iisra

INVESTIGATOR INITIATED - SPONSORED RESEARCH ASSOCIATION

Position Statement:

Setting Up an Investigator Initiated-Sponsored Research Program

Disclaimer: This document should not be construed as providing legal advice. Each company has its own unique program goals and level of risk tolerance. Ultimately, each company should consult their management staff and legal counsel when designing their IISR program.

Purpose

This Position Statement is designed to provide companies with "Points to Consider" in the development of an Investigator Initiated-Sponsored Research (IISR) Program. This Position Statement provides an introduction to topics more fully explored in IISRA's Best Practices Guideline.

Companies must consider several factors when developing and organizing an IISR program including: the placement of the program within the company's organizational structure; the scope of the program; the staff needed to support the program and the skills, experience, and training necessary for that staff; the development of standard operating procedures (SOPs) to ensure adherence to applicable local/global regulatory requirements; the processes for receiving and reviewing the proposals; the terms and conditions under which support will be made; the tracking of the progress of the research studies; and the communication of the program results internally and externally. The following is a list of points to consider for each of these critical issues.

Organizational Structure

Deciding where to house an IISR program within a company is not always easy. However, the guidance issued by the US Department of Health and Human Services Office of Inspector General in May 2003 clearly stated that to reduce risk, manufacturers should insulate support of IISR programs from sales and marketing influence. Each company should make the decision on where to house the program based on available resources, strategic alignment, and applicable laws and regulations.

Points to consider

- What part of the organization has the scientific expertise to support the program?
- Does the organization have the requisite resources to support each component of the program?
- What level of risk is the company willing to tolerate?

Defining the Scope and Strategy of the IISR Program

Companies need to clearly define the strategy, the scope, and the study areas that will be supported. Externally communicating the scope and areas generally considered supportable will reduce submissions that will not be approved, which save time for both the potential investigators and grant program staff.

Points to consider

- Products that will be supported
  - Marketed products
  - Investigational products
  - Both categories

- Types of studies that will be supported
  - Preclinical research
  - Clinical studies
  - Non-interventional studies
  - Retrospective data reviews
  - Cooperative group studies

- Support of global or ex-US studies

Staffing the IISR Function

Staffing on the IISR program will depend on the scope the program, the type of research that the company intends to support, and the number of submissions expected.

Points to consider

Assignments

1. Program management and development
2. Program design and workflow
   a. Policy establishment
   b. SOP and guidelines development
3. Regulatory requirements
4. Accounting requirements
5. Shipping fulfillment
6. Milestone tracking
7. Investigator communications
8. Contracting

9. Global regulations
10. Proposal review and approval team
    a. Statistical review
    b. Data management review
    c. Medical review (when necessary)
    d. Scope alignment review
    e. Budget and fair market value review
    f. Compliance review

Throughput analysis and forecasting

1. Number of ongoing projects
2. Anticipated number of new IISR submissions
3. Number of projects the IISR program can support
4. Budget
5. Platform to oversee program management

- Number of full-time and part-time individuals required to implement IISR program
- Expertise required to implement each of the roles within the IISR team

Staff Training

The IISR staff will need to understand the legal and regulatory requirements governing IISR programs, as well as the therapeutic areas they will be responsible for reviewing. Becoming involved in the IISRA is a great way to participate in education and training opportunities for IISR staff. IISRA also provides an avenue to network with others in the industry involved with IISR programs, which will allow IISR staff to learn from and contribute to the state of the art in industry practices.

Points to consider

- Prior experience in IISRA activities
- Prior experience in the relevant therapeutic areas
- Resources available for individualized review and training (eg, books, CDs)
- Available educational conferences
- Membership in IISRA
- Available budget for training
- Existing company policies and SOPs related to the IISR program

Proposal Submission Processes

Once the IISR program is established, the research proposal submission process needs to be defined. Appropriate expectations need to be set so that the process and time frame is generally understood by both internal staff and individual Sponsor-Investigators seeking support. A well-defined process can help the company to establish metrics for evaluating their IISR program.

Points to consider

- Potential requirement of submitting a preliminary study idea prior to a detailed protocol or study concept
- Development of proposal templates
- Submission method - Web-based, hard copy, or electronically by e-mail
- Documentation of submission and receipt of proposals
- Definition of required records per submission
- Submission of detailed budget
- Pre-defined limits for direct/indirect expenses

The Review Process

As companies develop their IISR program, another area of focus is the review process. The review process is often conducted by a standing review committee made of various disciplines from across the company. The size of the standing committee, the criteria used to evaluate proposals, and the method used to obtain any additional expertise needed must all be considered. Companies must also consider whether and how much information they will share with Sponsor-Investigators.

