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

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

SPONSOR

COLLABORATOR

- 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)

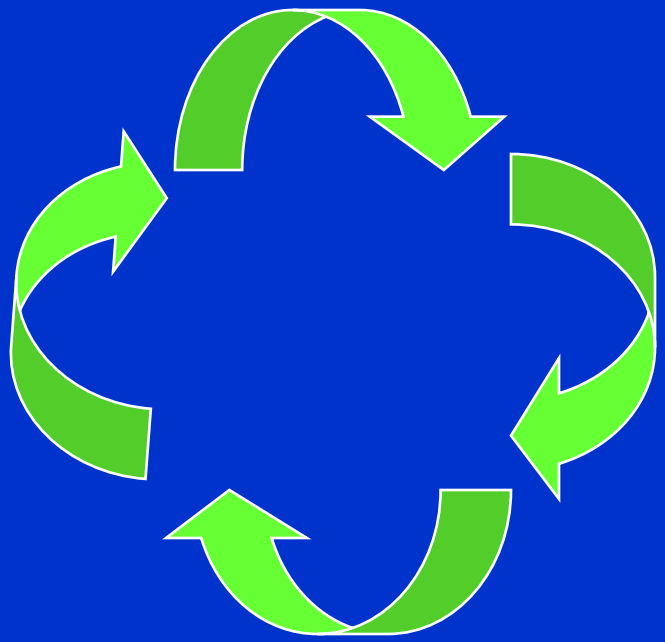
Standards of Accountability

- Federal Regulation
- ICH Guidelines
- State Laws
- Institutional Policy
- Contractual Agreements
- The Protocol
- Investigator SOPs

IIR: Responsibilities
Plan to Succeed
(or failing to plan is planning to fail)

Make a Plan

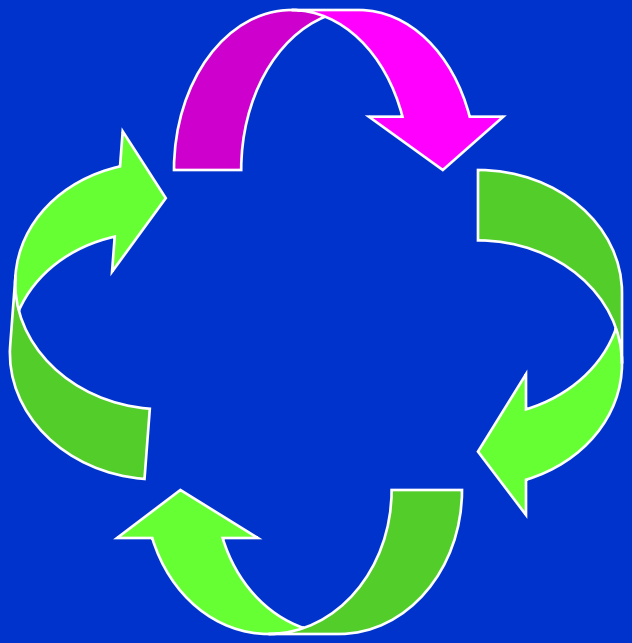
Report on the Plan



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:

[A]ny 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.

