CRIO

Case Study

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How Sponsors Can Leverage New Technologies To Lower Trial Costs

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OVERVIEW

Biotech organizations routinely rely on full-service contract research organizations (CROs) to manage all phases of their clinical trials. Sponsors often defer to their CRO's recommended processes and pre-qualified vendors, relying on their CRO's experience. After conducting a competitive bid/negotiation process, a sponsor may feel they have obtained the best possible market price, offering, and vendors.

Based on our combined 33+ years of experience working for sponsors, CROs (both large and small), and investigative sites, we know there is a better way--
– a leaner, nimbler operating model that leverages a new class of site-facing technology. In particular, we recommend the use of the CRIO platform which includes the industry's most popular site-based eSource application already used by upwards of 2000+ private research sites and site networks, and expected to be 4000+ within five years.

The "CRIO Model" eliminates the need for source transcription into the eCRF, improves protocol compliance, and reduces monitoring and data management demand because of fewer queries and increased remote collaboration abilities. When CRIO's eSource is used by research sites, it serves as an efficient way to capture data for their trials, improving site efficiency and allowing them to spend more time screening and enrolling patients. When CRIO's eSource and Reviewer solutions are used by sponsors and CROs, the eSource becomes a full-service Direct Data Capture (DDC) system that combines the eSource with the EDC - we refer to this as the "CRIO Model". Sites are now able to capture eCRF data directly in the exam room, with real time edit checks firing while the patient is present - thus reducing queries and protocol deviations.

This model eliminates the need for sites to perform the time-consuming task of double-data entry, and greatly reduces the need for costly onsite monitoring to perform source data verification. Indeed, the CRIO Model projects 30%+ savings possible on the combined cost of monitoring and data management for a trial - usually the two largest budgetary line items within CRO costing models. A 30% savings on these two areas may represent as much as 12-15% of the total budget for CRO services.

[1] Excluding investigator payments and vendor pass-throughs.

COST COMPARISON

To estimate cost savings, we constructed a representative pricing model of monitoring and data management costs - first, using the traditional model and second, using the CRIO Model, where the sponsor can leverage direct data capture. Our methodology is described in more detail at the end of this article.

We used the following parameters for a hypothetical phase 2 study:

- 20 sites
- 28 month duration (from start of CRO engagement through delivery of CSR)
- 300 subjects
- 10 visits per subject
- 30 unique CRF pages
- 45,000 total CRFs to review

The following is our summary of estimated costs by line item for the Traditional model vs. the CRIO model, and estimated savings. The total savings comes to $1.132 million against the original cost of $3.464 million, or 33% (all amounts expressed in USD).

Line item	Current Model	CRIO Model	Savings
Monitoring			
Central Monitoring	$570,000	$570,000	$0
Site Monitoring	$1,858,500	$1,252,500	$606,000
Travel (pass through)	$367,500	$135,000	$232,500
Data Management			
eCRF design / UAT	$120,000	$50,000	$70,000
EDC licensing (vendor)	$230,000	$230,000	$0
EDC Site User Support	$23,100	$0	$23,100
DM review and query resolution	$225,000	$45,000	$180,000
Data lock, delivery, archiving	$40,000	$20,000	$20,000
Reporting, coding, other	$30,000	$30,000	$0
Total	**$3,464,100**	**$2,332,500**	**$1,131,600**

[2] Total CRFs is a key volume driver. We estimate 25 CRFs for 3 of the 10 visits (Screening, Randomization and End of Treatment) and 15 for 7 of the 10, for a total of 145 per subject. 300 x 145 = 43,500, minus dropouts, plus unscheduled visits. For simplicity, we rounded to 45,000.

MONITORING COST SAVINGS

CROs typically charge a flat fee for every Interim Monitoring Visit (IMV) conducted. For onsite IMVs, we modeled $4,500 per visit, and an incremental $2,000 if a second day is required; in addition, we modeled $1,000 of travel per visit, and an incremental $650 of travel per second day. By contrast, for remote IMVs, we modeled only $2,500 per visit, with no travel. This fee structure reflects an implied assumption by the CRO on the number of hours spent doing productive work (monitoring, preparation and follow-up) versus time spent traveling. Remote monitoring enables CRAs to double productivity by eliminating travel days.

The CRIO Model drives savings in two ways. First, it reduces the number of total IMVs required because it increases the throughput of monitoring. By combining eCRF and eSource, Source Data Review (SDR) and Source Data Verification (SDV) occur simultaneously - thus freeing up a significant amount of a Clinical Research Associate's (CRA's) time. Additionally, by standardizing the collection of source data across all sites on a study, the number of queries and deviations are reduced through the use of real time edit checks. Based on our analysis and CRIO's case studies, we estimate that monitoring productivity - measured as CRFs per monitoring-day - can potentially double. However, for purposes of this case study, we assumed a conservative productivity increase of 50%, thus reducing the need for IMVs by about a third.

