Vendor Oversight Management as a Professional Skill and Function

Successful CRO Oversight: Mission Impossible?

With the biopharmaceutical industry outsourcing more than ever, Contract Research Organization (CRO) oversight has become increasingly important for the industry in recent years. As the ultimate accountability stays with the sponsor in outsourcing situations, companies are obligated to establish and execute effective CRO oversight strategies. At the same time, study oversight has come under scrutiny by regulatory agencies. Overall, there is a lot of frustration and disappointment at all ends. Sponsors are unhappy about what they receive from their vendors, CROs complain about the constant pressure, unrealistic expectations and change requests they receive from their clients, and regulatory agencies are concerned about the deficiencies in CRO oversight or the lack thereof. This article addresses the questions of why this is such a dilemma, what are the real issues, and what can be done to mitigate them?

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Outsourcing Modalities and the Regulatory Perspective

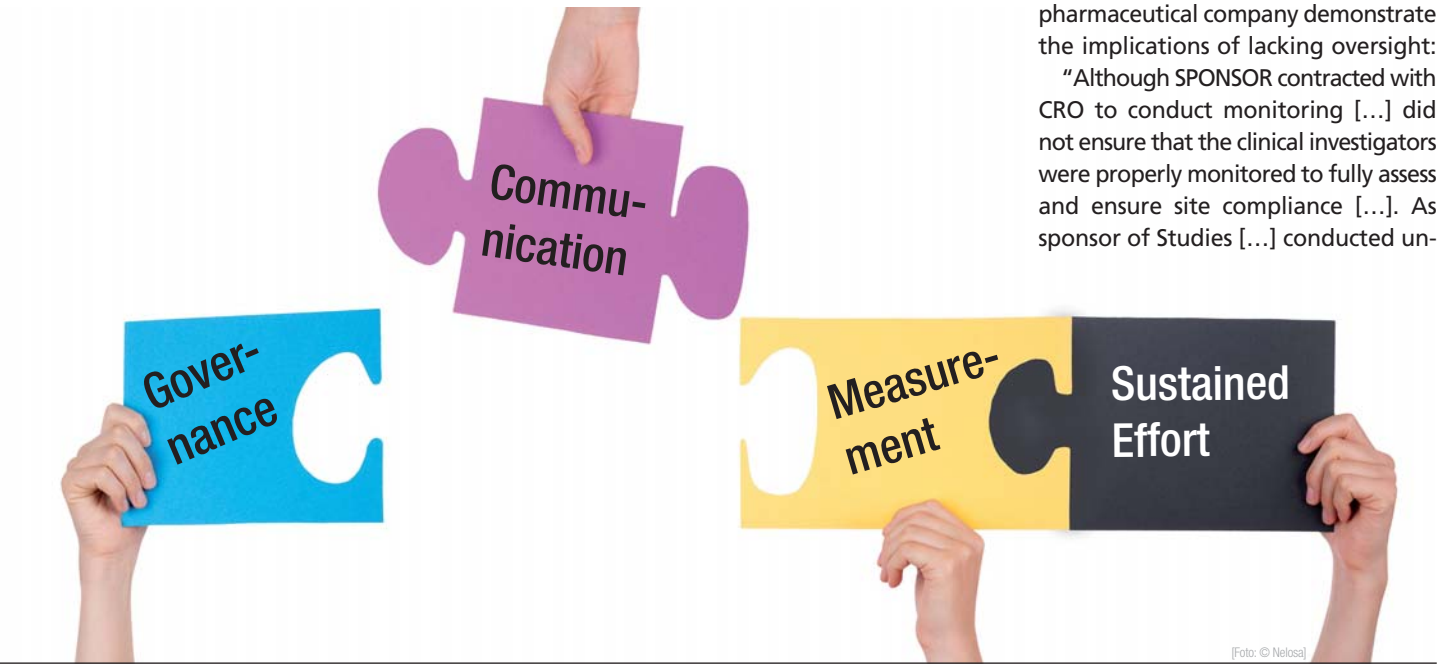
There is a broad range of different outsourcing strategies. It starts with the occasional need for "a little help this quarter" and ends with so-called "Partnerships". And in between one can find "full" outsourcing, program outsourcing, project outsourcing, skill outsourcing, functional outsourcing and low priority outsourcing. There are quite a few mixed forms of these modalities and often sponsors apply more than one at a time. The issues discussed below are not substantially different between these modalities. However, the extent to which they are visible may vary depending on the specific way a certain model is being applied.

