Category: Trial Start-up, Activation, Regulatory, and Protocol Development - Work in progress

Evolution of an Institution-Sponsored IND Program

B. Murphy, C. Angeles

Fred Hutchinson Cancer Center

1. Background

Fred Hutchinson Cancer Center (Fred Hutch) is an NCI-designated Comprehensive Cancer Center composed of a tri-institutional consortium, the Cancer Consortium. The Institution-Sponsored IND (ISI) Program provides operational structure to support the institution holding the IND instead of individual investigators, and ensures that ISIs are submitted, maintained, and overseen in accordance with United States Food and Drug Administration (FDA) regulations. The Program reports to the Director of Clinical Research Regulatory Affairs and Compliance within the Clinical Research Support (CRS) office and has institutional oversight from a committee made up of physicians, senior institutional leadership, general counsel, and compliance. The ISI portfolio includes the Cancer Consortium's highest risk and most complex INDs, and supports all investigator-initiated studies that involve manufacturing investigational product at Fred Hutch. Since the ISI Program was established in 2016, the volume and complexity of INDs and trials has increased by 300 percent, necessitating optimization of the operations to meet the demand while ensuring efficiency, safety, and compliance.

2. Goals

To implement and/or improve processes to:

- enhance safety evaluation and reporting
- support oversight of multicenter studies
- develop operational expertise to support ISIs requiring manufacturing external to Fred Hutch

3. Solutions and Methods

Safety Reporting:

- Consider attribution to standard of care and/or study procedures in addition to investigational product
- Strengthen adjudication process to capture supportive information from Medical Monitors regarding expectedness and relatedness determinations
- Create 22 study-specific safety review sheets identifying unique reporting requirements
- Implement bi-annual review of Investigator's Brochures

Multicenter Studies:

- Leverage use of existing tools when practical
- Cross-collaboration with other comprehensive cancer centers for best practices

External Manufacturing:

- Identify FDA-required elements for drug substance and drug product information
- Collaborate with industry experts to build Program expertise in product release requirements

4. Outcomes

Safety Reporting:

- Significant reduction of incomplete forms, missed reporting, and study team consults
- More robust assessment documentation
- Eliminated risks of late reporting per protocol-specific requirements
- At-a-glance directives for reporting safety events to financial partners
- Contemporaneous updates for expected risks

Multicenter Studies:

- Development of tools for site selection and activation
- Creation of workflows for multicenter studies requiring in-house manufacturing and shipping to external sites
- Draft templates and tools, including batch records, SAE reporting forms, and protocol templates

External Manufacturing:

- Enabled ability to support three projects with manufacturing outside the United States
- Development of a facility audit process for both domestic and international needs
- Deepened expertise in requirements for drug substance and drug product information, as well as product release requirements for all stages of manufacturing

5. Lessons Learned and Future Directions

Our primary lessons learned are:

- Process breakdowns provide the greatest opportunities to identify areas of improvement
- Simplification can be the most effective form of process improvement
- Cross-collaboration resulted in most significant outcomes

We are excited to continue efforts to support multicenter studies. The Program's next set of goals include expanding the scope to support a larger portfolio of INDs, establishing a centralized data and safety monitoring board (DSMB), and exploring implementation of electronic Common Technical Document (eCTD) format.