Second, because the model makes the sites' source data available remotely, by default (i.e. scanning and uploading paper source are not required), it shifts the vast majority of IMVs from onsite to remote. We assumed that the percent of the IMVs done remotely will increase from 20% in the incumbent model to 70% in the CRIO Model (i.e., still allocating 30% of IMVs as onsite). We kept the assumption that the Site Qualification Visits, Site Initiation Visits, and Closeout Visits would be performed either on-site or remotely depending on study requirements. Simply by shifting the structure of IMVs from onsite to remote, we reduce monitoring costs significantly, and drastically reduce pass-through travel costs.

DATA MANAGEMENT COST SAVINGS

For the EDC licensing fee, we obtained a quote from CRIO using the parameters above; this quote includes not just the licensing fee, but also a set of robust wrap-around services that they provide, including the study build, the data delivery, and the electronic archiving service for the sites. From experience, we know that incumbent EDC vendors will vary significantly in price; some of the lower-end quotes will come in lower than CRIO, and the quotes for premium systems will come in significantly higher. For purposes of this case study, we set the EDC pricing for the incumbent model to be the same as CRIO. The point of this exercise is not to show savings from technology fees per se, but from a shift to an operating model enabled by a fundamentally different approach.

In doing so, we identified that the CRIO Model not only reduces monitoring costs, but also data management costs. First, CRIO significantly reduces the cost of the study build, as they can deliver standardized study templates on a very cost-effective basis. This is because of their intuitive study configuration module, along with an extensive pre-built library of reusable templates across a wide range of therapeutic areas. This standardized library represents cumulative experience designing hundreds of study templates across numerous therapeutic areas. We took CRIO's price quote for study design, and then added in the estimated cost for completing the mandatory User Acceptance Testing, which is the responsibility of the sponsor and/or CRO.

Second, CRIO's quote includes the cost of setup, training and supporting the sites on the trial, including provisioning of a 24/7 multilingual Live Chat support. Other EDC vendors often charge separately for user administration/support. Thus, we eliminated the cost of user management.

Third, the CRIO Model greatly reduces the need for Data Management to conduct traditional "data cleaning" - the process by which clinical data managers view the eCRF to perform form-by-form, query-by-query review in consultation with the data review specifications (i.e. assessing for data completeness and/or issuing queries). We recommend and encourage sponsors and CRO's to invest more in utilizing data analytics and data reporting to identify safety and efficacy outliers, patterns and enrollment trends in as close to real time as possible. Therefore, we reduced the cost of this service by 80%.

Fourth, the CRIO Model facilitates data freezing on a continuous basis, especially since it's obtaining the Principal Investigator sign-off contemporaneously with each visit completion. This significantly reduces the flurry of activity associated with obtaining PI signature that is associated with data locks. In addition, users can extract data at any time through a self-service export feature, at no additional cost. Finally, CRIO will, as part of its quote, include the cost of archiving each site's

DATA MANAGEMENT COST SAVINGS (CONT.)

source data for the contracted length of period post-closeout. As the site is the custodian of their data, they will retain access to CRIO indefinitely after a study (with the ability to download and electronically archive locally), as they would with paper source. As a result, we only modeled the basic process costs associated with the final study data lock - project management, cross-system reconciliation, final checks, and site communication, etc. To be conservative, we cut the total cost in half.

Conclusion

The CRIO Model, where CRIO is used as a DDC tool for sites, enables a shift to a primarily remote monitoring model, enabling efficiency with CRA productivity and resourcing. In addition, much less effort is required from data management. As a result, sponsors are able to realize tremendous savings. CROs are able to increase quality by conducting more visits, utilize their resources more efficiently, and improve their own margins while speeding up timelines. Sites benefit from the reduced burden of data transcription from source to an EDC and preparation for on-site visits. Sponsors receive more touchpoints from their CRO at a steep discount compared to traditionally priced models. Overall, the sponsor, CRO and sites can all focus on what's most important - patient safety, data integrity, enrollment and retention.

Note on Methodology

Our economic model applies estimates based on market benchmarks in non-oncology therapeutic areas. Together, we have a combined 33+ years of industry experience, and have both presented CRO proposals to sponsors, and evaluated them from the perspective of a sponsor. As each CRO uses a unique pricing structure, we spent considerable time normalizing pricing quotes to identify a range of low to high pricing on a per-unit basis for each service line. We eliminated outliers and special situations, and chose a representative value (rounded for simplicity) in the midpoint. We then made estimates of the total volume of activity that may result from the study parameters provided, and applied the benchmark pricing. To simplify our review, we removed costs associated with non-EDC technologies such as ePRO or IRT, and ignored the provision of other common CRO services such as site startup, TMF, medical monitoring, safety, project management, or biostatistics.

To learn more about ALCOA Consulting, LLC and their services reach out to them at info@alcoaconsulting.com or visit their website www.alcoaconsulting.com.

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