Points to consider

Personnel reviewing the proposals

- Personnel coordinating the review
- Review by the IISR program staff or by a multi-disciplinary committee
- Disciplines required in the review committee
- Core membership versus ad hoc members
    - Medical Affairs
    - Legal
    - Compliance
    - Research & Development
    - Regulatory
    - Commercial Development
- Level of commitment needed by individuals conducting proposal reviews

- Executive/supervisor support for time needed for committee members to review proposals

Proposal review process

- Frequency of proposal review
- Proposal reviews during face-to-face meetings or written proposal reviews
- Documentation of reviewers' comments
- Reviewers responsible for approval of proposals
- Documentation of the review process
- Storage of records
- Personnel responsible for final approval of a submission

Criteria for evaluating proposals

- Scientific merit
- Alignment with IISR program strategy
- Clarity of the proposal
- Expertise of the Sponsor-Investigator
- Established knowledge of GCP requirements
- Budget
- Available drug/device supply
- Risks posed to human subjects

Feedback provided to the Sponsor-Investigators

- Suggestions for improvement
- Feedback on consent documents prepared by the Sponsor-Investigator if a template is not provided by the Company

The Contracting Process

Where possible, research agreements for supporting IISRs should begin with a standard research agreement template. It may be helpful to develop written negotiation parameters to facilitate the contract negotiation process. It is best to work with legal counsel in advance to define these parameters in order to facilitate the completion of the IISR agreement.

Points To Consider

- Development of a research agreement template
  - IISR program staff
  - Transactional counsel
  - Compliance counsel
  - Intellectual property counsel

- Negotiation of research agreements
  - IISR staff
  - A contracts group
  - Legal Department

- Critical components of research agreements
  - Compliance with applicable laws and global regulatory requirements
  - Assignment of regulatory responsibility for the project
  - Payment Structure
    - Milestone driven
    - Per patient
    - Invoiceables
  - Other support
    - Drug/device supply
    - Competitor products
    - Equipment

  - Milestone/status reporting requirements
  - Responsibility for reporting adverse events
  - Publication requirements/terms
  - Confidentiality
  - Ownership of inventions
  - Registration of study (eg, clinicaltrials.gov)
  - Indemnification
    - Product liability for manufacturing defects
  - Term and termination

Safety Reporting

Companies supporting IISR program will need to consider how to manage and report information relating to the safety of their products that results from their IISR studies.

Points to Consider

Reports from IISRs

- All adverse events
- Only serious adverse events
- Specific formats for reports
- Timing of reports

Roles of the Sponsor-Investigator versus the Company supporting the study

- Reports of adverse events to the applicable Regulatory Authority
- Obligations of the Company to review safety data
- Incorporation of safety information into Company documents
- Providing newly available safety data on products to Sponsor-Investigators

Program Management

Once an IISR proposal has been approved, it is important to maintain regular communication with the Sponsor-Investigator to assess how the project is progressing. The Company should consider requiring the Sponsor-Investigator to provide periodic update reports or milestone reports. Many companies have their field medical team conduct regular visits with the Sponsor-Investigator. The Company must also establish a process for closing the project.

Points to Consider

Communication with Sponsor-Investigators

- Main contact
  - IISR staff
  - Medical Affairs
  - Field staff
  - Scientific discipline

Reporting Requirements

Frequency and timing of reports - semi-annual, quarterly, annually, at close of project only

- Format for the final report
    - Template for reports
    - Publishable manuscript only
    - Public reporting on a results database

Close–out of the Project

- Documentation requirements
- Public disclosure of results regardless of outcome
- Documentation of financial close-out/reconciliation
- Return of unexpended funds
- Accountability of unexpended study drug
- Grounds for early study termination

    - Failure to move the project forward
    - Failure to comply with reporting requirements
    - Failure to report safety information in a timely manner
    - Unacceptable safety risks

Standard Operating Procedures

Organizations that create IISR programs need to develop policies and procedures to govern the processes involved. The policies and procedures should define responsibilities and scope of the program. In particular, the process should vest ownership of any supported study with the Sponsor-Investigator. In the documents that describe the procedures, the work flow should be well defined and appropriate benchmarks should be described. Documentation requirements should also be described in the policies and procedures.

Points to Consider

- Development of SOPs specific to the IISR program
- Final sign-off authority
- SOP topics
    - Global policies
    - Selection and term of Review Committee Members
    - Review process
    - Review criteria
    - Process for termination/close-out
- Review/update of SOPs
    - Annually
    - Ad hoc basis

Program Awareness

Each company will need to decide how they will create awareness of the program both internally within the company and externally to the public and the research community.

Points to consider

- Internal and external communications to create awareness of the program
    - Via the company's web site
    - Through field personnel

- Information to communicate regarding the IISR program
    - Areas of research interest
    - Corporate goals of the program
    - Submission schedules
    - Points of contact
    - Review criteria

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