The Direction of Pharma/CRO Relationships

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Introduction

The management of outsourcing and vendor relationships is one of the hottest topics across the pharmaceutical, biotech, and device industries today. All life sciences companies struggle with developing internal capabilities and infrastructure for proactively managing their outsourced development partners and programs. As the dynamics of clinical development - evolving regulations, complicated protocols, and financial constraints - increase the complexity of research and development, companies are moving toward outsourcing various components of a drug's development program to aid in balancing workloads. With this increased level of outsourcing, there is a need for sponsors to figure out the best way to improve and manage working relationships with contract research organizations (CROs). In building relationships with a CRO it is important to set expectations and take both an introspective and a proactive approach in defining and outlining requirements of the program and the working relationship with the CRO. As the sponsor, you need to articulate needs versus wants, outline the scale of the program, and define the timelines to hit milestones. Additionally, there is a need to identify who will be involved and what responsibilities they will have, what in-house expertise and resources for managing the project you will have, and what standard processes are in place and/or need to be developed for use in the managing and overseeing the program. Once you have these areas identified, you need to determine how the CRO will function as an extension of your company. What is the scope of your relationship with the CRO? How will the project be driven, how will you interact with the CRO, what type of core competencies and experience do they need, do they understand your product or therapeutic area – the list of questions is virtually endless. These questions are crucial to answer as you identify and evaluate vendor alliances so you can start to build a more effective partnership and understand where gaps in outsourced projects may lie.

Over the last fifteen years, the part CROs have played in research and development has changed. CROs are being required to handle more of the workload previously managed by sponsoring pharma companies. According to the Association for Clinical Research Organizations, between 2007 and 2011 the use of CROs by pharma companies increased 44%. Much of the work falls to offshore companies such as those based in China, which are growing at a rate of about 30% in the past five years. This increase in responsibility has made CROs more of an equal partner in the clinical development process rather than simply another hired gun. Transparency Market Research published information about the pharma/CRO relationship in 2013 and determined by the recent trends that outsourcing could reach $65 billion by 2018. These trends also indicate that the relationships are becoming more of a long-term working partnership similar to one large team rather than a short-term project mindset.

Strategic partnerships have the benefit of significantly reducing the need for the hands-on management that has contributed to the high cost and effort of previous pharma/CRO relationships. However, the decreased hands-on management in these types of partnerships can still ensure good information exchange. They can also reduce effort duplication because the contract research organization can take on many of the daily responsibilities of the project previously held by the sponsor. The average ratio of sponsor-to-CRO oversight can be reduced from 1:3 to 1:8 or even up to 1:15 in a strategic partnership model, saving around 20% of a CROs fees for each project.

All of these developments in the relationship between pharma companies and CROs mean that sponsor companies will need to be comfortable with identifying, qualifying, managing, and communicating with the vendors they use. Partnerships are derived from relationship equity, where ideas and innovations are shared equally and freely, and project goals and responsibilities are clearly defined. While relationship changes between sponsor companies and CROs are a major trend across the industry, that doesn't mean

that there aren't still relationship options for further collaborations. Defining expectations and clarifying roles and responsibilities will help you determine how to interact with your CRO and describe what is expected of each company, which will undoubtedly improve the relationship.

Determine What Relationship to Use

There are three major types of service agreements which will have an impact on what kind of working relationship you have, short or long-term. The three kinds of service agreements are:

- Transactional
- Functional Service Provider
- Strategic Partnership

A transactional relationship is a short-term relationship that has drug companies outsourcing one or several projects at once. Upon completion of the project(s) the CRO and drug company will have the option to go through another service agreement or not, at which point the drug company could change CROs. CROs work within their own infrastructure and provide the hands-on part of the process while the drug companies provide the ideas and concepts.

A functional service provider relationship can be either short or long-term. This relationship has drug companies outsourcing functions, such as monitoring, to CROs, which means that sponsors may be working with several vendors who fill specific roles and functions to accomplish one overarching goal.

A strategic partnership with one or more CROs is the relationship model that most drug companies are moving toward today. This relationship has drug companies outsourcing projects for an agreed-upon duration of time. Drug companies and CROs will also tend to work within the same infrastructure and have the responsibilities of both the ideas and the hands-on aspects. As the name implies, this allows the companies to be more strategy-focused on things such as cost and resources. It also means that the two companies will be constantly working closely with each other to achieve a goal.

In the past most CRO/pharma relationships were based on the transactional model which helped cut costs and reduce risk. These relationships were short-term, and the relationships, as such, were mainly financially-based. Short-term transactional types of relationships with CROs can be the most difficult due to the obvious lack of shared goals and cost-driven motives (leading ultimately to a lack of trust). This shows why the strategic partnership model may be the way of the future. Major pharmaceutical and biotech companies need to learn how to deal with a contract research organization on a very close and long-term basis.

