Category: Regulatory – Work in Progress

Eliminating Unnecessary Review of Offsite Adverse Event (Expedited IND Safety) Reports: Departmental Collaboration Leading to Institutional Position

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1. Background

FDA guidance indicates the sponsor is responsible for evaluating individual safety reports, assessing significance, performing aggregate analysis, and communicating actionable concerns to sites. OHRP has taken the position that it is neither useful nor necessary for reports of individual adverse events (AEs) in subjects enrolled in multicenter studies to be distributed to all investigators or IRBs [Unanticipated Problems (UPs)]. Individual AEs should be reported to investigators and IRBs after the sponsor has made a determination that the events meet specific criteria and are deemed actionable at the site. Sponsors and sites have not yet reached consensus on the process for distribution of individual reports. Most sponsors send all safety reports regardless of assessment and including those lacking action at the site. The University of Pennsylvania, Perelman School of Medicine (PSOM)'s Office of Clinical Research and the Abramson Cancer Center Clinical Research Unit (ACC CRU) have adopted an approach intended to limit administrative burden associated with unnecessary event report reviews.

2. Goals

Reporting AEs that are not serious, unexpected, and related to the study product creates administrative burdens for all site stakeholders including staff, faculty, and review committee members. The intention of the unified position was to reduce the number of uninformative AE reports being received, processed, and reported, unnecessarily, at the site.

3. Solutions and Methods:

We aligned practice for review of events to only those meeting a clear definition for action at the site and those communicated outside of bulk automated systems. A guidance document delineating this best practice was developed, in addition to supportive tools explaining the position; language has also been added to contracts between PSOM and sponsors. Since the position was not specific to oncology programs, and the ACC CRU focuses heavily on sponsored projects, the ACC CRU served as lead in developing the position which could later be applied more broadly across the institution. ACC CRU (department) and PSOM (institution) continue to collaborate to message the position, train faculty/staff, and collect stakeholder feedback.

4. Outcomes

The ACC CRU has seen drastic (nearly complete) reduction in administrative burden as most reports previously received were not actionable. Actionable events continue to be communicated in alignment with "Dear Investigator" letters, protocol amendments, and/or updates to the investigator's brochure. Sponsors have provided generally positive feedback on the position; negative feedback served to present an opportunity for discussion and education. Our confidence has been bolstered by three FDA inspections of trials employing the position with no related findings upon review of safety reports/IRB submissions.

5. Lessons Learned and Future Directions

Sites will gain momentum in pushing back on undesirable, inefficient processes by banding together to communicate a consistent message supported by regulation. Institutions can seek inspiration for broad

policy from internal departments as operational workflows and system requirements are realized during the day-to-day conduct of human subject research. As the ACC CRU continues to improve efficiency through review of process and implementation of new electronic systems, sustained enhanced communication and collaboration with PSOM will afford future opportunity for alignment with institutional policy.