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Supporting critical Phase I-III clinical studies by outsourcing supporting elements such as bioanalysis.

Dr Vikki Renwick, Pharmaceutical Services Sales Manager for Tepnel Research Products and Services, looks at the trends within the pharmaceutical industry for outsourcing, the challenges facing the industry when looking to outsource difficult services such as bioanalysis, and the critical factors for identifying the ideal outsourcing partner and for building an accretive and rewarding relationship.

The Pharmaceutical industry has experienced a number of difficulties during recent years. Only last year product registration was at a 24 year low ^[1], with only 18 new products launched in 2007, the lowest number since 1983^[2]. Greater competition from generics, with over 60% of prescription drugs being supplied from the generic market and increased gaps in the drug pipeline resulting in acquisitions or strategic alliances has led to an uncertainty in the bio/pharma market place. There has also been a change in the market place, with a shift from primary care to specialty drugs, the introduction of personalized medicine driving the need for biomarker/diagnostic technology and the introduction of biopharmaceutical product.

With the pressures of time to market, the associated costs of discovery, the attrition rate from generics, patent expiry and development in pharmaceutical products, pharmaceutical companies are increasing their investment in off-shoring and outsourcing. Whether this is strategic or tactical outsourcing with contract research organizations (CROs), the CROs need to be pro-active in responding to their sponsor's requirements for cost effective services. For example, by offering a breadth of services, an innovative approach and a commitment to the sponsor in terms of understanding and sharing risk.

As industry is constantly striving to achieve a reduction in development times, maintain quality, reduce development costs and boost productivity, there has been an increase in outsourcing spend. Since 2001, the pharmaceutical industry has increased its financial commitment to contract clinical services by 16% annually to a staggering \$6.6 billion ^[3], which is greater than the annual rate of growth in overall development spend (11%).

Key reasons for outsourcing analysis are:

- Strategic outsourcing allows pharmaceutical organizations to focus on its partners' core strengths and long term goals. This route allows the sponsor to maximize the internal resource and capacities of the vendor adding value to the product development process. This allows for a flexible service model.
- Tactical outsourcing relates to short term projects, which cannot be handled internally due to the lack of internal capacity or resource allowing for streamlining processes, fast turn around times and access to additional equipment etc.

The pharma head count has remained static and current challenges have altered the dynamics of the market with focus on R&D performance and strategy. With the influx of SME biotech enterprises, pharmaceutical organizations have become reliant on the CROs for a full service infrastructure, experience and greater efficiencies they can provide, supporting late stage PI to PIV. The problem of choosing the right outsourcing partner has been exacerbated by the growth in the number of Contract Service Organizations (CSO's) onto the market over the last few years. Often these organizations appear to offer similar services and returns for the customer thus making the partnering decision difficult.

With strategic outsourcing becoming the preferred outsourcing approach, more and more companies are looking to develop partnerships with CROs, however this requires initial assessment. Important factors should include, the right corporate culture, an effective cost structure, sufficient and relevant technology including software infrastructure and flexible human resources.

All of the above, coupled with effective communication lead to what I believe is the basis of a good CRO/pharma partnership of which supporting elements such as bioanalytical analysis are increasingly being outsourced adding value in additional scientific and operational capacities.

Bioanalytical outsourcing adds a further level of complexity in managing a CRO but allows for added value such as rapid but regulatory compliant method validation. The remainder of the article establishes the critical factors for identifying a bioanalytical partner. Let me start by outlining some of the important factors, which should be considered in aiding the decision for partnering with a CRO are:

- Quality and regulatory compliance.
- Scale and Flexibility, in capacity but also in understanding potential delays and variations in projects.
- Commitment to the project and associated risk, a clear understanding and shared vision allows for the basis of growing an excellent partnership.
- Costing vs. confidence in a bioanalytical partner. Technical expertise, a breadth of experience in method development, validation and clinical sample support is paramount.
- Communication, this is two way, and allows for clear up to date project status and managing expectations.
- Key performance indicators, all projects vary in complexity, but performance and track record measuring processes, people and the end result are key to understanding future project expectations.
- Contracts – clear goals and objectives established from the start of projects.
- Financial stability, ensuring your CRO partner is a reliable long term resource during lengthy studies.