US American Food and Drug Administration (FDA), European Medicines Agency (EMA), and other regulatory agencies mandate sufficient sponsor oversight of clinical trials. They have also been very clear with their expectations in an outsourced environment:

"Although sponsors can transfer responsibilities for monitoring to a CRO(s), they retain responsibility for oversight of the work completed by the CRO(s) that assume this responsibility" [1].

However, it seems this is not always working this way. The example below from an FDA Warning Letter sent to a pharmaceutical company demonstrate the implications of lacking oversight:

"Although SPONSOR contracted with CRO to conduct monitoring […] did not ensure that the clinical investigators were properly monitored to fully assess and ensure site compliance […]. As sponsor of Studies […] conducted un-



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der Investigational New Drug Application […], you were responsible for ensuring that these studies were adequately monitored for compliance with regulatory requirements […]" [2].

EMA does not publish their inspection reports but the quote below is from a presentation provided by an EMA official about inspection findings:

"No clear communication lines between investigator, CROs and sponsor, lack of communication; audits insufficient, no documentation which tasks are delegated from the sponsor to the CRO (the only documentation is an e-mail: '...trial is out-sourced to …')" [3].

These examples show that inappropriate CRO oversight is not only an inconvenience for the people involved but it also bears a considerable regulatory risk.

Issue Patterns

In our work with sponsor clients over many years we see issue patterns, which will be shown in this section. Instead of CRO oversight the term "Vendor Oversight Management" will be used here. Vendor oversight includes not only traditional CROs but providers of technology, e.g., Interactive X Response Systems (IXRS), Electronic Data Capture (EDC), electronic Clinical Outcome Assessment (eCOA), electronic Trial Master File (eTMF), and similar vendors where the issues are not any different, as well as other third-party service providers such as central labs, biomarker assay processors, imaging reviewers and so on.

A typical outsourcing situation involves a strong or even rapidly increasing pipeline. At the same time there is insufficient internal staff size, or the staff's experience level might not be sufficient. This combination, along with disappointing vendor performance, leads to a difficult discussion. Many times there is a debate about professional vs. service contributions of a certain function, while internal resources are constrained and underprepared.

One Size for All?

Frequently outsourcing decisions are made at a high management level. This may affect the outsourcing modality, scope and vendor selection. From a management perspective there are good reasons to keep this straight, consistent and simplistic. However, if this translates into a "one size fits all" approach across clinical development functions, for some of the functions this might become rather difficult. For example, to ensure sufficient site access from a clinical operations perspective, "global presence" may be an important CRO attribute for studies with investigational sites on all continents. For functions like biostatistics or medical writing, "global" may mean that their vendor counterparts are located many time zones away from where they are, which simply makes their work somewhat harder, with no strategic, economic or operational advantage.

It is not only in companies with a rather new outsourcing approach where you can find internal staff not skilled, not trained, or underprepared to manage vendors correctly. Staff may be qualified and experienced in certain roles and jobs for many years, and they may have performed great in those jobs. But now they are expected to supervise someone else's work – the work, which they used to do. Now their primary job becomes project management and people management – skills quite different from their previous job.

There is a high degree of uncertainty on how to check vendor deliverables

Figure 1: The Operational Mismatch

in general. This affects those individuals mentioned above who are inexperienced or not sufficiently trained in handling third party vendors, but is not limited to them. Without corresponding guidance, individual practice may be quite different. One extreme is the complete "hands off" approach, which basically lets the vendor do the work and mostly trusts in their proper execution. On the opposite side we have been in sponsor situations where every deliverable has been checked in detail – for instance, every single analysis table was re-programmed. Of course neither of these two approaches is demonstrating reasonable vendor oversight or efficient vendor management.

Internal Dysfunction

Some outsourcing collaborations suffer from inefficient processes and complicated communication paths. However, there are many cases where the root cause for this does not lie in the interaction itself or on the CRO side. Instead it might be that the sponsor's internal study team collaboration is suboptimal. We have observed conflicts about who is doing what in an outsourcing environment. Who manages a data manager when data management is done outside? Who is endorsed to interact with the external medical writer or the Interactive Voice Response System (IVRS) provider? In other words: the definition and execution of sponsor internal roles in an outsourcing environment can be the issue.

