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Contract Services

Strategies for Outsourcing Pharmaceutical Development and Manufacturing

Dilip M. Parikh


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Strategies for Outsourcing Pharmaceutical Development and Manufacturing

Dilip M. Parikh



Today's cost-containment pressures and the need for a reliable supply of product are requiring companies to form long-term relationships with their suppliers. With careful planning, these partnerships will result in a virtual integrated company for the future.

Contracting or outsourcing development or manufacturing of a pharmaceutical product has been used by the pharmaceutical industry for a long time. In the early days, the driving force to seek an outside entity was to provide additional development or manufacturing capability or to have another company handle difficult products. An outside company was also contracted at the development or manufacturing stage if it had unique technology or equipment to offer.

The 1990s ushered a new era into the healthcare environment. The impact of these changes on the pharmaceutical industry is evident in the mergers and acquisitions that have

taken place in recent years. Governments and managed care organizations in most of the major pharmaceutical markets have imposed price restrictions on prescription products. In the United States, the use of managed healthcare not only has affected the way pharmaceutical companies approach the sales of products and pricing factors but also has forced many to adopt a very different long-term strategy. Companies such as Merck, Eli Lilly, and SmithKline Beecham have moved vertically to position themselves as providers of integrated health services. Although pharmaceutical sales staffs visit doctors to persuade them to prescribe their products, the primary responsibility for deciding which products are bought and ultimately used now lies more with the purchaser. In Europe, increasing regulation of pharmaceutical prices has become a characteristic feature of the healthcare system. The increase in competition from producers of generic products has been significant in many national markets. The switch of as many products as possible from prescription to over-the-counter (OTC) status had introduced further changes to the industry. The consumer-driven OTC market is growing fast and is devoid of the price pressures seen with prescription products.

These changes have forced internal restructuring in the industry. In many companies, executives have scrutinized the areas that traditionally absorbed a high proportion of pharmaceutical company budgets, and rationalization is becoming more common, particularly in research and development. Many companies recognize that they can no longer master the entire spectrum of skills and have focused on the strengths they would like to have. In the United States it is evident that a number of companies are concentrating on discovery and distribution while outsourcing development, manufacturing, and marketing. The formation of virtual companies has accelerated the need for contract research organizations (CROs) and contract development and manufacturing establishments.

In the United States, according to a privately circulated survey, the outsourced market for contract development was \$625 million, and the contract manufacturing market accounted for \$900 million in 1995. This survey encompasses all dosage forms and covers the range from clinical research,

Dilip Parikh is the general manager of Atlantic Pharmaceutical Services, Inc. (APS), 11200 Gundry Lane, Owings Mills, MD 21117, tel. (410) 413-2001, fax (410) 413-2000, e-mail (dmp@niroinc.com).

analytical development, stability testing, preformulation, clinical supplies manufacturing, and final dosage form manufacturing and packaging. The list at lower right shows the types and providers of outsourced services.

OUTSOURCING PHARMACEUTICAL DEVELOPMENT

The research function in R&D consists of the discovery process and preclinical trials; development encompasses clinical trials and filing of the NDA or ANDA. The lengthiest and most expensive stage of the development process is Phase III of the clinical trials. It is here that one can strategically outsource certain aspects of complex R&D to reduce costs. The driving force for outsourcing development activities comes from two sources: downsized R&D departments of major pharmaceutical companies and the proliferation of virtual companies without any plant or technical staff to carry out development activities. In the

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product development area, outsourcing is rapidly becoming established industry practice. Clinical trials and registration processes have become increasingly complex as regulatory requirements become more extensive. The development process incorporates the same generic milestones across the industry, largely because FDA strictly defined much of the process. Because of the range of discrete tasks and departments involved in the development process, a whole contracting industry has grown around this area. This enables companies with minimal staffing to take the product from discovery to market in less time than it would take if all functions were performed in-house. Outsourcing can thus be used as a strategic move in product life cycle planning. By maintaining in-house core competency with minimal staff, the sponsor company can outsource the work and maintain control of the project.

The contract development process starts with the preliminary evaluation of a contract development organization by the sponsor company. Some of the issues this preliminary visit should investigate are

- technical capability
- laboratory services
- staffing level and competencies
- financial strength
- indication of a resolve to fulfill the contractual obligations that both companies are about to go into.

After the initial facility visit, a formal audit can be conducted, which would be a typical CGMP/CGLP audit. If the sponsoring organization is unable to provide the staff to handle such an audit, it can hire a consulting organization to carry out the audit.

Once the outsourcing organization is selected, the sponsoring organization and contractor should be partners in the development project. A legal document that lists in detail the terms, conditions, and disclosure agreements is signed. At this stage, project managers should be appointed from each organization. The scope of the project and milestones are established and a payment schedule is discussed. Experimental designs, reporting requirements, and a schedule for the work to be done are agreed upon.

