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HOW TO CHOOSE THE RIGHT OUTSOURCING PROVIDERS FOR YOUR ONCOLOGY CLINICAL TRIALS

OUTSOURCING STRATEGY

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SELECTING THE RIGHT OUT SOURCING PROVIDERS

FOR YOUR ONCOLOGY CLINICAL TRIALS

With the growing trend towards global drug development strategies, today's sponsors face a growing number of uncertainties. A well thought-out risk management strategy is vital to securing a competitive drug development position since the stakes have never been higher and because there are so many factors that can potentially spin out of control. Choosing the right service provider and proactively managing the relationship is one way to tip the odds in your favour.

Biotechnology companies are realizing they do not have the in-house expertise to lead their drug development ventures and that they must partner with the right service partner for their particular needs. There are an increasing number of service providers emerging as the development of drugs and devices become ever more specialized. We are seeing an emerging trend towards niche service providers who act more as strategic allies than transactional one-stop-shop suppliers. This article will highlight some of the key issues to keep in mind when deploying a well thought out outsourcing strategy.

CURRENT ECONOMIC CONDITIONS

Current economic conditions dictate that R&D investment will be monitored even more closely by upper management to ensure that money is spent wisely and that internal resources are being fully utilized. This means that if the decision to outsource is warranted then "best in class" partners should be selected to maximize the ROI.

We have noticed a hiring freeze, and in some cases, a reduction in R&D staff among the larger biopharmaceutical companies, which has led to experienced people being deployed in three main areas:

1) Consultants, who offer a "niche" expertise;
2) Contract research organizations (CRO) to perform services on behalf of drug sponsors;
3) Small biotechnology companies that require a particular expertise.

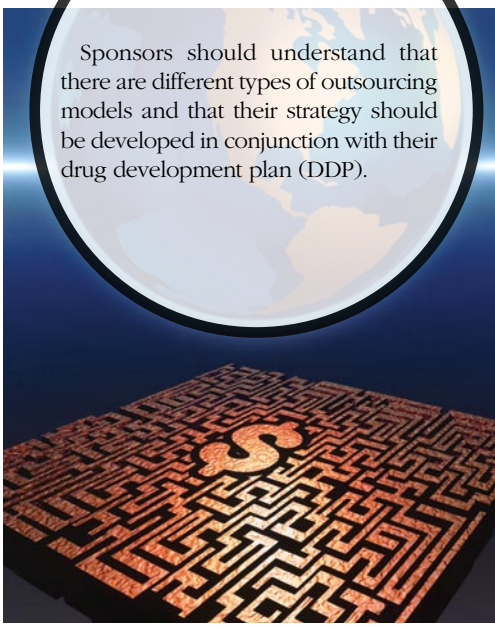
In the first two areas, we see qualified individuals who can apply their knowledge on behalf of clients, while in the third scenario these people are looking to outsource to compensate for a lack of internal resources and/or expertise.

Outsourcing is on the rise and the result has been a plethora of service providers entering the market, which has made the task of choosing the right one exceedingly difficult.

To select the ideal outsourcing service provider, a company's management team must first identify their drug development objectives to ensure the right fit.

OUTSOURCE WHAT TO WHO

Sponsors should understand that there are different types of outsourcing models and that their strategy should be developed in conjunction with their drug development plan (DDP).



The DDP will not only identify protocols but will also evaluate market potential from a financial, epidemiological, and regulatory point of view. Embarking on a colorectal cancer study in Japan or a multiple sclerosis study in India, for example, may not be a wise decision, due to a low incidence of disease in those countries.

Similarly, the return on investment may be more advantageous in countries where a medical need has been identified and governments are willing to pay for the proposed drug or device.

Study design may dictate that a placebo is acceptable in one country but inappropriate in another. Although the purpose of this article is not to discuss the merits of one country versus another, the point is that your outsourcing partner must be well connected in that part of the world

Your outsourcing strategy should also take into consideration your internal resources, which may fluctuate over time. Most sponsors outsource because they currently do not have the in-house resources or expertise for a particular function.

Here are a few of the various outsourcing models that exist to help you evaluate which providers would be best suited to your needs:

1 Agency approach:

A specific skill-set is required in-house for a particular task and that person works at the sponsor's facility on a full-time basis. The sponsor is responsible for overseeing that individual's workload.

2 FTE model, (Full time equivalent):

This model is similar to the agency approach, however the service provider's employee works out of his or her home office and work instructions are provided by the sponsor via e-mail or phone.