After defining these three relationships you can see that each requires a different plan and specific methods to create the best working relationship in order to reduce future problems. This is where developing a working strategy will help you define your roles and responsibilities, improve communication, and eliminate confusion. Going through the process of creating a strategy will speed up the entire process and help everyone focus on the work rather than the issues.

Develop a Working Strategy

To develop a strategy that helps you best identify and interact with a CRO and accomplish the goals you set, you must first define what you want the CRO to do. Part of this challenge is determining high-level needs versus wants, understanding key challenges of the program, and defining the specific activities required of the vendor. Different types of vendors offer different services so you need to understand the vendors and their service offerings.

Table 1 – Differences between Vendors

Big, Broad, and Basic	Small, Slim, and Specialized
Experienced	**Flexible solutions**
Focus on large customers	**Less overall capacity**
Broader array of services	**Focused on customer**
Well-defined processes	**Boutique offerings**
Client must fit in processes Large,	**Potential for more outsourcing Typically**
global presence	**not global**

There are numerous challenges that a sponsor company and a CRO face when collaborating. Ways of vetting these challenges include:

- Understand the differences in corporate cultures and operating structures (sponsor/CRO).
- Create a clearly defined "Transfer of Obligations" document outlining responsibilities of each vendor.
- Write an RFP to best communicate your needs.
- Perform a Comparative Bid Analysis, especially when bids are extremely different.
- Ensure review contracts and "Transfer of Obligations" to identify work, deliverables, and services you don't need.
- Craft your final contract to protect your investment (e.g., payment terms, responsibility for issues, method of dispute resolution).
- Maintain control and clarify expectations by kicking off the project on the right foot.
- In order to identify and close performance gaps, define when and how to address issues in the quality of services performed both internally and externally.
- Ensure all people involved are completely informed and unified in a set plan and goal (this means communication at all levels).

While many of these concepts are seemingly simple, managing these requirements on a global level, across different time zones and myriad regulatory cultures can present dynamic challenges, which could manifest as major turbulence in a sponsor/CRO relationship. Many of these issues are especially pertinent in today's globally connected business culture. It is a good idea to consider these and other possible challenges going into a relationship with a CRO. It can help to have a list if, during the project, any of these challenges need to be specifically addressed or if they are becoming a problem and need to be looked at again. This ability could play a big role in overcoming any common relationship or communication problems.

In order to create a cohesive collaboration and team environment, the following solutions and practices can be implemented to prevent or limit issues between sponsor companies and CROs:

- Understand that the sponsor has the ultimate responsibility for all clinical research activities.
- Selection and training of qualified individuals managing delegated activities.
- Constant communication and involvement on all levels and to all levels with a clear communication structure (who communicates with whom).
- Set specific and regular times to communicate live (not via email, e.g. telephone-based or visually via digital means).
- Create and document defined roles and responsibilities for everyone.
- Specific goal(s) and expectation(s) for the pharma company and the CRO.
- Be goal or project oriented.
- Trust and care. These go both ways but trusting the other company can do their job well and showing that you care about what they are doing and in their company will foster better partnerships. This is especially important in a long-term situation.
- Commitment to excellence. Always striving to improve and be better means that neither part of the equation becomes sedentary or moves forward without the other. If you require this same attitude of your CRO, you will create a collaborative, encouraging and productive partnership.
- Both parties should succeed. If the focus is constantly about who is doing better, than a strong team atmosphere will never thrive. If both parties aren't winning then neither is.

Considering the direction that pharma is taking in becoming more integrated with CROs for management of daily operations, creating a simple outline of key strategies as you begin to plan your development program will be instrumental in building and maintaining a good working relationship.
Ideas for creating a symbiotic relationship include:

Creating an RFP with the right detail and flexibility.	The more detail you provide the vendor, the better able they will be to provide you with what you want and need. **Include:** • Context/background, study design for your project. • Identify specific reports/data for regulatory filings and required format. • Identify when certain processes are required GLP/GCP/GMP. • Identify third party or outside vendors (IVRS/WRS, eCRF, ECG)

Request clarity on specific competencies that may be qualitative.	• Experience in therapeutic area or formulation type. • Staffing and project management, request detail on how project will be staffed at all levels and insist on identification of processes that will be outsourced, and to whom. • Request detailed description of project management services including frequency and type of contact and a detailed rationale for deviation from requested services.
Transfer of Responsibility	• The document should clearly define the roles and responsibilities that you wish the CRO to manage and perform. • Define the role of the sponsor and other vendors.
Create a Joint Steering Committee or Operation Committee	• Define risk sharing
Create a well-defined communication plan	• Vendors are humans, too (really!) and they need continual contact from their client
Identify metrics to judge the level of service	• Select several review point meetings with vendor over the course of the program. • Consider weighting metrics at the beginning and end of the studies.
Managing oversight and due diligence.	• Define quality processes. • Corrective Action planning: while you can only correct for mistakes once they happen, review and corrective action can prevent reoccurrence.

