WHITE PAPER

Overcoming Common Challenges of Clinical Data Review

Introduction

Clinical data review is an intrinsic component of clinical development aimed at assuring patient safety, determining drug efficacy, and assessing data quality. It involves rigorous analysis of a broad variety of clinical trial data and often necessitates integration of data from multiple sources in order to extract actionable insights. Answering key questions during clinical data review requires being able to rapidly identify and combine relevant data sources - despite the inherent "complexities" of clinical trial data – to provide near real-time reporting. Here, we look at some of the main challenges of clinical data review and discuss effective strategies to address these, before explaining how PerkinElmer's Clinical Analytics solutions can be deployed to bring urgently needed therapeutics to patients faster.

Challenges of clinical data review

Every clinical trial is unique. But one thing all clinical trials have in common is a critical dependency on clinical data review to assure patient safety. Generally, this involves monitoring variables such as adverse events, laboratory results, concomitant medications, and medical history, with efficacy analysis becoming integrated at Phase II and beyond. The overriding aim of clinical data review is to identify risks as early as possible, however a widespread inability to perform self-service analytics in near real-time has long hampered clinical research. Without strategies in place to address this need, users face several common challenges.

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- **Risk of missing an unexpected safety signal**

The primary focus of any clinical trial is to ensure the safety of the subjects enrolled in a study. This means having processes in place to rapidly identify any unexpected safety signals or adverse events so that risk to the patient is minimized. Reduced risk equates to a better-quality trial, shorter timelines and, consequently, lower cost, highlighting the value of a near-real-time view as subjects undergo screening. Equally important is the ability to quickly analyze study-specific objectives and endpoints in accordance with changing needs since this can decrease time to insight for faster, safer study completion.

- **Tools that cannot be tailored for specific therapies or use cases**

A major drawback of many existing analytics tools used to review clinical data is that they cannot be tailored to the unique aims of a study. Whilst there are certainly some similarities between clinical trials, study-specific endpoints, objectives, and data points must also be considered. These can only be properly analyzed using a tool that can adapt to a particular use case and that is designed with clinical analysis in mind. The key lies in striking a balance between common metrics used across all studies whilst at the same time focusing on stated objectives, endpoints, and safety risks that are relevant to a specific study and/or therapeutic area. This is fundamental to supporting scalability throughout clinical development.

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• Difficulty in drawing relationships

Another limitation of current technologies and processes used to review clinical trial data is that they prevent users from seeing the bigger picture. Despite electronic data collection (EDC) systems and vendor lab systems being widely employed for data centralization, the practice of using independent line listings, basic spreadsheets, and static analyses to sift through data remains surprisingly common. Adopting such an outdated approach makes it difficult to view adverse events in parallel with the corresponding lab results and concomitant medications in a single view or on a patient profile. It also prevents users from analyzing all laboratory results at a population level before selecting abnormal data, drilling down to a patient level, analyzing the corresponding medical history and concomitant medications, then finalizing the review on a line listing. Rapid identification of relationships and trends is vital to minimize risk and to avoid slowing down clinical development.

• Existing technologies or processes slow down data review and decision-making

The COVID-19 pandemic has emphasized to companies of all sizes the value of working remotely. Perhaps nowhere is this more apparent than within the realm of clinical data review, where information is generated across sites, across geographies, and by multi-site internal and external research groups specialized in many different areas. Being able to review data in near real-time without depending on outside organizations for analytics reporting - be they another group within the same company or an external contract research organization (CRO) - is key to keeping clinical development on track.

• Reliance on data reporting from outside groups

Relying on a middleman rather than going directly to the data source can add considerable time between question and answer. As such, insourcing clinical data review is often a preferred approach to alleviate regulatory pressure while ensuring compliance with ICH guidelines stating that ultimate responsibility for the quality and integrity of trial data always resides with the sponsor[1]. Moreover, the financial incentives to quickly determine safety and efficacy mean that performing clinical data review in-house provides a faster route to understanding success or failure and adapting accordingly. Currently, many clinical data review teams are forced to request data in a standardized format from data management groups, biostatisticians or external vendors, a process which inevitably incurs delays and extra costs. In contrast, having direct access to source data that is easily manipulated into a workable format provides those performing clinical data review with faster time to actionable results.

• Each team is reviewing their own reports

One further challenge of clinical data review lies in avoiding inadvertent study biasing that can occur when clinical data review teams rely on data management groups, biostatisticians, and external vendors to provide manual reports and analysis. This interdependency not only invites significant delays, but it can also lead to the generation of individual analyses that are difficult to share, impossible to reproduce or compare across domains, and that typically have to be recreated every time new data becomes available. Since clinical development is a team sport that requires verifiable results, having a centralized view and collaboration mechanism is essential to avoid any errors that can jeopardize the entire process.

