CHALLENGES IN CONTRACT MANUFACTURING ORGANIZATIONS IN PHARMACEUTICAL INDUSTRY

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ABSTRACT

During our survey from 2009 to 2012 we had found some different issues regarding outsourcing in Pharmaceutical companies which were beneficial and non-beneficial for large multi-national pharmaceutical companies as well as smaller ones, other side of our study we had found there were some Challenges in Contract Manufacturing Organization in Pharmaceutical Industry. The study included of about 40 pharmaceutical outsourcing companies.

KEYWORDS: Contract Manufacturing Organization, Outsourcing, Pharmaceutical Industries, Food and Drug Administration, Good Manufacturing Practice.

INTRODUCTION

A Contract Manufacturing Organization (CMO) is otherwise known as Contract Development and Manufacturing Organization (CDMO). CRO is meant for research & development and CMO is meant for manufacturing.

Services offered by CMOs are follows, Pre-formulation, formulation development, stability studies, method development, pre-clinical and Phase I clinical trial materials, late-stage clinical trial materials, formal stability, scale-up, registration batches and commercial production.

EVOLUTION OF CMO

In the pharmaceutical industry, if R & D has to outsource that can be provided through contract research organizations (CROs) and for outsourcing manufacturing than contract
Contract manufacturing means a firm manufactures the products for another hiring company or firm as it is a form of outsourcing. In this type of business the hiring firm approaches the contract manufacturer with a new design or formula to develop and create a new project with the help of contract manufacturer. The contract manufacturer will decide the quotation based on land, labor, capital, and organization, generally they investigate in market and make a research on the quotation of material and tools. Production of goods by one firm, under the label or brand of another firm. Contract manufacturers provide such service to several (even competing) firms based on their own or the customers' designs, formulas, and/or specifications. Also called “Private Label Manufacturing.”

Contract manufacturing organizations (CMOs) offer a wide array of manufacturing services to the pharmaceutical and biotechnology industries. These services can range from production of small quantities of materials for R&D purposes, larger amounts for clinical study usage and ultimately full-scale production for commercial purposes. The global contract manufacturing market primarily includes solid and liquid dosage forms and injectables. The growing use of generic drugs and complex pharmaceutical products has also induced many CMOs to offer active pharmaceutical ingredient (API) manufacturing services to their clients. In 2011, total global spending on contract manufacturing reached $31.9 billion according to a 2012 Informal report entitled "The CMO Market Outlook to 2017". The CMO industry had experienced double digit growth in the past two decades and that trend is expected to continue for the next five years. By 2017, the size of the global contract manufacturing market is expected to grow to about $63 billion. While, in recent years, there has been a steady growing demand for API manufacturing, solid dosage formulation remains the largest segment of the CMO industry by revenue. The solid dosage market is expected to expand over the next five years at an annual rate of 12.5% and as much as $55 billion will be spent by 2017 on CMO-based solid dosage manufacturing.

Challenges In Contract Manufacturing Organization

Many pharmaceutical companies, big and small, have been outsourcing work to contract research organizations (CRO’s) and contract manufacturing organizations (CMO’s).
are several advantages and disadvantages. In spite of these numerous advantages, there are many challenges to working with CRO’s and CMO’s: The bottom line of every project is “getting work done” and “meeting with the timeline”.

1. **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.

2. **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.

3. **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.

4. **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.

5. **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.

6. **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.
7. **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:

A. **Language** – They may not be fluent in American-English.

B. **Time** – A difference of 6 to 12 hours due to time-zone changes is very common.

C. **Cultural variation** – A difference in work hours and holidays.

D. **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.

E. **Patent issues and local politics**

F. **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.\(^4\)

**REVIEW OF LITERATURE**

Our study were also correlated with the other studies carried out by, Nick Taylor in his article was conveying “US firm offering modular plant leases as alternative to CMOs” published in outsourcing-pharma.com, 2011. The author was conveying in his article that US firm offering modular plant leases as alternative to CMOs. He was mentioning that Biologics Modular is leasing its mobile production facilities to help clients make FDA regulated drugs without fixed plants. Biologics Modular thinks the model will appeal to research park innovator biopharm that need access to flexible and affordable GMP (good manufacturing practice) production capacity.

The author in his article he was mentioning the quotation given by Clark Byrum, Jr, president and CEO of Biologics Modular “The current business model for drug manufacturing companies is changing, and as we see more onsite research and development, there is a growing need for affordable quality facilities”.
The author was conveying that Biologics Modular is pitching the model as an alternative to outsourcing to contract manufacturing organisations (CMOs). Instead of outsourcing manufacture of clinical trial materials biopharma can have a Biologics Modular facility temporarily installed at their site to handle production.

The facilities are manufactured by Biologics Modular at its site in Indiana before being qualified and validated. Clients also receive support with process validation, GMP quality control and regulatory strategies.

By taking this modular, pre-constructed, pre-tested approach to facility design Biologics Modular claims it can deliver a plant within 20 weeks. Validation and commissioning is said to take days.

The author was explaining about Building a facility, which are housed in steel shipping containers. Inside the containers Biologics Modular installs pre-constructed, pre-tested modules, like giant Lego pieces, to equip the production facility.

