CLINICAL RESEARCH OUTSOURCING

Outsourcing of business activities is the new mantra in business. Companies, today outsource a part or whole of the work to another company (often in another country) since there is money to be saved in this. There is a difference between off-shoring and outsourcing. In off-shoring, the functions are performed in a foreign country by a foreign subsidiary (transfer of work to its own branch overseas); in outsourcing, the work is transferred to another organization.

When one talks about outsourcing, Business Process Outsourcing first comes to our mind. The BPO industry in India has become so well known, that people think this is the first example of outsourcing. In fact outsourcing has been a way of life for time immemorial.

Outsourcing is the fundamental principle of civilization, and man has been outsourcing many of his activities to others with special expertise. In the past, the royalty employed wet nurses to feed their babies, however the logic of this outsourcing does not fit into modern business methods. In today's world, outsourcing has a more logical basis and is done to save, time or money or simply because of lack of manpower or expertise.

Sending children to school to learn, or sending fabric to a tailor to stitch clothes are examples of outsourcing. Thousands of years ago, people realized that they were not capable of teaching their own children and the era of the schools arrived. People with special skills in teaching set up institutes where in they took the children of others for training. This was probably the earliest example of outsourcing.

We have, over years learned to outsource, almost all our daily requirements and become interdependent on other members of the society. Each person with a different expertise helps another with the task in return of some consideration. Thus, different professions came into being, which are all necessary in the modern society.

Outsourcing is done for a number of reasons, firstly because of lack of expertise. We go to a tailor or a cobbler simply because most of us do not have the expertise to stitch clothes or make shoes. If each person had to learn each of these special tasks, our education would never be complete, and we would die before completing it.

Secondly, we outsource some activities that require low level of skills to lesser paid individuals. When one employs a driver, housemaid or a gardener, one is offloading these activities to another person so that the time we save can be more fruitfully used. This outsourcing is mutually beneficial, since a person with limited skills gets a job and hence a steady income, while we can devote our time to higher paid activities, or earn more.

Lack of human resources is a common reason to outsource. If an individual were to plan to build a house, he would probably find it difficult to round up the masons and stone workers to help him. Outsourcing the whole job to a contractor, makes it simpler, because the contractor has on his rolls the required people with the required expertise.

A large number of pharmaceutical companies, involved in new drug development had limited exposure to clinical research, and hence research outsourcing began. A number of organizations came up, whose main business was to conduct research on contract. These companies were never involved in new drug development or marketing of drug products, and these came to be known as Contract Research Organizations (of which Quintiles is the largest).

Pharmaceutical companies found it easier to outsource their research projects, rather than set up their own research units. Setting up research units would entail employing more staff and the companies would have had a problem with the staff once the projects were completed. Research staff was also inexperienced in routine manufacturing or other activities; hence job rotation was not feasible.

CROs and Pharmaceutical companies formed symbiotic and synergistic alliances which allowed both of them to prosper. Since both were separate business entities, they formed short term alliances during the trial and went their separate ways when the trial was over. Legal agreements like Confidentially Disclosure Agreements and Clinical Trial Agreements ensured that the CROs did not take any advantage of the knowledge the sponsors shared with them.

Some sponsors make long term arrangements with CROs, while others make agreements which are limited to the project in hand. Long term relations have some advantages but sponsors who had only one or two research molecules in their pipeline could not opt for that arrangement. They made short term, trial specific agreements which terminated when the trial did.

The advantages of long term alliances were many. Sponsors came to know and understand the CRO well, and so did the CRO. Each party was able to identify the strengths and weaknesses and help the other to improve. Such alliances also meant that they could rely on each other in times of need. If a sponsor needed some work done on priority, the CRO would oblige. They could exchange information and at times even staff. Short term agreements did not carry any of these advantages with them.

Sponsors also had strategic or tactical alliances (most long term alliances were strategic). The CRO was carefully chosen before an alliance was made, and sponsors could evaluate all the CROs in the market before zooming on one. The choices were deliberate and not forced on either party.

A variety of sponsors outsource clinical research to CROs. Leading among these are biotech companies, which are generally small and led by technocrats. With limited resources these companies are forced to outsource trial work. Other companies who outsource work are :

- Pharmaceuticals
- Medical device companies
- Diagnostic instrument companies
- Research institutes
- Virtual companies

There is no limitation of what can be outsourced, it all depends upon the sponsor and the CRO undertaking the work. Generally, the jobs that are outsourced are :

1. **Pre-clinical**
    a. Lead identification
    b. Lead optimization
    c. Toxicity
    d. Pharmacological studies
2. **Clinical**
    a. Monitoring
    b. Site management
    c. Recruitment services
    d. Auditing
3. **Documentation**
    a. Protocol writing
    b. CRF design
    c. ICF preparation

d. CSR writing

4. Project / Program Management

a. Study management

b. Full product development plan management

5. Data management and Statistics

a. Data entry

b. Data cleaning

c. Data analysis

6. Safety Services

a. Pharmacovigilance

b. Laboratory testing services

c. Special central evaluations such as ECG, MRI, CT

d. Drug level testing in biological fluids

7. Regulatory Services

Creating dossier for regulatory submissions such as IND, NDA, ANDA, etc.