Foster Team Environment and Collaboration

Some of the simplest aspects for managing a sponsor/CRO relationship include a kickoff meeting, weekly "milestone updates", and routine monitoring checks, both formal and informal.   The collaborative team environment stems from the culture you create. An oversight strategy can give both companies direction and create the possibility for them to feel as though they are working together toward the same goal but actually *having* a collaborative culture takes everyone - every individual, top to bottom. Having this culture means having the right people for each job at every level. Too many times, sponsor companies complain that they are getting the CRO's "B-team" – instead of giving the sponsor the right people for the job, CROs simply utilize whoever they have available, regardless of experience. Culture is also based mainly in the behavior of people rather than a specific strategy, so attitude and mindset make the most difference when you are interacting. Developing a sense of equality starting from the very top can also be extremely useful in generating this culture. Whether working in the same building or being spread out across the world, drug companies and CROs can create this environment when using the right tools and sharing the proper

mindset. Communication and goal orientation are the most useful tools you can use to produce this kind of relationship. Bringing everyone together to share in a common goal as well as being open, even across the individual company divisions, can create a team relationship.

Traditionally, the relationships between pharma companies and CROs have been based more on sources of cheap labor rather than partnerships. For both sides to work effectively together it is crucial to show each other cooperation, trust, and unity.

What to Expect from Your CRO Relationship

Every good relationship has certain expectations that each side must meet in order for them to work well together. The same is true for any sponsor/CRO relationship. You should always have specific expectations of a CRO which should be communicated and agreed upon before you enter into a relationship with them. Doing this will save you from many of the common problems that occur when companies need to collaborate. It is also a good idea to go over these expectations occasionally to make sure they are clear to your CRO and that they are being met. These are some ideas for expectations you should have for your CRO and the partnership.

- Clearly define expectations and responsibilities. As mentioned earlier these should be discussed and agreed upon by both parties. *Make sure your CRO is really following through on what they agreed to, and don't be afraid to hold them accountable.*
- Make sure a CRO can deliver what it has promised. Have your CRO create a plan or outline for you on what they would like to do or accomplish. If it seems unrealistic, you should question it and have them prove that they are capable of delivering what they promised.
- Include everyone in the very first collaborative meeting and expect them to be there (in some way) and participate. This includes all vendors (laboratories, eTMF, ECG, EDC/eCRF, IVRS/WRS) to ensure that everyone is informed and on the same page. It also helps each vendor know what others are doing and its specific role in the project.
- Make sure that the CRO you choose is really "in the same boat as you." Creating a true partnership with a CRO means that both companies feel they are as one. They should not only be integrated but able to contribute to the overall needs and wellbeing of the partnership. A good sponsor/CRO relationship is made from what each can contribute to the whole. If your CRO is not contributing, you should let them know what changes they could make to improve instead of just pointing out their failures.
- Know when to make a fuss. Give vendors the benefit of the doubt, but contact them immediately if you think something is not working right. Vendors are required to follow processes and they would rather hear about problems while they can still fix them.
- Pay attention to the signs. Typical vendor management problems include: ineffective project management, falling behind on timelines, and ineffective communication. Personnel changes in the midst of the project may occur; you must be cognizant of good personnel being transferred to bigger projects and understand this is not strictly a vendor's decision.

Conclusion

The number of sponsor companies looking to CROs to provide much of the workload as both the "thinkers" and "doers" is increasing rapidly. Sponsors and CROs are also re-evaluating their traditional relationships

and more commonly opting for long-term strategic partnerships. This means a foundation for the partnership must be well formed for the relationship to work. Strategies should be implemented early on and agreed upon so the sponsor and the CRO feel united. Continuous communication, a collaborative culture, and focus on a joint goal can help pharma companies and CROs either improve or maintain a partnership that can ultimately be beneficial for both. Clear expectations should be made and roles defined so that no confusion can delay a project's progression or inhibit relationship growth. Checking-in often helps to make sure the plan is still straightforward and understood. It can also show that both companies are working together for the same goal.

With many pharma companies sending projects to CROs overseas, communication can be difficult and corporate cultures widely varied. When considerations are made on both ends, the improvements to an international relationship are immediate, but the effort must be made. Given the money being spent, pharma companies should have high expectations for the CROs they work with and hold them accountable. The CROs must also be plainly invested in the relationship between the companies and not act as just another vendor.

If you have a well thought out partnership strategy and work to create a collaborative culture, your relationship with your CRO can be better – and more profitable – than ever.

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