1. Quality

Quality of work is of paramount importance to bioanalytical studies and is a measure of the systems in place within a CRO to facilitate timely delivery of high quality data and reports. Important elements when considering a CRO are what quality systems are in place and the principal elements should include:

- Whether the vendor's quality systems are adequate such as SOPs and accreditation to GLP
- A pro-active inspection of the quality process, review of procedures and peer review steps and adopting any changes in the regulatory environment
- The length of maintained accreditation and the level of sponsor audits and any feedback positive/negative to allow an informed decision.
- Complete training records and an adequate training program therefore having a technically astute resource for projects.

2. Commitment to the project and associated risk, a clear understanding allows for the basis of growing an excellent partnership

With the time and financial commitment in planning and outsourcing clinical and supporting bioanalytical analysis, commitment between the sponsor and CRO enables an effective partnership. Each project is individual and can vary in size but by implementing the following ideas; this can lead to an effective partnership.

- A shared vision – planning and forecasting future workloads

- A single point of contact within the CRO and continued project updates ensuring all parties are aware of changes in the projects and timelines
- On-going assessment of quality
- Having a shared understanding of the risk and sharing the successful outcome of a project.
- Having a master services agreement in place and detailed contracts allowing the CRO to understand the exact requirements from the project outset.

3. Communication

A structured and disciplined approach to communication can help deliver desired business benefits which should include:

- Frequent face to face meetings
- Effective kick off meetings stating clear expectations, milestones and delivery targets.
- Clearly define roles and responsibilities of the sponsor and CRO.
- Tools, templates and formal process for documenting sponsors expectations prior to the start of any project.
- A recognized format for feedback through the course of a project, such as a project manager or status reports.
- Review a project using KPIs/ratings to allow timely sharing of knowledge and information to re-enforce the relationship/partnership.

4. Balancing Cost and Confidence in a bioanalytical partner

When faced with the prospect of outsourcing you must be convinced of the viability and robustness of your decision to hand over control of a project to a third party. As the project manager, you must also be confident about getting value for money, quality and delivery.

Cost is often a key factor but is very rarely the most important. You will be reluctant to spend even a small amount of money if you are not confident in the CSO's ability to deliver on time and to the right quality. Poor performance in achieving agreed targets can be very costly to both your company and yourself and absorbs valuable time.

Indicators to good service provision are:

- Appropriate Quality standards
- CROs understanding of sponsors expectations
- The CSO analysts are enthusiastic and helpful thus indicating problems will be dealt with promptly and effectively.
- Knowledge and competence of the staff, with continuous training.
- Involvement of the staff in improving their knowledge and competence through networking and membership of scientific groups.
- Presence of a robust training plan which includes both scientific and commercial development.

5. Managing the Outsourcing Process through Contracts (Protocols)

Setting up contracts can sometimes be seen as a contentious issue and as the project manager you may be unwilling to commit to a contractual agreement. There are advantages and disadvantages to contracts that need to be addressed.

There is a need to define the types of "contract" required:

1. A Confidentiality Agreement is needed to ensure protection from fraudulent use of your intellectual property. Most pharmaceutical companies have a standard template which can be quickly issued to a CSO on request

2. A Technical Agreement detailing the nature of the testing and also the way in which both parties conduct business. Included in this are the official names and addresses of each company and details of quality standards for example. There should also be a template for this available within most organisations.
3. A Financial Agreement needs to be drawn up to define the payment schedules.
Often the above can be seen as an obstructive series of hurdles delaying getting the work started and just additional work for the project manager. This does not have to be the case and a good CSO should take the initiative and make this process as smooth as possible by providing in-house templates and promptly signing and returning documents.

Like any business decision there are many contributing factors in the process of choosing your laboratory partner. However, we believe the above should be key steps in the selection.

Collectively, they indicate the competence of an organisation and more importantly, their willingness to move that little bit further to make your project a success. There will be regular dialogue between the CSO and yourself before, during and after the project so it is extremely important that you feel comfortable with the company and staff involved.

The key areas discussed in this article can be investigated in a relatively short time frame and can go a long way to giving you the confidence to commit company resources to an audit and ultimately the partnership.

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[1] Pharma outlook 2008, drug discovery and development 1st Jan 08)

[2] IMS health industry forecast

[3] Contract Pharma 2007 outsourcing survey.