8. Documentation Services

a. Research report writing

b. Study publications writing

c. Narratives for Adverse events

9. Information Technology related Services

a. IVRS

b. Electronic data capture services

10. Manufacturing Packing Services

a. Active ingredient manufacturing for testing and trials

b. Clinical trial packaging and QA services

11. Consultancy Services

a. Regulatory consulting

b. Clinical expertise

c. Medical expertise

12. Storage Services

a. Study drug storage

b. Study sample long term storage

c. Study documentation storage and archival

There is no dearth of CROs in the Indian market and one can find CROs of all sizes, from single individual run companies to large organizations employing thousands of employees. There are full services CROs, as well as those working in niche areas. For best results the choice of the CRO needs to be judicious and the following criteria may be considered.

1. Therapeutic Area of Expertise

Medicine is a vast field, and not all CROs can claim expertise in all fields. Some CROs specialize in niche markets such as dermatology, while others are ready to venture anywhere. A specialized CRO makes all the difference when speed and quality is required.

2. Costs

Outsourcing saves money, but outsourcing also costs money. CRO charges vary considerably and one needs to choose a CRO as per ones budget. This may be done by following either a bidding or a non-bidding process, as follows.

(a) Bidding – request from proposal from several vendors.

(b) Limited bidding – request for specific or pre-selected or short listed vendors to bid.

(c) Reverse bidding – open bidding from short listed vendors for the lowest quote.

(d) Direct allocation – without bid.

3. Timelines

Timelines of delivery vary from organization to organization. Small CROs are often nimble while larger CROs may require more time.

4. Quality

Quality of work is an important consideration, in fact with cost and timelines it forms the triad on which clinical research stands. The quality of a CROs work is a very crucial parameter for choice.

5. Geographic Coverage (countries)

Many CROs are regional, and some are national. Very few Indian CROs work on a worldwide basis. Hence, the choice of the CRO also depends on the geographic area where the sponsor wants to conduct the trials.

The method for choosing and tying up with a CRO is important for getting optimal benefits from the association. There are many models for working but the following points are worth considering :

1. Decide the way to go about the collaboration.
2. Shortlist the entities that suit your requirement.
3. Evaluate their credentials from the perspective of the present work.
4. Make double sure they can comply with requirement.
5. Choose the first winner and a back up the one suits the most.
6. Negotiate for a budget and requirements acceptable.
7. Define the specifications.
8. Requirements such as number of sites, patients, countries, recruitment rates.
9. Timelines – start of activity, first patient in, last patient completed, data cleaned, statistical analysis, final report etc.
10. Specifications of services required.
11. Quality issues such as monitoring frequency, % of data verification, reporting requirements.
12. Management issues such as whom to report, who is responsible for what activities.

On the sponsor's side the following decisions have to be taken :

1. Who would participate in discussions and negotiations.
2. Who will evaluate the proposals.
3. What are the parameters to be evaluated and their importance and priority.
4. Timelines for bid submissions and review and decision.
5. Any strategic area need to be taken into consideration.
6. Discuss and grade internally based on team inputs.

7. Short list the preferred vendor and back up as required.
8. Negotiate, if required and allot to the most suitable vendor.
9. Define payment schedules.

After the choice of the CRO for outsourcing, the sponsor should discuss certain financial issues the following activities are necessary for a smooth working relationship :

1. Complete the legal contract formalities for the project, if delayed, define an interim process.
2. Keep an eye on activities to confirm that the agreed processes and timelines are being followed.
3. Process any changes for contractual agreement with vendor and agree on modifications of terms, conditions and budgets.

At the end of the trial, when the contract ends, the sponsor should analyze and evaluate the collaboration :

1. Confirm the contract completion and date of completion.
2. Check if the payments are clear and there are no other obligations.
3. Was the contract completed :
    a. On time
    b. On budget
    c. With quality
4. Check if any changes need to done in the process for future projects.
5. Ask concerned staff for feedback for any process changes and comments from the projects.
6. Convey the comments to the vendor.
7. Comment on the possible improvements and changes in the process that should be implemented.

It should be remembered that in business, outsourcing is not a one time requirement, but could be a regular feature. Building a database of vendors (CROs) would help in choosing one, when it is needed. The experience that is gained from one contract can be very valuable while signing another, and no opportunity should be lost in optimizing this relationship.

Global Pharmaceutical companies based in developed countries are increasingly turning to developing countries and emerging economies around the world for conducting clinical trials. Reduced costs combined with easy availability of patients with varied diseases makes developing countries favorite destinations for clinical research outsourcing.

According to US government publications, today, 8.9% of clinical trials registered with US health authorities are conducted in emerging countries of Asia − 7.4% in Latin America, 7.1% in Central and Eastern Europe and 1.6% in Africa. India has become a hub for clinical trials outsourcing and this has advantages both for CROs as well as professionals aspiring to join them.

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