“A Guide to GCP for Clinical Data Management”
Mark Elsley, 2017, 46 pages, Canary Ltd., £8.95
Review by Norman M. Goldfarb

“A Guide to GCP for Clinical Data Management” provides a clear and concise summary of the elements of clinical data management GCP. For example, here is chapter 11:

**Have Input into Risk-Based Approaches to Trial Management**

Data management has a large role to play in risk-based approaches to trial monitoring (RBM) and quality management. This modern approach is being advocated by most regulators around the world, including the European Medicines Agency (EMA) and the US FDA, who have both published guidance on this topic.

ICH GCP E6(R2) also provides guidance on RBM. It requires sponsors to develop a systematic, prioritized risk-based approach to monitoring clinical trials. The aim of this is to improve the effectiveness and efficiency of trial monitoring. The sponsor may choose on-site monitoring, a combination of on-site and centralized monitoring, or when it can be justified, centralized monitoring only. A monitoring plan is required that provides details of the selected monitoring activities for the trial. Regulators will expect this to be adhered to.

**Select appropriate data monitoring tools**

Together with the biostatistician, the data manager should therefore have input into the monitoring plan and the selection of appropriate data monitoring tools. They should also have input into the risk assessment, particularly in relation to data integrity issues. Data managers should have input into the monitoring of risk registers and take accountability for the data management risk registers. The identification of critical data and plans to protect data integrity are crucial. Data managers should also have appropriate data integrity input into risk identification, risk evaluation, risk control, communication, review and reporting. Data managers may also have a significant impact on maintaining the trial blinding and the impact of breaches.

**Consider suitable centralized monitoring approaches**

Centralized monitoring is an evaluation of accumulating data away from the study site. This has to be performed in a timely manner by suitably qualified and trained personnel. Data managers and biostatisticians should have a significant role in this.

The FDA guidance supports risk-based approaches to monitoring clinical trials. It argues that the types of monitoring activities and the extent to which centralized monitoring practices can be employed depend on various factors. These include the sponsor's use of electronic systems, the sponsor's access to subjects' electronic records, the timeliness of data entry from paper CRFs, and the communication tools available to the sponsor and study site.

Sponsors who plan to use centralized monitoring processes should ensure that the processes and expectations for site record keeping, data entry, and reporting are well-defined, and should ensure timely access to clinical trial data and supporting documentation.

According to ICH GCP E6(R2) Section 5.18.3, centralized monitoring processes can be used to:

- Identify missing data, inconsistent data, data outliers, unexpected lack of variability and protocol deviations.
• Examine data trends, such as the range, consistency and variability of data within and across sites.
• Evaluate systematic or significant errors in data collection and reporting at a site or across sites, or potential data manipulation or data integrity problems.
• Analyze site characteristics and performance metrics.
• Select sites and/or processes for targeted on-site monitoring.

Some of the metrics that might be measured include serious adverse event reporting, time to CRF completion, numbers of deviations from predefined tolerance limits, high rates of withdrawals, and high rates of eligibility criteria breaches.

Central monitoring activities should be undertaken early and well before the end of a trial. Anything detected could then be used to trigger a monitoring visit and perhaps prevent further protocol violations or data integrity issues.

When centralized monitoring is undertaken, the reporting of activities should be regular. These reports form an important part of the Trial Master File. The reports should be detailed enough to demonstrate that the activities defined in the monitoring plan have been undertaken. Any deviations from the plan must be explained and justified.

The booklet includes 11 chapters:
• Ensure that Staff are Suitably Qualified and Trained
• Create, Maintain and Follow SOPs Describing the Clinical Data Management Processes
• Validate and Control All Computerized Systems Used to Collect and Handle Clinical Data
• Ensure that the Flow of Data from the Source to the Database is Well Documented
• Ensure that Source Date Meets ALCOA+ Standards
• Create a User-Friendly CRF and Database
• Check CRF Data for Accuracy, Consistency and Completeness
• Produce, Maintain and Archive High-Quality Documentation
• Ensure that CROs are Suitably Qualified and Experienced
• Use a Risk Register at Functional and Study Level
• Have Input into Risk-Based Approaches to Trial Management

Each chapter is accompanied by citations to pertinent ICH guidelines. An appendix provides a GCP checklist for clinical data management.

**Reviewer**

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