MEDIDATA | WHITE PAPER

Is the future of Data Management finally here? Indeed it is.

Table of Contents

This white paper is the first in a series that will help the audience understand the current data management landscape, where their organization currently sits within this landscape, and finally how to implement the necessary changes to optimize and rebrand their Data Management (DM)Risk and cleaning strategies.

Introduction

For roughly 10 years, we have heard about the changing role of the Clinical Data Manager. Whether this was discussed at conferences, via webinars, or white papers, the message was everywhere: Clinical Data Management (CDM) needs to change and needs to change fast. Due to the increased complexity of electronic health records, data wearables, sensor data, and the advent of risk-based quality management, it was these capabilities that would ultimately disrupt the old school, heads-down data cleaning methods data managers were enabling and executing. In this series of white papers, we will dig down into the whys and hows of this transformation, but to start we will focus on what exactly is meant by the “future of data management”.

Modernizing Clinical Data Capture and Management with Medidata Clinical Cloud

Traditional methods for data acquisition and management in clinical trials have been disrupted in ways never before seen. This disruption has forced both regulators and the industry to think progressively about how to enable and execute new methods for delivering care to patients. Innovative thinking and modernized data governance platforms have allowed for the implementation of continuity solutions to accommodate the ongoing conduct of clinical trials while maintaining subject safety and data integrity. However, CDM processes and technology have not progressed at the same pace as the industry's accelerated clinical trials - giving rise to mounting pressure on data managers and data analytic groups.

To that end, intelligent, automated data review and detection with actionable analytics must now be the backbone of the clinical data ecosystem and leverage the benefits of risk-based approaches and Quality by Design, as outlined in ICH E6 (R3) and ICH E8 (R1) respectively.

The Transition to Modern Data Management

Clinical Data Management should implement a systematic, prioritized, risk-based approach to clinical trial monitoring. Adapting to the modern CDM paradigm involves setting up informed central monitoring strategies to continually analyze the data coming in from EDC and other sources. To avoid post data base lock surprises, sponsors and CROs will proactively identify and mitigate any trends or patterns in the data that would cause issues at the time of analysis for biostatistics. To date, ICH Good Clinical Practice (GCP) E6 (R3) has been adopted by multiple regulatory bodies and is essential for rapid, study start-up, ongoing data cleaning, and data analytics.

Organizational Impact of RBQM

The clinical data management industry is known to be risk-averse, with well-entrenched processes following sometimes decades-old regulations. Institutionalizing significant changes included in ICH E6 (R3) in this highly regulated atmosphere requires a thoughtful strategy, change management plan, and implementation. In ongoing COVID-19 trials, we have seen the significance of the rapid change in organizations and the impact of identifying who is affected, what changes are needed, and how change is communicated. Moreover, it has brought to the forefront that traditional methods do not scale in all cases and would not have been able to support the real-time review and analysis required. Here are some of the key features enabling this optimization of ICH E6 (R3) through a focused implementation team that will identify affected people, processes, culture, and a strategic long-term approach:

- Agility - study designs must be more data acquisition focused
- Common data model - governance model must support a wide variety of data to ingest from a diverse group of sources
- Patient-centric - a study designed with the patient first to enable changes in data capture to meet the patient, site, and study needs
- Scalable - data capture must allow for all types and volumes, ranging from lab to devices
- Security - data security is the custodian of patient trust

Process Change

“The life science industry has seen accelerating interest and adoption of decentralized trial technology in the wake of the COVID-19 pandemic,” said Anthony Costello, president, patient cloud at Medidata. “Sponsors and CROs are increasingly turning to decentralized trial models in an effort to bring increased efficiency, security, and accessibility to the clinical research process.”

> With this shift, new or updated technology may likely be the best solution to address aspects of ICH E6 (R3), decentralized trials, patient diversity, data abundance, and clinical complexity. data analytics tool to give us early visibility into missing data.

Any gaps due to data re-entry, multiple systems, and resulting data latency or data errors create unacceptable risk. The velocity of decentralized clinical trial data capture requires monitoring tools that put sponsors and CROs as temporally close to the data entry as possible.

Sponsors and CROs have extensive access to process experts who can analyze existing states, design future state processes that maximize value from the technologies chosen, and create robust implementation plans to ensure organizational alignment.