As already described above, it is pretty common for sponsors to handle multiple outsourcing approaches in parallel. This may appear to increase flexibility, but for the people who are doing the day-to-day interaction with vendors this increases complexity. The share of responsibilities between sponsor and vendor may be different depending on the model, and even within the same model but with different vendors.

Vendor oversight management is further complicated and obstructed by the contract. Nowadays the legal or procurement department mostly determines the content of contracts. On the one hand people working in these groups usually are not experts in the work they are contracting out. On the other hand, even if the experts' input is requested, it is hard for the operational staff to have the time or understanding to review a contract properly. So neither the professional researcher nor the professional contractor should be left alone to the task.

In consequence this increases the risk of suboptimal contract issues, which does not get noticed until execution. This may include some administrative overkill, such as a high degree of documentation needs on the sponsor side. We also noticed contracts, which have been very specific about "bonus" but very unspecific about "penalties". If the experts have not been asked for their advice on payments triggers (or did not looked at them), you can frequently find payments per the wrong items (e.g. query resolution, per check, per table, …) and high costs for rather repetitive tasks (e.g. programming of tables, listings, and figures – TLF programming). Overall it seems that there is a pretty high tolerance for failed milestones anyway, as eventually the sponsors just "want to get things done". Many of our clients who have experience with contracts containing bonuses and penalties report that they do not find them very effective either, but even counterproductive, depending on how they are actually implemented.

The Operational Mismatch

The most fundamental and overarching issue is the operational mismatch between service providers and their customers. Figure 1 illustrates the differences in operating models between pharmaceutical companies and CROs – which do not quite fit together. There is (big) pharma on one side – a complex organization with its multi-million dollar projects and with the target to bring their medical innovations as quickly as possible to the market. And on the other side there are the CROs, which are more organized like a "Unit of Work" factory, for which quarterly cash flow goals are most important.

This is no argument about the size as we already have some CROs being bigger than some pharma companies. It is more about the incompatibilities of company cultures. Changes of priorities, project success and project failures are common when working for a sponsor. Biopharmas have worked hard over the last 15 years to tear down intra-company silos and to attract and develop broadly qualified people. Vendors tend to lag behind in this regard. In practice this leads to significant expectation mismatches. Where the sponsor expects flexibility and a solution-focused approach, CROs often have a more formalistic, "one step after the other" approach, and silo thinking is much more pronounced than on the sponsor side.

This description of issues may be overly simplistic and exaggerated. It is not complete either. And of course you will not find all of this at one place or in one specific sponsor/vendor situation. However, none of the above is theoretical, these are all concrete examples of client situations. And it is important to understand what can and what does happen before looking into potential improvements of the vendor oversight situations.

Leverage Categories

Conceptually there are four categories to be considered when vendor oversight is under review:
– Governance
– Communication
– Measurement
– Sustained Effort.

All of these play their role and are equally important. The sustained effort needed has a prominent position though, as it makes this change management effort so challenging. Without sustained effort the change will not "stick". There is no quick solution and no immediate healing.

Governance

It may sound contradictory to readers who live and work under "Partnership" agreements with their vendor counterparts, but our experience is that to assert control over vendor counterparts is essential in developing a successful vendor oversight strategy. There is a sponsor at one end of the equation who takes the risk and the costs for the clinical trial endeavor. At the other end there is the service provider who does certain things for the sponsor and gets paid for it. This sponsor/service provider relationship should be named what it is. Any attempts to blur these lines are misleading and have not helped to improve clinical trial execution. The sponsor needs to lead this collaboration from the basis of authority no matter what label the sponsor/service provider collaboration has. Ronald Waife, a colleague of the author, wrote an extended column about this topic a couple of years ago [4].

The basis of a successful sponsor/vendor relationship is an ongoing, thorough and strong vendor performance review on the study level. This is where the experts from both parties talk to each other, discuss issues and track study progress. Further up, committees are usually used to govern sponsor/vendor collaboration. Typically there are too many of them. Two committees are usually enough. One higher-level committee should be focusing on long-term review, planning, and business strategies. Another committee, which discusses status and escalated issues from the operational level, can complement the governance structure.