3 Full outsourcing:

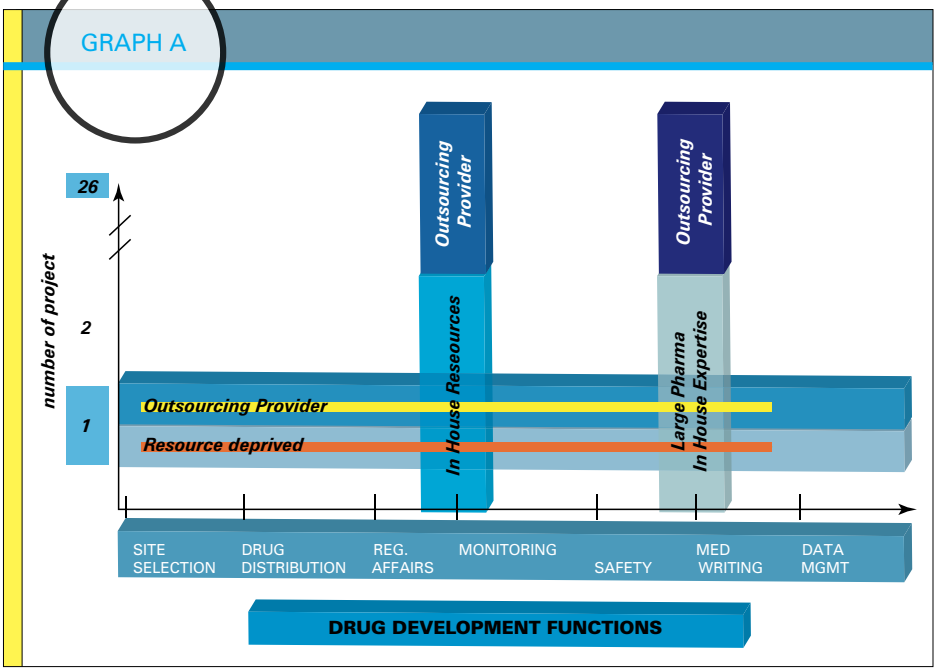
The employee reports to the service provider's Operations Manager (or clinical leader) and the delegation and scope of work occurs between the sponsor's executive team and the service provider's Manager (or clinical project leader).

The culture or organizational fit of your outsourcing provider is also very important. Size, processes, communication and decision making procedures are all key components that make for a good fit.

Smaller organizations tend to have people with a lot of decision making authority. They may wear many hats, but due to their broad range of responsibilities they typically manage fewer projects at a time.

Larger organizations usually have very detailed processes and procedures, leading to a certain degree of specialization. As the volume of work expands there is a tendency to develop an expertise in a very narrow function. We see this trend in large CROs and in large pharma companies. Communication and decision making go hand in hand as you ideally want a partner who shares the same vision and interest in ensuring that the project moves forward as quickly as possible. (See Graph A)

GRAPH A



It is, therefore, extremely important that both you and your outsourcing provider understand these seemingly subtle differences that can have a big impact on the outcome of the trial.

A larger service provider will be geared more towards functional outsourcing, which is in response to a particular need of a specific type of client. For example, a monitoring manager may require one or more clinical research associate(s) for a six month period to cover a specific geographic area during a data crunch. Or a medical writer may be asked to produce a clinical study report as part of a regulatory submission. It is very important that the right service provider is selected for this task to ensure that the expertise required for that particular function is available.

Once you know what you need, how do you find the right CRO? What should you expect from them and how can you measure it?

Once you have identified your needs, you can search the internet, speak to colleagues, consult industry directories, pick a few and proceed with a Request for Information (RFI) to identify strengths and weaknesses of your prospective partners. The more time you spend identifying what it is you really need, (by gathering different points of view from people within your organization) the more likely you are to make the right choice. There is also the intangible chemistry between team members that should be taken into consideration. After all, the process is similar to dating, whereby you get to know your partner before deciding there is a good fit and signing a long-term wedding contract.

IS FUNCTIONAL OUTSOURCING A COMMODITY MARKET?

If a sponsor is simply looking to have data monitored should a science background with SOP training be sufficient? The following graph (See Graph B) illustrates the importance of specialization when selecting a service provider (be it a company or an individual) to review your data to maximize the ROI.

