'During the Audit'. Each box provides specific guidance and contact information for study teams.

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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

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Home

ORRS

Study Files

IND Submissions
IDE Submissions
FDA Reporting
Templates and Forms

SERVICES


Monitoring
ClinicalTrials.gov
FDA Audit Coordination

RESOURCES

Educational Resources
ORRS Contacts
Related Links

Study Files

Organized and Complete Study Files are the Key to Smooth Sailing versus Sinking in Paper!



Throughout the course of a clinical research investigation, multiple documents and records are generated relating to the study and its participants. To ensure a well-managed study that can be readily verified as compliant with applicable regulations, these study and subject files must be complete, accurate, traceable and retrievable in a timely and efficient manner.

Using a 3-ring binder with labeled tabs to divide sections is the standard for organizing study documents. Understanding what should go into the Regulatory Binder and keeping it updated as study activities proceed is an excellent way to remain confident that you are accounting for required documentation and maintaining an audit-ready study.

For your FDA Regulated studies, contact the ORRS for binders, dividers and pre-labeled tabs to organize your study documents and records.

STUDY FILE ORGANIZATION - Helpful Tools and Tips

Use the **Checklists and Quick Reference Guides** in the table below to help you determine which documents to maintain in the regulatory binder and subject files for each study.

FDA Regulated DRUG STUDY	FDA Regulated DEVICE STUDY	NON FDA Regulated Study
Study File Management Checklist	Study File Management Checklist	Study File Management Checklist
Quick Reference Guide	Quick Reference Guide	Quick Reference Guide

STUDY LOG TEMPLATES

Customize these templates for your study and include in the Regulatory Binder.

Delegation Log #
Training Log #
Monitoring Log #
FDA Communication Log #

NEW! FOR ELECTRONIC DOCUMENT STORAGE - eBinder Templates are now available for FDA-regulated drug and device studies as well as for non FDA-regulated studies.

Use these templates to set up your system for organizing electronic study files.

Laboratory License and Certification Information
Print and retain CAP and CLIA documents to verify certification.

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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			Check one	
A. Study Documents			Yes	NA*
Tab or eFolder Label	Documents to include in binder			
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 Device Study	Investigator's Brochure	Include all versions. Alternatively, may include a product package insert here if there is no IB.		
	Investigational Device Information	Summary document describing the device under study.		

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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)

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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

Home

Support for ClinicalTrials.gov Study Registration

ASSISTANCE

- Study Files
- IND Submissions
- IDE Submissions
- FDA Reporting
- Templates and Forms

SERVICES

- Monitoring
- ClinicalTrials.gov
- FDA Study Coordination

RESOURCES

- Educational Resources
- ORIS Contacts
- Related Links

The Office of Research Regulatory Support (ORRS) provides services to support research teams with registration and results reporting of clinical research trials on ClinicalTrials.gov.

Registration Requirements
Assistance with ClinicalTrials.gov
When to Report Results and Adverse Events

Online Education: My Learning
Overview of ClinicalTrials.gov
- Registration and Requirements
- Short course (20 minutes) through My Learning (LMS)
- Overview of ClinicalTrials.gov site
- Tip on how to enter information into ClinicalTrials.gov

Quick Reference Guide: The following quick reference guides are available for use or printing for future reference.

- Basic Assistance with ClinicalTrials.gov
- Information on logging in, locating your study, closing your study, and releasing a study
- Tip to Enter Study Information on ClinicalTrials.gov Registration System
- Tip on entering information in certain fields on ClinicalTrials.gov. Answers questions such as: What is a unique protocol ID?
- Quick Reference Guide: Tips to Specify Arms, Interventions and Outcome Measures
- Includes examples for entering arms, interventions and outcome measures.
- Determination of Registration Requirements
- Information on what studies are required to be registered on ClinicalTrials.gov, who is responsible, and when to register.
- Completing FDA Form 3674
- Reference document is intended to help Hays Clinic Investigators when filling out

Access Links
Log In Screen to ClinicalTrials.gov
First Time users: establish account for ClinicalTrials.gov please email: ORRS

Related Links
NIH ClinicalTrials.gov registration FAQs
ICHM Guidance (Journal Editors)

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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

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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

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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

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CTMA Tools Q Investigational Drugs - Devices

General | IRB | FDA Annual Report | IND/IDE Transfer

IND Number: Cancer Center: Yes No

Drug Name:

Drug approved for any use: Yes No

FDA Center: CDER CBER CDRH

Date Submitted to FDA:

Date Received by FDA:

Effective Date:

IND Status (per FDA):

Single Patient: Yes No

IND Sponsor (Holder):

Training Required: Yes No

Mayo Investigator:

Sponsor Location:

Non-Mayo Investigator:

Drug from Company: Yes No

Company Name:

Any Manufacturing Steps at Mayo: Yes No

Manufacture Location:

FDA Contact:

Phone:

Email:

Other Mayo Research Contact:

Mayo Regulatory Contact:

Notes:

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Best Practices to consider for Investigator Initiated Research

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- 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
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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)

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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”

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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.

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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

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Thanks for Your Time and Attention!

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