Best practices for clinical data review: Five strategies that work

Five key strategies underpin a successful approach to tackling the challenges of clinical data review, namely:

- Speed
- Agility
- Customizable analytics
- Workflow flexibility
- Collaboration

The first of these - speed – recognizes the need for a solution that can rapidly be deployed and that allows visualization of near real-time data as soon as a study begins enrolling. It also references the capacity to promptly identify safety, efficacy, or data quality issues, as well as the ability to adapt quickly to any given changes in a study.

Complementing speed, an agile solution highlights the requirement to handle protocol amendments, data changes, multiple data sources, and the specific metrics of a study or therapy. It segues neatly into customizable analytics since striking the right balance between common and study-specific analysis solutions is critical. With the effectiveness of clinical data review hinging on being able to interrogate unique objectives, endpoints, and safety risks, as well as being fully amenable to scalability, it is vital that customized analytics can be used to augment standard safety metrics for faster time to actionable insights.

Workflow flexibility means providing a user experience that helps highlight risk and relationships to streamline data discovery. Having the capacity to drill down from population to subject and then also across related safety domains naturally paves the way to more efficient clinical data review. Lastly, with collaboration being pivotal to the success of any clinical data review process, analytics solutions must be designed with teamwork in mind. Users should be able to clearly track the data review process, share results, receive feedback from peers, and communicate findings to stakeholders. In combination, these strategies allow for rapid identification of adverse events and swift resolution of any issues with the potential to impact safety in a larger population.

Clinical Analytics solutions for clinical development

Until now, clinical research has lacked a solution enabling clinical data review teams to perform self-service analytics in near real-time. However, by providing a suite of Clinical

Analytics solutions covering the entire clinical development process, PerkinElmer has removed many common barriers that would normally delay the delivery of urgently needed drugs to patients. These solutions, powered by TIBCO Spotfire®, can be integrated within an existing ecosystem or can instead be used as stand-alone platforms to support a specific clinical need.

Common clinical challenges that can be solved using PerkinElmer's Clinical Analytics solutions range from biomarker discovery and subject selection, through clinical data review and medical review, to operational effectiveness and identification of key risks to assure patient safety. PerkinElmer's Clinical Analytics solutions are also applicable to broader use cases; because the use cases are modular, they can easily be mixed and matched for specific needs or scaled as a solution to meet the requirements of an entire portfolio.

PerkinElmer's Clinical Analytics solutions include:

- Clinical & medical data review
  - Efficacy analysis
  - Safety analysis
  - Pharmacokinetics
  - Query review
- Operations & risk-based monitoring
  - Site selection and initiation
  - Protocol deviation analysis
  - Study milestones
  - Site status
  - Recruitment
  - Query cycle times
  - Abnormal labs
  - Lab tracking
  - Central site monitoring
- Pharmaco vigilance & Safety data reconciliation
- Real world evidence

Using Clinical Analytics solutions, PerkinElmer has been able to address everything from a 12-study tailored clinical data review and operations analysis at a small sponsor, to a full service medical monitoring program deploying six studies per month at a mid-sized sponsor, to a 20-study safety and efficacy analysis with study biasing prevention at a large sponsor.

Since the overriding aim of clinical data review is to ensure patient safety, PerkinElmer's Clinical Analytics solutions are designed to address the multifarious challenges of analyzing clinical trial data and putting in place robust strategies to overcome these hurdles. In addition, they provide users with speed, agility and tailored analytics to identify risks as early as possible. Moreover, with unrivalled workflow flexibility to support dynamic collaboration, PerkinElmer's Clinical Analytics solutions are accelerating the delivery of urgently needed therapeutics to patients.

Reference :
1) https://www.fda.gov/media/93884/download

For more information on PerkinElmer's Clinical Analytics solutions please visit: https://www.perkinelmer.com/uk/category/clinical-analytics

This white paper is based on a PerkinElmer webinar: "From Safety to Efficacy: Top 5 Strategies to Improve Clinical Data Review", presented on May 19, 2020 by Brent Myers, Director of Clinical and Translational Analytics, and James Bullis, Senior Software Service Specialist.

CTA – view the webinar

What is the Biggest Challenge Faced by Clinical Data Reviewers?

- Data quality – 63%
- Trial complexity – 50%
- Inadequate technology to support the trial – 47%
- Patient safety – 38%
- Regulation – 16%

Source: "From Safety to Efficacy: Top 5 Strategies to Improve Clinical Data Review" webinar poll

- I need to better manage my data quality – 62%
- I need to synthesize disparate data across multiple domains – 47%
- I need to identify safety signals sooner – 41%
- I need to make decisions faster – 38%

Source: "From Safety to Efficacy: Top 5 Strategies to Improve Clinical Data Review" webinar poll

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