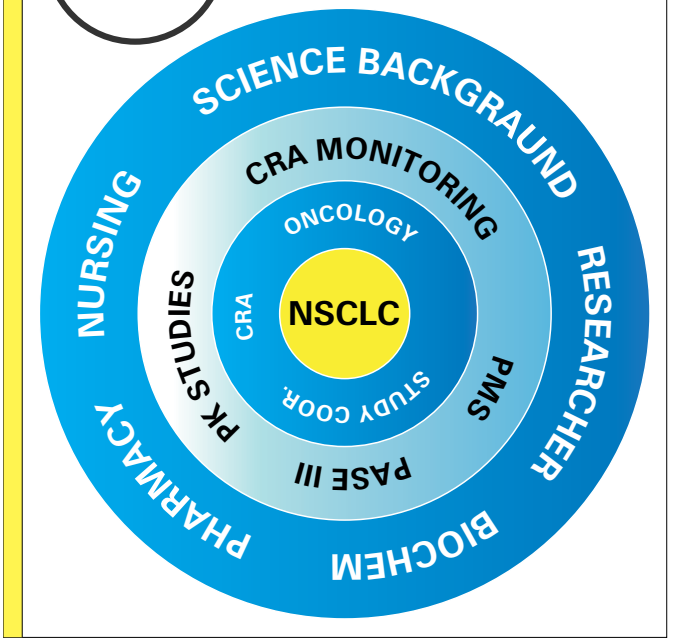
There is certain uneasiness when it comes to having an outside company or individual review key safety data. What if the SAE is not reported? What if the benefits of the investigational agent are not properly documented or reported to the authorities? Does one run the risk of having false positive results? The decision as whether or not to pursue the development of a drug is driven mainly by the safety and/or efficacy of the agent being tested. Does it not then make sense to hire an expert to monitor your data?

This is where "niche" or "therapeutic specific" CROs are bringing considerable value to the table. Expertise in a given therapeutic area or functional area has two advantages:

1) Quality: proper training and experience to pick up anomalies or recognize poor work and the knowledge to provide suggestions on how to fix it;

2) Efficacy: a knowledgeable and experienced individual will likely perform the task faster, thereby reducing costs.

GRAPH B



The need to have the right people reviewing key data has become even more important in recent years as is evidenced by the increase in the number of drug recalls, boxed warnings and health authority warning letters. The cost of this review can be mitigated by identifying key data points across all patients and by hiring experts who can review more data in less time and with fewer errors. If an individual takes 20% more time to review the same amount of data, (i.e. reviews one patient data in 9.6 hours as opposed to an experienced CRA who takes eight hours to review the same patient data) it is important to note that a 20% increase in the hourly rate may be well worth it.

It is no secret that reviewing data is a costly process. It has been estimated that it can cost up to $10,000 per data point in a case report form. This includes study coordinator costs, CRA review costs, data management, DSMB (data safety monitoring board) and Endpoint Committee Reviews. This is why being proactive and looking at CRF design, site selection and monitoring plans can help reduce costs without sacrificing quality.

Significant amounts of time and money are spent to collect, review and monitor the accuracy of clinical data. It is, however, much more cost effective in the long run to select quality data producing sites than to continuously clean data after the fact. A feasibility study is often the best way to determine whether the study will be successful in a given country or site.

The following issues are uncovered:

1) Patient availability with that pathology;
2) Competing studies for the same population;
3) Study start-up times including resource allocation at the site and ethics committee approvals;
4) Scientific interest in the investigational product and feedback on the study design.

1) Transactional

The mandate is well defined. It is usually for a set period of time, occurs once and allows both parties to understand how they function and communicate with one another. This step is key to building trust and moving on to the next step.

2) Preferred Provider

The sponsor will tend to stick with a given provider based on a positive past experience. This usually means there was perceived value in the relationship and a certain level of trust has been earned over the course of previous mandates.

3) Trusted Advisor

The sponsor perceives their service provider as an expert in their field and is confident that they understand the context of their business and their organizational idiosyncrasies. They begin to turn to them for advice. They also begin to offer their partner advice on how they can increase their value to them.

4) Strategic Ally

This step is typically contractual in nature it allows both parties to share company information, resource allocation, pipeline progress and even developmental strategies. At this point the outsourcing provider has become an integral part of how the sponsor delivers value to their customers. The relationship is collaborative which enables the partners to address current strategic priorities, as well as anticipate future challenges and opportunities.

Not only is this information itself useful, but the conditions under which it was collected is also important. Data collected on Boxing Day via fax is not likely to be as pertinent as a face-to-face or teleconference with a key investigator. Investigators are bombarded with study requests and you run the risk of either getting no response or a hasty response without much thought behind it. There is also valuable insight to be gathered by investigators who take the time to turn your project down, as it may reveal aspects of your study that were not picked up on by other researchers. It is, therefore, very important to work with an outsourcing provider who has these privileged relationships with potential investigators.

Niche CRO's in oncology, for example, are typically well aware of ongoing clinical studies and have privileged relationships with a principal investigator that will give you an honest opinion of your study and who will add credibility to your results.

Patient recruitment is the number one concern facing drug developers and we are often asked whether recruitment figures actually reflect this reality. It has been said that if you want to eradicate a disease all you have to do is run a clinical study and patients will disappear.