Meetings are the No. 1 time consumer in today's business. This is true across industries, including the pharmaceutical industry. Particular attention needs to be paid to the frequency of meetings. With good intentions, regular meetings are used as the governance means of many sponsor/vendor relationships – the quarterly steering committee, monthly project and weekly study team meetings. However, we found it much more efficient to adapt meeting frequency to project needs rather than to the calendar. Sometimes there is no need to meet on a monthly basis if there is not anything to talk about. On the other hand a weekly study team meeting may not be often enough during a critical phase of a study.

Governance structure, meeting philosophy, and any other aspect of the collaboration should be described in detail in one internal document, which could be called the "Vendor Oversight Plan". This fundamental repository serves as the basis of proper vendor oversight. It is the reference for everyone, the basis for training, and the foundation for healthy sponsor/vendor relationship.

Communication

A primary factor of success in vendor oversight and collaboration is effective communication. Table 1 summarizes some recommendations for the sponsor side.

It is essential people on both sides understand and use each kind of communication mode appropriately. The

Table 1: Suggestions for Effective Sponsor/Vendor Communication	
Insist on a single point of contact at the operational level.	A single point of contact for each functional group is an important enabler of proper expert-to-expert communication. This helps to ensure that interactions between sponsor and vendor are consistent, transparent and establish accountability on both sides of the relationship.
Have frequent face-to-face contacts with service provider personnel.	This solidifies the personal relationship by reinforcing the fact that on both sides there are real people with a common goal, and that counterparts are not just another voice on the phone or teleconference, or just an e-mail correspondent. The project budget should factor in these face-to-face meetings. E-mail should be used as a last resort or when it is important to have a record for documentation purposes.
Avoid passive-aggressive behavior and request vendors to do the same.	An example of this is copying everyone on e-mail when a simple direct one-to-one communication is sufficient (which is nearly always). This is especially important when the e-mails discuss something contentious in nature. Passive-aggressive behavior only serves to drive a wedge in the relationship, as each party feels threatened by the other and is less apt to trust and work well together.
Select vendor with counterparts co-located whenever possible.	Distance drives a wedge into relationships just by the fact that it takes more work and effort to get in touch with someone who is multiple time zones or thousands of kilometers away, notwithstanding the other inherent difficulties of managing from afar.
Request that status reports, for the most part, have the form of exception reports.	Exception reports should show only outliers on both ends of the spectrum to be addressed. This will help make the oversight more efficient and focus specifically on the items that need to be recognized.
Self determine the content of meetings with your service providers.	The vendor is more than welcome to bring up topics to be discussed and suggestions for agenda items are also appreciated. However, in general the sponsor sets the agenda.
Lead and facilitate meetings with your service providers.	Leading and facilitating reaffirms the governance and ensures that the required topics are addressed and that the meetings are productive and efficient.
Provide frequent, open and honest feedback to your service providers.	Feedback focuses on facts and not on subjective information.
Feedback provided should be positive and negative.	In particular recognizing achievements as well as exceptional performance. You should assume that most people at both sides come to work wanting to do a good job; positive feedback boosts morale and the recognition goes a long way in promoting a healthy working relationship.
Encourage proactive engagement on both side of the vendor and sponsor relationship.	If something important needs to be discussed, the topic should be brought up immediately and nobody should wait until the next scheduled meeting to do it.
Motivate your internal team members to be role models for your service provider counterparts.	Transparent, fair expectations not only allow for effective relationship building but also provide solid objective data on performance measurements that can be discussed frankly and professionally.
Establish proper internal communication about vendor performance.	Have issues solved at the lowest level possible and set the expectation that internal leaders are on top of things and are knowledgeable of all current issues. This allows management to escalate and focus on the most critical issues.

importance of effective communication for the collaboration cannot be overstressed.

Measurement

The definition and application of some vital and objective metrics is key to assess vendor performance based on facts. It does not help to have many Key Performance Indicators (KPIs) or metrics, as the volume is not important. In the worst case too many metrics may even mean that nobody is paying attention to any of them. So the art is to identify those few items which are important and which may make a difference to the organization. If these few numbers are monitored regularly, issues can be identified right after they occurred. The review of vendor output on an ongoing basis is also important since process compliance and quality of deliverables are interrelated and require permanent attention and not at the study end only.

