

PI Supervision and Oversight: Multi-Center IITs

A. Shah, K. Brown, N. Shuman, B. Halmos

Montefiore Einstein Comprehensive Cancer Center

1. Background

Traditional Investigator Initiated Trials (IITs) have been single centered, however as the clinical landscape of cancer therapies and treatments evolve, the focus shifted to collaboration on a multi-institutional capacity. Multi-center IITs assist in ensuring a clinical trial reaches its enrollment goal at a faster pace than a single center IIT and a diverse population of ages, races and ethnicities are included which is an FDA and industry focus right now. The challenge is how to successfully implement a clinical trial with adequate lead sponsor-investigator supervision and oversight when their offices are in different geographical areas. Per Title 21 of Code of Federal Regulations (CFR), specifically 21 CFR Part 312 and Part 812 Sponsor-investigators must supervise and oversee clinical investigations conducted under Investigational New Drug (IND) and Investigational Device Exemption (IDE). This presentation explores how sponsor-investigators can ensure adequate supervision and oversight in multi-center oncology clinical trials. It also provides insights into the U.S. Food and Drug Administration (FDA) guidance on “Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects”.

2. Goals

- Develop an institutional Principal Investigator (PI) Supervision and Oversight Plan for multi-center IITs based on FDA guidance and ICH-GCP.
- Educate and familiarize PIs and clinical research staff with the essential elements of conducting multi-center trials as the lead coordinating center.
- Outline the PI Supervision and Oversight Plan from the perspective of an NCI-designated comprehensive cancer center, incorporating best practices.
- Serve as a model for structuring and implementing multi-center IITs effectively.

3. Solutions and Methods

The Supervision and Oversight Plan is structured into three key stages that align with the lifecycle of a clinical trial: startup, maintenance, and closure. Organizing PI supervision and oversight elements within these stages enhances clarity and promotes compliance among research staff. (Figure 1).

4. Outcomes

Advantages

- Assists sponsor-investigators in understanding their responsibilities under federal and local regulations.
- Serves as a tool for demonstrating subsite supervision and oversight during inspection or audit.
- Enhances the efficiency and effectiveness of clinical trial implementation by providing a well-documented and structured process.
- Supports subsite staff to adhere to the protocol and comply with coordinating center requirements.

Challenges

- The plan must be comprehensive enough to cover all aspects of establishing and maintaining a clinical trial while allowing stakeholders the flexibility to follow their own practices.
- In some instance deviating from the plan may occur due to study specific incidents. Complete and adequate documentation can help remedy it.

5. Learned and Future Directions

Lessons Learned

- PI Supervision and Oversight Plans must be adaptable to trial-specific and institutional needs.
- This discussion emphasizes key FDA guidance elements that are frequently missed or inconsistently followed.
- PIs often lack familiarity with administrative complexities, requiring additional support and education.
- Comprehensive training for clinical research staff is essential for successful multi-center IIT implementation.

Future Directions

- Create eLearning training programs to enhance PI and research staff understanding of oversight responsibilities.
- Develop standardized templates to improve compliance with 21 CFR Part 312 and 21 CFR Part 812.
- Implement continuous assessment strategies to refine and improve PI supervision and oversight plan.

Figure