The more information that is provided to the investigator during the feasibility study, the more accurate the estimated number of enrolled patients will be. It has been our experience that for a sample of 10 sites or more, if you remove highest in predictions and take an average of expected patient recruitment you should obtain a fairly accurate forecast.

Feasibility studies do have a shelf life though. Studies come and go, staff at the sites change, and competing trials are always a moving target. We usually estimate that the information collected is accurate for up to six months.

To summarize, niche CROs provide valuable information because they are able to discuss the merits of a study with key investigators and their presence in a given country gives them good insight into standard of care and treatment patterns in that particular country.

Key Performance Indicators (KPI) also known as metrics are tracked by sponsors and CROs alike. Is it fair to evaluate a CRO based on metrics that are set by the sponsor? The answer is yes, but only to a certain extent. If the CRO is being evaluated based on the time

between protocol sent at site and first patient in (FPI) but the sponsor has not given the CRO all the tools or responsibility to perform the job, then the CRO's performance should not be criticized. A case in point would be a situation in which contract negotiation with the site was handled by the sponsor. Since the study cannot start until the contract has been signed the KPI would only be as good as the weakest link in the process – in this case the contract negotiation.

The definition of certain metrics is also relative. FPI in a country is different than FPI at a given site. Drug import or a central IRB approval can be an obstacle to a country's FPI, on a smaller scale the start of a study or FPI at a given site can be affected by a different set of parameters.

Different individuals track different metrics. For example, the Clinical Project Leader is looking at patient enrollment, site start up delays and CRF flow, but the procurement/accounts payable department is looking at costs on a monthly basis, and time remaining to LPI etc. The service provider must adapt to respond to the demands of different stakeholders within the sponsor's organization. Strong relationships are developed when the CRO cares about the success of the sponsor. This caring is best demonstrated by the attitudes of the individuals who perform the work and is tangibly measured by the actions taken. These actions are discussed at a kick off meeting to understand the sponsor's key performance indicators (KPIs) and to ensure that the CRO respects timelines and tracks recruitment results. Experience and a proactive approach to handling issues that arise during a project is also extremely valuable to the sponsor. If the service provider cares about the success of the client, issues that arise can be dealt with promptly and honestly.

Niche CROs have more at stake, since their expertise in a given therapeutic area requires them to build solid relationships with physicians who share the same specialty. If they are negligent with some sites, they cannot fall back on other therapeutic areas to assure their livelihood and long term existence.

Sponsors are familiar with the activities and tasks they require to be performed by CROs.

Pharmaceutical companies often monitor studies, write protocols and manage data internally and often suffer from "sticker shock" when they decide to outsource because they typically do not notice all the costs associated with having an employee handle the tasks. Issues like employee benefits, travel cost, competitive marketplace for resources and hidden cost such as IT, training and overhead all are included in a CRO's hourly rate.

The cost of hiring a CRO is only a portion of the overall cost of running a project.

The following is a breakdown of some key project costs, which are not all necessarily outsourced.

1) Medical writing includes protocol + Final Study report
2) Regulatory filing + reports to the health authorities
3) Investigational entity manufacturing cost + labeling + distribution cost (could be placebo)
4) Control over
5) Project management
6) Monitoring clinical + medical
7) Clinical grants including EC review + pharmacy
8) Imaging, ECG's, randomization systems
9) Data management + statistic
10) Clinical grants to investigator
11) Clinical trial management systems

The cost of time to perform a particular activity such as monitoring or site start up is usually based on tangible assumptions, however project management or site support activities are more variable and as a result, more difficult to accurately predict.

Inefficiencies and poor planning is where costs can easily climb both in time and money. As the old saying goes, if you fail to plan you're planning to fail. It's better to take an extra day to plan as it will save you both time and money at the end of the study. Expertise and experience will allow you to properly plan and proactively solve issues.

As the treatment of diseases such as cancer becomes more and more personalized, it becomes progressively difficult to review safety data post approval. Sponsors run the risk of delaying the release of a medication and health authorities are torn between ensuring the safety of patients and delaying the potential benefits that new medications could provide the public.

The early phases of drug development (I to III) may not have collected sufficient data to rule out safety concerns, so it will be important to continue to track safety issues post approval. The right expertise will be required to ensure that products are not withdrawn prematurely due to erroneous information.

As the complexity of drug development continues to rise, there will be even more outsourcing to properly track events over the long term.

Companies have to move beyond paradigms. They have to collaborate and form strategic partnerships with CROs if they are to realize their true value. This means taking the time upfront to negotiate a greater number of contracts and proactively manage a greater number of relationships. These variables can be controlled and should be an initiative that is undertaken regularly by drug developers who wish to establish or maintain a competitive drug development position.

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