Investigator Initiated Research: Establishing Practice for Regulatory Submission Studies

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Why Do Investigator Initiated Research?

- Improve Science/Data
- Patient Benefit
- Support a New Use/Indication
- Supports Product Strategy
Considerations

- Who are the parties?
- What are their roles?
- How can you manage the risk of IIR?
- What are the criteria for an appropriate IIR project?
- How should IIR be reviewed and processed?
Undefined Roles
What Am I?
(And what are they?)

Sponsor
Collaborator
Investigator
Investigator-Sponsor
A person who takes responsibility for and initiates a clinical investigation. May be an individual or company, government agency, academic institution, private organization, or other organization.

21 CFR 312.3
• Financial Support
• Protocol Development Assistance
• Provision of Product
• Anything other than a contractual statement and/or listing on the 1571 designating “Sponsor”
Investigator

An individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject).

21 CFR 312.3
Sponsor-Investigator

Individual who both initiates & conducts a clinical investigation, and under whose immediate direction the investigational drug is administered or dispensed.

The term does not include any person other than an individual. The requirements applicable to a sponsor investigator under this part include both those applicable to an investigator and a sponsor.

21 CFR 312.3
Potential Risk Perspective

Institution / Investigator

• Local sponsorship ambiguity
• Inadequate resources to act as sponsor
• Presentation / publication of data that may not have been validated (False Claims).
• Pivotal impact for research subject safety
• Legal issues from non-compliance to regulation
• Lack of indemnification of site from funding sources.
Subject: Risk to Benefit Ratio

An invalid study resulting from the inappropriate/incomplete conduct of any study, places the subject at risk, potentially without providing any benefit....even to medical generalizable knowledge.
Categories of IIR

- Traditional IND/IDE
- Non-IND/IDE Drug, Biologic, or Device studies
- Non-Drug, Biologic, or Device studies

(Each may be industry/association sponsored or not)
Standards of Accountability

- Federal Regulation
- ICH Guidelines
- State Laws
- Institutional Policy
- Contractual Agreements
- The Protocol
- Investigator SOPs
Plan to Succeed
(or failing to plan is planning to fail)

IIR: Responsibilities

Make a Plan

Report on the Plan

Follow the Plan

Record the conduct of the Plan
Make A Plan

- Protocol (including oversight)
- Infrastructure Review
- Contracts
Protocols and Oversight Plans

• Sample size (power) of study appropriate for study design and purpose.

• Appropriate Endpoints

• Detailed plan for oversight of study conduct, subject safety, validity of data
Review of Infrastructure

- Knowledge Base
- Personnel Resources
- Facility (space, services and equipment) Resources
- Recruitment Potential
- Financial Resources
Functional Infrastructure

Infrastructure appropriate for:

- monitoring regulatory submissions
- oversight of study conduct (including qualification and education of staff)
- oversight of data and research subject safety
Start Responsibly

- Spell out roles and responsibilities in contracts with sponsors or collaborators.
- Read all agreements or conditions of awards
Financial Budgets

Assure that budget is representative of full study costs.

- Personnel
- Procedures
- Supplies
- Facilities
- Recruitment
- Training
- Monitoring
Warning: Assure not in violation of anti-kickback statute.

OIG:

Any remuneration from a manufacturer provided to a purchaser that is expressly or impliedly related to a sale potentially implicates the anti-kickback statute and should be carefully reviewed.

To reduce risk, manufacturers should insulate research grant making from sales and marketing influences.

Contract Financial Considerations

- A written budgetary agreement should be in place, specifying the type of the research services to be provided and the basis for payment for those services.
- Investigator compensation should be reasonable for services performed.
- Payment should not be tied to study outcome.
- The Investigator team (or their families) should not have conflict of interest related to the product being studied.
Maintain the IND or IDE as required

Qualify investigators and monitors (all sites)—CV’s, 1572, financial disclosures

Ensure proper monitoring (all sites)

Ensure appropriate study conduct (all sites)

Inform FDA and investigators of significant new AEs or risks with respect to the drug.

Maintain accountability of investigational product (all sites).
Follow the Plan

- Obtain approvals
- Stay the course
Record the Conduct of the Plan

Essential Documents:

• Who?
• What?
• Where?
• Why?
• How?
Essential Documents:
(see ICH E6 Consolidated Guidance, Section 8)

Examples:
- Protocol/Investigator Brochures
- Informed Consent and Recruitment Materials
- CV/License/Certifications
- Approvals
- Key Communication
- Accountability of test articles
- Training
- Staff permissions (not delegation)
- 1571 & 1572 when applicable
- Adverse Event reports
- Source documents and CRF when applicable
Report on the Plan

- Waivers, Deviations, and Amendments
- Continuing Review
- Progress Reports
- Interim and/or Final Analysis
- DSMB reports
- Clinical Study Report/Manuscripts to IRB, FDA, and perhaps collaborating group