In some situations it is difficult to operationalize the review of deliverables, which are less quantitative (e.g., statistical analysis plan, clinical study report). Therefore certain criteria need to be defined which allow a systematic and consistent assessment.

To take the example of the clinical study report, the following categories might be used:

– Content
– Accuracy
– Compliance
(with formats and standards)
– Completeness
– Timing.

Of course content and accuracy are most important, but having the document in the wrong version or the vendor template incomplete or much too late – this impacts the overall sponsor satisfaction with the report. There are different approaches to further operationalize these or similar categories, starting with simply counting errors or using a certain score (including weights) for each category. Most important, however, it is to de-

velop a consolidated and consistent approach for the assessment.

Sustained Effort

What makes change management projects in vendor oversight so challenging for sponsors is the fact that substantial efforts are needed after the initial definition and implementation. Essentially, implementation almost never stops, as the new way of vendor management needs to be applied repeatedly for each project and every study.

All of the efforts necessary for governance, communication and measurement have to be sustained throughout the life of the trial or program.

This requires appropriate training and mentoring and the soft skills factor must not be under-estimated. Consistent and repeated messages, and actual support from management, need to go along with this, in particular when it comes to issues or disagreements with the vendor.

First Steps

Depending on the status and preparedness of an organization, it can take a while and some effort to develop and implement a new vendor oversight strategy. So where to start? What to do first?

The obvious answer is to start with some homework, i.e. identify areas for internal process optimization. If for instance your study start-up processes are inefficient or not working well, this may become a roadblock for better vendor management. If a company's electronic Case Report Form (eCRF) design is not up-to-date this may lead to site dissatisfaction, many queries and a lot of work (= costs!) for the monitoring vendor. This is also an example where the CRO could well be "ahead" of the sponsor. A review of standards to be developed and to be used by vendors will help to streamline the corresponding interactions. The definition of those "vital few" objective metrics/KPI's, corresponding information sources, reporting methods, and their application serve as the foundation of objective assessment of vendor deliverables. Collect all fundamental aspects of the collaboration and develop the vendor oversight plan. This plan will be the guidance for everyone to apply proper risk-based vendor oversight.

It is also important to align with key stakeholders on functional needs at an early stage. Although very much desirable, not all departments may follow the same vendor oversight strategy and approaches. Therefore the relationship and responsibilities of in-house managers need to be clear. As part of interdepartmental alignment it should also be clarified who is in charge of overall vendor control and who does functional oversight. This begs the question as to whether staff is qualified for the oversight, and may lead to soft-skill training requirements.

The Way Forward

The guiding principle for a healthy sponsor/vendor relationship is that the sponsor (big or small, experienced or naïve) should govern the relationship with service providers. Although some vendors are still suggesting to strive for the "we are one team spirit" [5], in fact managing sponsor/provider communication and control from a position of accepted authority is key to establish appropriate vendor oversight. Collaboration should never mean abdication: the authority needs to be natural and fact-based. Some further points to be considered:

- A team cannot be the responsible party – only a single individual is responsible.
- Meet only when there is a good reason to do so.
- Nobody is perfect, including you.
- Learn and communicate reasonable expectations.
- Model good behavior to your providers.
- Manage through facts and your eyes.

In our experience clinical development organizations are typically not prepared and not staffed to set up a successful vendor oversight management strategy. Instead sponsors jump to another vendor or another outsourcing model. There is never time or money to set up something sustainable from scratch. In consequence the learning effect of bad experiences is negligible.

This may sound pessimistic but it need not be; there is no "one-size-fits-all" solution for vendor oversight management any more than there is only one approach to managing vendors. Although issues might be similar, sponsors are different. They are as different as their key business drivers are different. And those key business drivers should drive the solution. Things like an increasing or downsizing pipeline, in-licensing or integration efforts, cost-containment, community labor commitments, absorbing entirely new therapeutic areas, or any other high-level company targets may lead to very different solutions for a given set of sponsors. What is common to all sponsor situations however, is to approach vendor oversight management as a professional skill and function requiring professional development and a robust function-driven strategy. Not an impossible mission, but a challenging and unavoidable one. |

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