

# In-house Contract Research and Manufacturing

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Many pharmaceutical companies, big and small, have been outsourcing work to contract research organizations (CRO's) and contract manufacturing organizations (CMO's). There are several advantages in doing so.

## Advantages of Contract Manufacturing

- **Cost savings:** No capital expenditure for plant and equipment
- **Access expertise:** CRO's and CMO's are specialized in a particular field or operation and are generally up-to-date with the current technology.
- **Low labor cost:** Being a small company, the CRO's and CMO's have lower salary structure and benefits.
- **Flexibility:** Based on the current business trends, work scheduling can be reshuffled easily without affecting work on other products.
- **Diversification:** Normally companies work with several CRO's and CMO's. This diversification provides stability in operations and provides flexibility to the management staff.
- **Focus:** The parent company managers can focus on core competency and can let CRO's/CMO's do mundane operations.
- **Geographic advantage:** If the CMO is located in another country and if it is in close vicinity with the API supplier, it will provide tremendous logistical savings.

In spite of these numerous advantages, there are many disadvantages to working with CRO's and CMO's: The bottom line of every project is "getting work done" and "meeting with the timeline".

## Disadvantages of Contract Manufacturing

- **Quality control:** In the early years of the relationship, it is difficult to understand the company value system of the CRO and CMO, which will generate conflicts (despite making a quality agreement). Once a quality issue is raised, an investigation and resolution can become time-consuming, expensive and a headache.
- **Accountability:** If things are not in place and fall through the cracks, it is easy to criticize personnel within the CMO. However, this might have long-term ramifications because the project manager has to continue to work with the CMO staff to ensure operational streamlining.
- **Flexibility:** One assumes unlimited flexibility with CRO's and CMO's. It is assumed that the production schedule with the CMO can be modified, shifted, decreased or increased whereas the reality of the experience could be the total opposite.
- **Paperwork:** The CMO may be running a very lean operation and may not have staff to keep track of paperwork. This may pose difficulties when filing the product with the FDA.
- **Supply chain issues:** Being a small company, the CMO may not have well developed procurement and systems. This could put the corporation at a major disadvantage.
- **Intellectual property risks:** Even after signing an appropriate contract, one may face breaches in intellectual property safe-keepings. CMO's work with many clients and in spite of many precautions taken, the probability of critical product information being leaked is greatly increased. There is an increased probability of leaking of critical product information.

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- Acquisition and management change: After a long-term relationship and understanding, the CMO could be acquired by another company. All the previous relation-building may go down the drain. In some cases, the value system of the new management may not be on the same wavelength with the previous management. If the company has to change the CMO at this point, the company has to spend on product transfer (time and money expenditure).

If the CRO or CMO are in another country, there are several other barriers such as:

- Language – They may not be fluent in American-English.
- Time – A difference of 6 to 12 hours due to time-zone changes is very common
- Cultural variation – A difference in work hours and holidays.
- Corruption – People in the parent company may not have knowledge to deal with the corrupt officials in another country. The difference in the value system can generate major conflicts and face challenges to company policies.
- Patent issues and local politics
- Exploitation of a multinational company: It is hard to plan to minute details and the contract written could be more general. As the project develops, if the parent company does not have a physical presence in the foreign CMO, the CMO will tend to exploit and the company can lose the cost advantage.

A poorly planned agreement with the CRO or CMO in the US or in a foreign country may result in quality and supply issues. It could result in a shortage of products or even an obsolete inventory. If the product quality is at stake, a poorly planned agreement may lead to product recalls, subsequent law suites and loss of credibility in the market. Additionally, the company may need special staff (which could be very expensive) to fix the problems. With this, the advantage with the lower manufacturing cost might get wiped out. If the employees from the parent company leave, a lot of information on the project and developed relationship will be lost.

Working with CRO's and CMO's could be extremely beneficial but also can be extremely detrimental. The parent company has to have a commitment to build and manage a strong relationship with the CRO or CMO.