Once constructed the facility is relocated to, for example, a leased light industrial warehouse. When the plant is no longer needed it can be decommissioned and in most cases, Biologics Modular will handle the removal.[5]

Dustin Ensinger’s objective in his article “Pharmaceutical Outsourcing threats” was the U.S. pharmaceutical industry is no longer immune to the outsourcing phenomenon, which poses major risks for American consumers. The author specifies India is becoming a major destination for American pharmaceutical companies seeking to boost their bottom line. Taking their cues from other American multinational corporations, they are doing so by outsourcing their manufacturing to the Indian subcontinent according to The New York Times. The author also pointed a comment in his article raised by Panos Kalaritis, the chief operating officer of Irix Pharmaceuticals, a Florence, S.C., contract research and manufacturing company, that “Cost is one issue, and yes it is important, but there are two other critical factors: intellectual property and quality and safety issues,” in The New York Times. He has mentioned that Americans were losing jobs and Indians were gaining jobs due to outsourcing. The employment in American pharmaceutical industry came down five percent from the last year and India’s pharmaceutical industry grew 13 percent in case of hiring employees. The Food and Drug Administration issued approvals for 12,000 plants in India and China. He has
mentioned the quality issue where last year, 1,742 drugs were recalled and just 338 drugs were recalled in 1999. Even the simple over-the-counter drugs have been recalled because of safety concerns. Even some of those products were manufactured in the U.S however their components came from outside the U.S., and due to the lack of manpower at the FDA, much of it goes unchecked until a problem is discovered.[6]

“Up to 40 percent of the drugs Americans take are imported and up to 80 percent of the active pharmaceutical ingredients in those drugs come from foreign sources,” Food and Drug Administration Commissioner Margaret Hamburg, M. D., said, according to *The Buffalo News*.

Dore explained in his article “cut your outsourcing risks.” He explained toll processing relationships, with respect to chemicals, active pharmaceutical ingredients and finished drug products. In this article he explained that both large and small pharma companies turned to toll processing after commercial drug product introduction, typically when manufacturing tasks had become routine. The Toll processing relationships resources dealing with the operational, safety, contractual, legal, regulatory and other aspects of these transactions is quite limited. He explained even the U.S. Food and Drug Administration's (FDA) 2001 Guidance for Industry Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients provides only that, all contract manufacturers should comply with the Good Manufacturing Practices (GMP) defined in this guidance, companies should evaluate any contractors. to ensure GMP compliance of the specific operations occurring at the contractor sites, a written and approved contract or formal agreement between a company and its contractors should be made available defining in detail the GMP responsibilities, including the quality measures of each party, a contract should permit a company to audit its contractor's facilities for compliance with GMP, where subcontracting is allowed, a contractor should not pass to, a third party any of the work entrusted to it under the contract without the company's prior evaluation and approval of the arrangements, manufacturing and laboratory records should be kept at the site where the activity occurs and be readily available, changes in the process, equipment, test methods, specifications or other contractual requirements should not be made unless the contract giver is informed and approves the changes. He finally concluded that cut your outsourcing risks.[7]

Daya Mukherjee was insisted in his article that “Look before You Sign Your Outsourcing Contract” He explained the factors that a firm needs to look for before signing the
outsourcing contract. He explained clearly that the contract should typically cover scope of work, little flexibility in the contract, problem resolution such as monetary compensation, problem escalation, terminating the contract procedures, repatriation clause etc., terms & conditions agreed upon, the service level agreement, and non-disclosure agreement should signed by both the parties. [8]

OBJECTIVES
1) To examine the challenges in CMO in Pharmaceutical Industry.
2) To examine the reasons for not choosing CMO in Pharmaceutical Industry.

HYPOTHESIS
Whether outsourcing is non-beneficial to the pharmaceutical industries?.

METHODOLOGY
Data Collection Method
The study depends on primary and secondary source.

Primary Source Data
Primary data has been collected through the direct personal investigation in the form of the questionnaire and Indirect oral investigation in the form of personal interview.

Secondary Source Data
Secondary Data will be driven from, books, journals, company records, company web sites.

RESEARCH DESIGN
Research design means the basis of defining the research problem. The preparation of the design of the research project is popularly known as the research design. The study aims to find out challenges in Contract Manufacturing Organization in Pharmaceutical Industry.

SAMPLE DESIGN
For the purpose of the study, a sample of 40 pharmaceutical outsourcing companies taken into consideration, 25 pharmaceutical outsourcing companies taken into consideration of which 10 pharmaceutical companies were into blend of both outsourcing and in sourcing within the India and 15 pharmaceutical outsourcing companies taken from outside of the India mostly from USA.
RESULTS
40 Different companies were representing for challenges in CMO in pharmaceutical outsourcing companies. 70% of companies were showing for Loss of Intellectual Property, 60% of companies were showing for Quality Control & Time Delays, 50% of the companies were showing for Flexibility and 25% of the companies were showing for Change in Management.

TABLE 1.

<table>
<thead>
<tr>
<th>Particulars</th>
<th>Number of Companies</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Quality Control</td>
<td>24</td>
<td>60</td>
</tr>
<tr>
<td>Flexibility</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Loss of Intellectual Property</td>
<td>28</td>
<td>70</td>
</tr>
<tr>
<td>Change in Management</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Time Delays</td>
<td>24</td>
<td>60</td>
</tr>
<tr>
<td><strong>No of Companies To Be Studied</strong></td>
<td><strong>40</strong></td>
<td><strong>100</strong></td>
</tr>
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DISCUSSIONS AND CONCLUSION
We would like to conclude that though outsourcing in pharmaceutical industries plays an significant role in Cost Saving, focusing on drug discovery, Less Capital Investment, Geographic advantage and Flexibility however, there are other factors such as Quality Control, Flexibility, Loss of Intellectual Property, Change in Management and Time Delays were also very important which are to be considered by client before they outsources their non-core business activities. If an organization really wants to outsource their products/projects to CMO’s then first they should make a survey about the third party service provider whether the employees are well qualified, they have capability to complete the job and whether they respect intellectual property rights. If the third party is unknown to the client then they should check the references about the third party. If all these issues are sort out then there won’t be any of these lacunas in outsourcing and certainly CMO’s can provide better solutions to their clients in many ways.
REFERENCES