Case Study

Clinical Data Quality Assessment

YourEncore found CRO data quality problems prior to submission for a $2 B peak-sales product

As clinical trials grow more complex, the need for improved quality checks becomes greater and more critical for submission readiness.

When asked for their opinion on the root cause of the recent increase in FDA warning letters, a majority of firms cited "outsourcing of clinical trials."
Source: CRO Outsourcing Survey, Avoca Quality Consortium

As biopharma firms continue to find ways to reduce costs in drug development, clinical trial responsibilities are being transferred to CROs. This creates an increased pressure on the pharmaceutical companies to ensure data coming from the CRO are properly validated prior to submission.

For CROs, the rapid growth and high turnover have led to gaps in consistency of delivery and training. CRO partners, often selected for their broad capabilities across multiple functions and geographies, may not have best-in-class capabilities across all functions, leaving potential risks in key data quality areas.

OPPORTUNITY: CONFIRM DATA QUALITY

A YourEncore client utilizing a CRO for its Phase III clinical trials was concerned about quality and timeliness of deliverables of submission data. The primary focus centered around issues in programming, data management, and data flow.

Facing the tight timelines of completing a review of the data and submission, as well as findings from previous submissions, the client required assurance that the submission quality would be acceptable to the regulatory agency. Internal resources were stretched too thin to dedicate the necessary time and attention, so the client turned to YourEncore to provide a comprehensive, objective assessment of the data quality.

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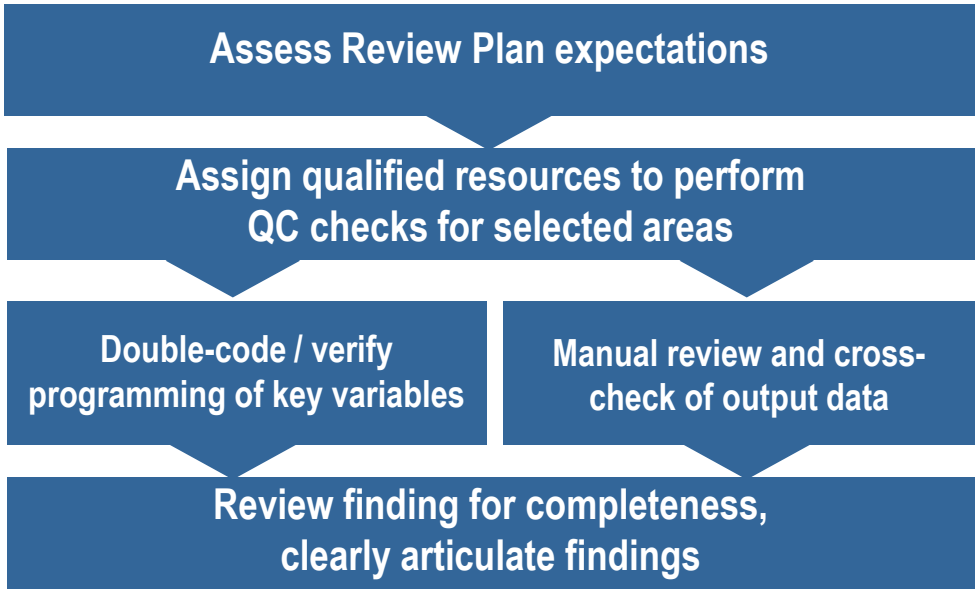
APPROACH

YourEncore built a customized team of experts in the areas of statistics, clinical, statistics, statistical programming, and data management to complete a data quality check of study data.

The team developed a detailed review plan to check clinical data tables, listing and figures (TLFs) as well as Integrated Summaries of Safety/Integrated Summaries of Efficacy (ISS/ISE) data in the submission.

While the scope for each data quality review varied, the standard approach for each review included these steps:



Throughout the process, regular communication between the YourEncore project leaders and the assigned client lead ensures real-time updates on the findings.

YourEncore has completed data quality assessments with teams specializing in multiple therapeutic areas, including:

- Oncology
- Cardiovascular
- Musculoskeletal
- Rheumatology
- Pain

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OUTCOMES

In a short timeframe, the team determined the extent of the data quality issues and identified a remediation plan, prior to the agency's return visit. The client passed the inspection and their drug has been approved, with an estimated annual peak sales of over $2.0 Billion.

Based on the success from this project, the team has become an integral part for helping to resolve these quality issues.

The client identified key outcomes from the YourEncore data submission quality project:

- **Mitigated delays in submissions.** Internal findings prior to data lock ensure the submission data are accurate.
- **Sponsor confidence.** The objective, top-to-bottom review of submission quality gave the sponsor confidence that the best possible package was being delivered to the agencies.
- **Objective partnership metrics.** The company and its CRO partners have objective information from a third party with defined improvement measures. The CROs took those improvement opportunities and build capabilities in-house.
- **Foundation for evolving quality system.** Issues identified by the YourEncore team provided input in a remediation plan that helped provide input into missing elements of a comprehensive quality program for products entering Phase II and Phase III.

ONGOING PARTNERSHIP FOR DATA QUALITY ASSESSMENTS

Based on the success from this project, the team has become an integral part of the quality organization, helping to resolve these issues before giving the agency the opportunity to find the issues themselves. The client sited three key reasons for continuing to use YourEncore for these data quality reviews with tight timelines:

- The YourEncore team is trained on client processes
- The YourEncore team has worked together before to solve similar challenges.
- YourEncore has the flexibility to include specific therapeutic area expertise to provide an additional layer of confidence in the findings

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Deployed Data Submission Quality Project Leaders

Biostatistical Quality

- PhD, Statistics; MS, Statistics; BA, Mathematics
- Statistician with nearly 15 years of pharmaceutical and biotechnology industry experience, in addition to experience as a consultant for clients in the biotechnology, ethical pharmaceutical, contract research and managed care industries. Strong background in statistical strategy and operational statistics, in addition to vast experience in document writing and in process improvement.
- Former Director, Statistics, at Aastrom Biosciences, Inc., expert was responsible for statistical strategy for the clinical plan. Provided statistical expertise for design and optimization of clinical trials, including sample size, and analysis of data. Contributed to the development of materials for regulatory agencies, key opinion leaders, professional meetings, press releases, and manuscripts. Performed data content and study document review, including blinded data review (BDR), and review of draft study reports and regulatory documents.
- As Statistical lead for Metabasis Therapeutics, Inc., expert participated in the development of standards for case report forms and data presentations (tables, listings, and figures).

(Expert # 13658)

Clinical Trial Expert

- MS, Clinical Nutrition
- Director with 13 years of pharmaceutical industry experience focusing on drug development in Phases I – IV. Clinical trials were transformed from concept through execution and reporting phases.
- Vast experience with protocol writing, study start-up phase, patient narratives, authoring Investigator Brochures, IND Annual Reports, operational oversight of clinical trials, and reviewing study data. Championed many process improvements at Metabasis and Pfizer.
- Now, owner of a high-quality consulting company assisting clients in reviewing clinical trial data to uncover potential quality concerns prior to NDA submissions; also involved in reviewing and coding Adverse Event and Serious Adverse Event data.
- As Clinical Study Operations Manager, served as the main point-of-contact for the operational activities of clinical trials in various therapeutic areas. Successfully launched national and international Phase II and III clinical trials, remaining within budget and enrollment targets.
- Expert has been a CRA, traveling extensively to study sites to ensure proper data handling for clinical trials, ensuring data accuracy and Good Clinical Practices. Worked closely with QA for site audit preparedness.

(Expert # 10551)

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