## Large vs. Small Companies

It is accepted that R&D units of large pharmaceutical companies are not as efficient as the units in small biotech companies. Large companies have purchased many products from small biotech companies. In some instances, the large company ended up acquiring small biotech companies just to obtain their products.

The reasons for success of small biotech companies are:

- Drive: Management and personnel in small biotech companies have a strong drive and desire to succeed.
- Structure: Large companies have too many layers of management and create unnecessary bureaucracy. It makes the operation very inefficient. Decisions are made very quickly in small companies.
- Quality standards: It is good to have high quality standards. However, due to fear of market forces, large companies tend to go way beyond the quality expectations. Consequently, they tend to spend more time, money and resources, making their operation very inefficient. Small companies run more efficient operations and conduct the bear- minimum number of experiments to develop or manufacture the products.

- Labor cost: Employees in large companies have higher base salaries and get more financial benefits. This is normally not the case in small companies. Also, in general, people in small companies tend to work longer hours thereby increasing their output.
- Work ethics: It is not true for every large company, but the atmosphere in many large companies is relaxed. On the other hand, people in small companies are put under tremendous pressure. Also, employees in large companies are compartmentalized and focus on a narrow skill set. Contrastingly, employees in small companies get to do a variety of jobs – whatever comes their way. This way, projects move faster and there is a sense of team work.

## What is In-house CRO or CMO?

In recent years, many pharmaceutical companies underwent acquisitions and mergers. Many companies have started working with CRO's and CMO's in Europe, India and China. As a result, locally (in the US), there is excess plant capacity and many facilities are standing vacant. Many a times, large companies sell off equipment at a throw-away price or sell the units. Many employees are laid off (the unemployment rate is currently over 10%).

The idea of In-house CRO or CMO is to set up an operation in such a way so as to benefit from the advantages of working with a CRO or CMO and eliminate the disadvantages. First of all, the CRO or CMO will be local and essentially, in the facility of the parent company.

### *Operational lay-out:*

The parent company will lend their facility and if possible, equipment to a CRO/CMO to set up an operation. The parent company may develop a conglomerate of various CRO's and CMO's in the same facility, each one being specialized in various functions. Each unit will run independently of the others and independent of the parent company. However, they will work towards to the same goal – develop products for the parent company and manufacture them to fulfill the requirements of supply chain. The parent company will not micro-manage day-to-day operations of individual CRO's/CMO's. However, they will coordinate overall activities of various CRO's and CMO's and resolve disputes.

### *Advantages to the CRO's and CMO's*

- Resources: Being a small entity, CRO/CMO's are low on resources. Working under the wing of a big organization will provide them sufficient financial and logistical resources.
- Focus: Small companies are under tremendous pressure every day to get new contracts. With a helpful big brother next door, the CRO/CMO can focus on their core operation (technology), making them more efficient.
- Advantage of a conglomerate: With many CRO's/CMO's in the same facility with different specialties, it will be easy to resolve technical issues through scientific exchanges. New ideas can be pursued in partnership.
- Project management: Because different CRO's/CMO's residing in the same complex can work on the same project(s), the project management function will be much easier, especially in bringing all the team members together. Face to face meetings in general are more effective and in this case, one doesn't have to worry about time differences. Also, people working in the consortium will have similar cultural backgrounds and will have less relationship building issues (in the US, people may come from various cultural backgrounds, but still it is a melting pot and people blend in easily).

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## Advantage to the Parent Company

- Utilization of facilities: All the vacant facilities and equipment will be used effectively and will get high return of investment (high ROI).
- Efficiency of product development: This is the most important advantage. It will help overall productivity, profitability and growth.
- Society: Companies are built to make profits. But they also build community and help our society. Increase in local employment will improve the economy and make it strong.
- Intellectual property: Since all the CRO's and CMO's are in the same facility and are not working for other clients or competitors, it will be much easier to protect intellectual property.
- Decentralized operation in a centralized facility: As companies grow, they reach a point when their large size actually becomes a disadvantage. GM is a recent example which eventually collapsed. Creating in-house CRO's/CMO's will make the operation decentralized, but because they are in the same facility, proper control can be exercised and the parent company can run profitably for longer time.