Source: OIG Pharma Compliance Guidance – 68 Fed. Reg. 23736

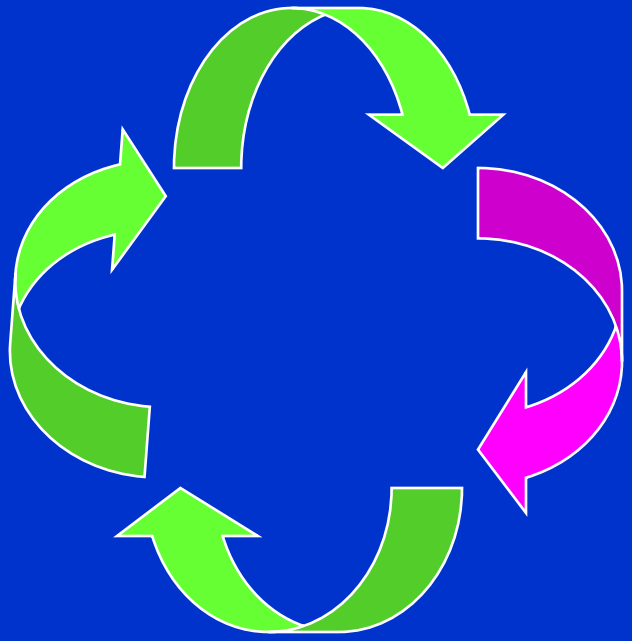
Contract Financial Considerations

- 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.

Sponsor-Investigators 21 CFR 312.50

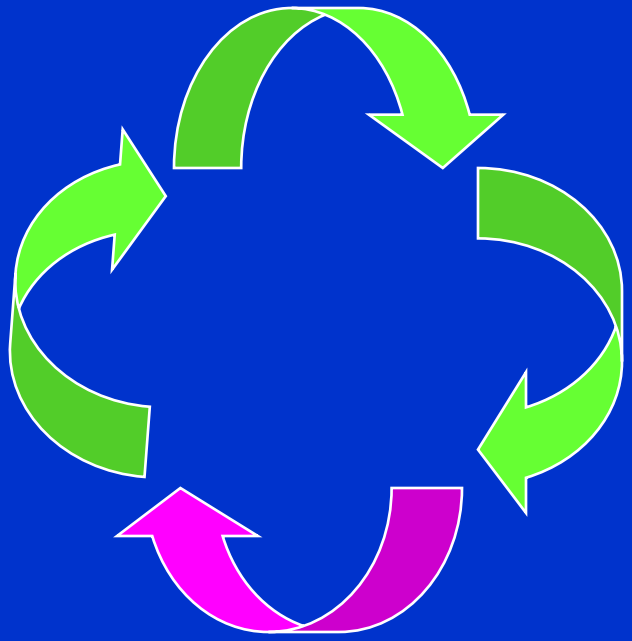
- Maintain the IND or IDE as required
- Qualify investigators and monitors (all sites)—CV's, 1572, financial disclosures
- Ensure proper monitoring (all sites)
- Ensure appropriate study conduct (all sites)
- Inform FDA and investigators of significant new AEs or risks with respect to the drug.
- Maintain accountability of investigational product (all sites).

Follow the Plan



- Obtain approvals
- Stay the course

Record the Conduct of the Plan



Essential Documents:

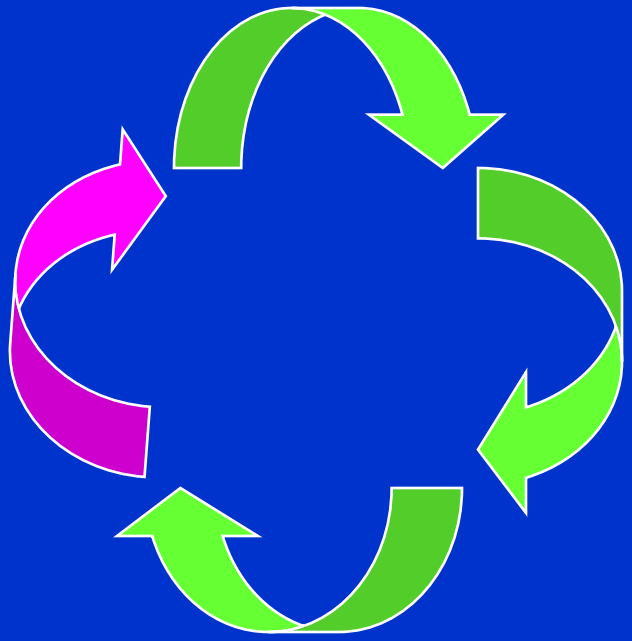
- Who?
- What?
- Where?
- Why?
- How?

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