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The CRO View: Sharing Opportunity Vs Risk In Drug Development

by Sean Russell

Premier Research's chief commercial officer, Sean Russell, describes how the CRO has turned risk-sharing negotiations from a black art to a predictable process.

We hear a lot about risk-sharing in drug development these days, and it's a healthy trend in an industry often defined by high costs and the pressure of project deadlines. Drug development thrives on cost and schedule adherence, and the inextricable link between the two leads increasingly to risk-reward arrangements between drug makers and their clinical research providers.

Having been involved in many of these, I like to avoid "risk-sharing" and other terms that can cast these agreements in a negative light. When we look at clinical development, I prefer to focus on *opportunity*-sharing — not so much avoiding failure as improving clinical trial productivity and efficiency.

After all, if you start a clinical development program assuming you're going to fail, you'd better find something else to do.

First, A Definition

Risk- and opportunity-sharing is still a pretty new concept, and there are different types of these arrangements. In this article, I'm describing agreements between drug makers and clinical research organizations under which CROs are rewarded, or penalized, based on their performance versus contract terms and milestones.

As CROs increasingly assume the role of professional adviser as opposed to service provider, sponsors expect us to have some skin in the game by connecting performance and reward. And the basis of a well-designed incentive arrangement is this: Sponsors want their CROs to succeed because successful clinical trials are essential to getting new drugs to market. No risk-reward

deal set up as a trip wire — "you missed these deadlines and now we're going to extract our penalty" — has any chance of succeeding.

The Carrot, Not The Stick

So with growing frequency, we're using a performance-based pricing model as a tool for negotiating and managing opportunity-sharing agreements. Sponsors pursue these deals hoping we reach those incentive milestones and happily pay for performance that meets or exceeds targets. We share these payments as project team bonuses to motivate our employees, recognizing that happy employees are engaged and stick around — even in the clinical research business, which is famous for rapid employee turnover.

Of course, bonus payments alone cannot provide the impetus needed to motivate our teams to the level of performance we aim for. Many factors drive high-functioning teams, such as the satisfaction of collaborating with talented colleagues and teaming with sponsors on work that has the potential to advance science and improve lives. But bonuses can be an important part of the mix in improving employee retention.

We've come a long way in evolving toward this ideal in the past couple of years, leaving in the wake of risk-sharing's checkered past some classic non-starter ideas. They include penalties without corresponding rewards (an unthinkably bad deal) and CROs signing up for royalties from future drug sales (a long wait for a very uncertain return).

Opportunity-Sharing Milestones

These arrangements began as a sort of afterthought in the contract negotiation process, offered by sponsors as a way to help close the deal. Recognizing the potential for mutual benefit, we developed a template outlining the sorts of terms we'll consider for inclusion. We'll typically put a percentage of the total contract value — or alternatively, our project management fee — at stake, tied to milestones such as:

- Time from contract award to opening of the first study site.
- Time from contract award to first patient screened.
- Date of database lock relative to last patient last visit (incentive rises for every week that lock date precedes LPLV).
- Percentage of sites activated within a prescribed period.

To cite a recent example, a double-blind trial of a treatment for major depressive disorder tied incentives and penalties to five factors: US patient enrollment (40%), enrollment in two other countries (7.5% each), database lock (30%), and first patient screened (10%).

There are other performance measures — mostly factors beyond your control — that should not be part of a risk negotiation. For example, because CROs have limited influence over enrolled patient numbers, that's a metric that's best avoided. So are customer-induced delays from any number of origins, such as contract approvals, implementation of protocol amendments, and late reviews and approvals.

Many other factors can cause delays and should likewise be excluded from risk-sharing agreements. These include product safety issues, import complications, unanticipated standard-of-care changes, and unforeseen regulatory intervention.

Assessing The Level Of Risk

For a successful negotiation, the CRO and sponsor must agree on several fundamentals to ensure that both parties share equally in the financial and performance benefits and risks. We'll assume risk only at a level commensurate with the control we're allowed over the study's execution — things like:

- Protocol design and site selection, which have a significant bearing on patient recruitment, retention, and compliance.
- Appropriate level of feasibility assessments to be performed.
- Operational strategy, such as recruitment plans, monitoring, strategy, data management platform and process, and statistical analysis planning.

In creating this structured approach, we have advanced risk-reward negotiation from a black art to a process that's straightforward, predictable, and repeatable. And we've witnessed compelling results — for example, greatly improving performance in a recent Eastern European study to evaluate an adult schizophrenia drug for a biopharmaceutical customer. Our incentivized team moved up the timeline for the 400-person study and, to a person, remained for its full 22-month duration.