Example: Process Change Related to Timing of Study Risk Management

A sponsor had historically delayed structured risk identification and mitigation discussions until the conduct phase of their studies when subjects were already enrolled. This sponsor found that when they shifted the timing of their study risk assessments to take place before final protocol approval, they realized both quality and cost savings. The risks identified during protocol design allowed study teams to "de-risk" the draft protocol, thus decreasing the number of avoidable protocol amendments. For example, one study team included an additional third-party lab to track an important KRI that was brought up during the risk assessment.

First, we must understand that the future is no longer years away. We can thank both the ICH E6 R3 release as well as Covid-19 for giving Data Management organizations worldwide, the kick starts it needed to realize that data and data cleaning would have to be swift, flexible, risk-based, and quality-driven. ICH E6 R3 gives guidance regarding the identification of critical data during the protocol writing process, the risks associated with these critical data, and the likelihood of such identified risks occurring. The FDA has endorsed these ideas and does expect that Clinical operations, as well as Data Management, will work in this critical data risk-based approach. Covid -19 taught us that the typical office visit and site data entry may not look the same. Data could be coming from a variety of technologies and DM would have to integrate and reconcile the critical pieces.

To learn more about ICH E6 guidelines, visit www.ich.org

Cultural Change

Cultural change is the second type of change that must be managed. Teams need to adjust their thinking and priorities on their role in the clinical trial. Although it can be tempting to merely state that all data must be reviewed and validated, it is better to communicate the positive results that come from adhering to the new guidance and recommendations that risk-based monitoring, data governance, and technological solutions bring, such as:

- Early access to trial insights for mitigation
- Improved identification of safety issues
- Reduced review times of disparate data sources
- Decreased mundane manual activity through access to technology
- Faster cycle times from last patient last visit to a submission-ready database

Example: Cultural Change Related to Targeted Source Document Verification (TSDV) Implementation

One sponsor implemented Medidata Rave TSDV and rolled out a targeted approach to verifying only critical data points defined by the study team. This sponsor tracked value metrics to look at time and cost savings derived from clinical research associates (CRAs). While they verified only a subset of source data in the targeted, risk-based approach, they were surprised to see virtually no change in SDV levels across their studies.

Providing options that are adaptive with flexible "site" workflows and the ability to ingest data from various media (i.e., telehealth, sensors, wearable devices) will require analysis and restructuring of many clinical operations. We will explore how the increase of data from multiple sources data management will need to reformulate their approach from onsite data cleaning and monitoring to using analytics to monitor, analyze and clean the data.

The major shift required post-ICH E6 (R3) was related to the call to conduct oversight activities and produce artifacts of documentation to show that the oversight was done. After two decades of static guidelines for ICH GCP, new terminology was introduced for risk identification and mitigation. Although it was clear that a risk-monitoring strategy would need to be adaptive, the ambiguity around how to operationalize this guidance led to industry working groups and toolkits for identifying Critical to Quality (CtQ)" data and processes.

Sponsors are informed in the revision to identify risks to critical trial processes and data. Additionally, sponsors are informed in the revision to identify risks to critical trial processes and data. Additionally, the revision calls for evaluation of the identified risks against existing risk controls considering the likelihood of the errors occurring. This evaluation is coupled with an assessment of both the extent to which errors will be detectable and the impact of such errors on human subject protection and the reliability of trial results. From there, clinical trial sponsors and CROs struggled to define meaningful risk indicators and prospectively identify quality tolerance limits.

RBQM adoption is a process versus a technology solution.

Core to the process is the tenets that early access is needed for trial risks. This paves the way for mitigations and other interventions contemporaneously as issues arise. Quite possibly the biggest barrier to industry adoption of ICH E6 (R2) is a demonstrable reluctance to operate with reduced SDV. The COVID-19 pandemic necessitated more centralized statistical monitoring and less reliance on traditional SDV. Importantly, nearly every global regulatory body which released COVID-19 specific guidance noted the importance of performing risk assessment activities.

ICH E6 (R3) is significant because it will address the reality of many disparate data sources in modern clinical trials and expand guidance to include the use of technology to ensure the quality of the trials. Notably, the updated guidance includes an emphasis on the design of oversight indicating that a one-size-fits-all methodology will be inadequate. The draft version includes Annex 1 (addressing interventional clinical trials), and Annex 2 (providing any needed additional considerations for non-traditional interventional clinical trials). The overarching principles document and Annex 1 are intended to replace the current ICH E6(R2), and ICH E6 (R3) clarifies that clinical trial teams are to be designing quality into the study protocol and processes. These activities should be applied during the early planning stages and across trial operations. R3 is supportive of an improved and more efficient approach to trial design and conduct.