OUTSOURCING PHARMACEUTICAL MANUFACTURING

Pharmaceutical companies have outsourced production of individual product lines for many years, primarily because of lack of capacity. Recent trends in outsourcing in contract manufacturing can be identified as follows:

Existing large pharmaceutical companies have outsourced their least popular or more problematic products (such as hormonal products or antibiotics) to contractors for years, and they continue to do so.

Mergers and acquisitions have created extra manufacturing capacity in large pharmaceutical plants that is offered for contract manufacturing. The only downside to this situation is that the contract manufacturer has its own priorities for its products, and any third-party manufacturing is offered if its own product does not require the capacity.

Virtual and start-up companies without manufacturing expertise are contracting with the outsourcing organizations for the manufacturing along with contract development work.

Manufacturing outsourcing is also taking place because of the unique drug delivery systems offered by the contract developer and manufacturer. Such systems may include transdermal patches and products, sustained-release systems, and inhalers. In many cases, the company responsible for the initial clinical trial manufacture of a product and subsequent scale-up to full capacity is the same company that originally patented the technology.

The client and the contractor must truly be partners in outsourcing the manufacture of a product. For a successful partnership between two companies, there needs to be a mutual fit.

Typical outsourced services and providers

Services

- Analytical development and stability testing
- Preformulation
- Clinical trial manufacturing
- Scale-up
- Process validation
- Commercial manufacturing

Service providers

- Large pharmaceutical companies
- Universities
- Clinical research organizations
- Contract development organizations
- Contract manufacturing organizations
- One-stop shop

Table I: Technology transfer documents.

Manufacturing/Packaging	Analytical
Product description	Raw material specifications
Qualitative and quantitative composition	Raw material testing procedures
Process flow diagrams	Sampling procedures for raw materials
Manufacturing method description	In-process sampling protocols
Process summary and critical process variables	Cleaning validation
In-process controls and tests	Raw material release specifications
Cleaning procedures	Specifications for release of finished product
Specifications for packaging bulk product	Specifications for testing and release of packaging containers and closures
Packaging/labeling	
Bulk storage stability	

Both companies must be financially strong. Technology leadership in complementary areas makes a partnership in manufacturing more successful. This enables a long-term relationship in which the contract manufacturer becomes the integral part of the client’s product supply strategy. This is truly a win-win situation. The contractor must receive fair revenue for manufacturing the client’s product, and the client needs to have assurance that the product will be available as needed in the mar-

nering thus makes it mandatory for the contract manufacturer to have a long-term relationship with the client and to work to assist the improvement of the process and manufacturing. The client company cannot take the product out to the existing facility without substantial work and expense, even after the implementation of SUPAC-IR and SUPAC-MR guidelines. Thus there is enough incentive for both parties to establish a long-term relationship based on mutual trust.

The selection of the outsourcing manufacturing organization is made in a manner similar to the selection of a contract development organization. The outsourcing of a product for manufacturing is a decision the client should not take lightly. The success or failure of a product in the marketplace depends heavily on the contractor’s ability to deliver the product in a timely fashion. The effort starts at the technology transfer stage. The technology transfer activity is a very critical step for establishing a robust process. Without a process that is production-friendly, it is difficult to complete successful process validation and subsequent assured production requirements. The contract manufacturer must be an active participant and consultant at the technology transfer stage. Table I lists some of the important documents needed for the technology transfer of a product.

Contract manufacturers traditionally looked for smaller contracts to eliminate having all their eggs in one basket. But current industry strategies demand a closer working relationship.

ketplace. The objectives of the partnership need to be defined at the outset and maintained throughout the contractual period. Partnerships that disintegrate are those in which the scope of the partnership was not defined correctly. There are several reasons why relationships become unmanageable:

- false promises made by the contractor
- wrong pricing that cannot be amended
- a lack of a quality commitment from the supplier
- unrealistic expectations from the client
- poor market forecasting by the client.

Contract manufacturers traditionally looked for smaller contracts to eliminate having all their eggs in one basket. But current industry strategies demand a closer working relationship, and partnering is becoming a way of doing business. This part-

CONCLUSION

Mergers and acquisitions have created economic pressures on the pharmaceutical industry. Outsourcing has become the focal point because of the need for cost containment and assurance of product supply in the marketplace. Strategic outsourcing is becoming part of the pharmaceutical planning process, and as such the formation of a long-term client–supplier relationship is becoming a necessary way of doing business.

The multidisciplinary team that comprises purchasing, manufacturing, development, QA, and regulatory personnel makes the selection of the outsourcing organization. The close partnership between the client and supplier will result in a virtual integrated company for the future. ■