## What Kind of In-house CRO's and CMO's will be Beneficial?

The pharmaceutical field encompasses various functions such as discovery of drug molecules, assessment of pharmacological effectiveness, determination of toxicological and pharmacokinetic/biochemical characteristics, development of formulations and appropriate package, development of analytical methodology, determination of stability of product, clinical studies (Phase I, II and III), and commercial manufacture.

Functions dealing with drug discovery, animal experiments, formulation support and Phase I clinical trials can be conducted by the in-house CRO's and CMO's. However, large-scale clinical trials should be conducted at various sites in order to check the effectiveness in different groups of people (better sampling). Also, some OTC products are made under very large scale and may be a stand-alone operation. Overall, the In-house CRO and CMO companies are small specialized units. The parent company may choose the type of CRO or CMO to be housed in their facility based on their needs. For example, they may start with setting up analytical labs or labs to conduct toxicological, pharmacological and pharmacokinetic experiments on small animals (rats, mice, rabbits etc.).

## Conclusion

Based on the project and situation, companies can decide which functions can be brought in with the in-house CRO or CMO so as to benefit maximum. But, certainly, in-house CRO's and CMO's can provide better solutions in many instances saving time and cost for the parent company.



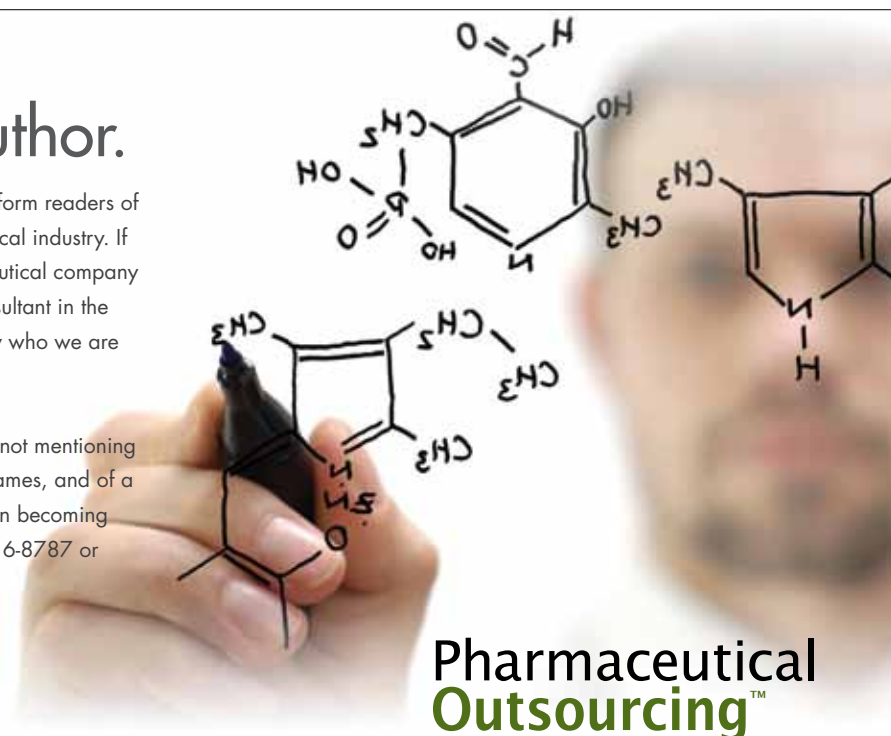
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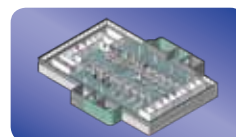
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