Category: Investigator-Initiated Trials – Work in Progress

Building IND Infrastructure to Ensure Compliance and Enable Growth

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1. Background

IND regulations are complex and require a high level of subject matter expertise to ensure compliance. Historically, Lineberger Comprehensive Cancer Center (LCCC) relied on centralized university resources to submit and maintain its INDs. In 2016, LCCC identified substantial noncompliance with FDA regulations across its IND portfolio and decided to build infrastructure to move IND management in-house.

2. Goals

The goal of this initiative was to develop an IND management system with appropriate checks and balances to ensure LCCC's INDs followed appropriate regulations and to detect early indicators of noncompliance.

3. Solutions and Methods

Root cause analysis identified several contributing factors to noncompliance, including lack of written procedures defining IND management; investigator involvement and awareness; and training at all levels of the organization. The methods implemented were focused on addressing these root causes and ensuring that all management steps relied on a system as opposed to a single individual to ensure compliance. Ten sets of IND-specific SOPs, work instructions, and templates were developed covering topics ranging from IND safety reports to distribution of FDA communication. The SOPs described automated processes that heavily relied on utilization of custom reports generated from OnCore to track submission deadlines. Subject matter experts in protocol development and IND management were hired within LCCC, expanding from 1 FTE solely supporting protocols to 5 FTEs over protocol development and IND management. Their addition was justified by the need to address noncompliance, growth in portfolio, and expansion in IND and protocol development services. Additional FTEs were also added in data management to develop IND reports. Electronic data reports were optimized to ease IND annual report writing and were released under a stringent quality assurance system to ensure the accuracy and completeness of the data. Additionally, a principal investigator (PI) training lecture was launched and covered IND-related hot topics with a focus on lessons learned. Furthermore, a series of lectures targeted to staff were developed and well received.

4. Outcomes

Prior to solution implementation, internal audits revealed that within the 5 years prior there was only 56 percent compliance with submitting IND serial submissions per the regulations. Furthermore, of the serial submissions that were provided to FDA, 64 percent of the submissions were late. This means that LCCC's IND overall compliance rating with FDA regulations was only 20 percent. Internal audits were completed in 2022 of the 5 years after intervention implementation and showed 100 percent compliance with the regulations. Importantly, the IND portfolio grew in complexity within the 5-year period post-intervention with the addition of 10 INDs for internally manufactured products covering 15 clinical protocols. Prior to the transition, LCCC had only 1 IND covering 1 clinical protocol for an internally manufactured investigational product. Therefore, compliance increased significantly despite increased complexity.

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5. Lessons Learned and Future Directions

Two major lessons were learned during this process:

1. PI understanding of IND regulations at a high level is key so they know when to reach out with questions
2. Automated systems that are independent of a single individual are necessary to ensure long-term compliant oversight of the IND portfolio