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Managing the Client-Contractor Relationship

Increased bio/pharmaceutical outsourcing demands new management skills

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Bio/pharmaceutical outsourcing is increasing in both volume and scope. Greater outsourcing requires greater oversight of projects, and this is creating managerial problems. Even before the current economic situation, bio manufacturers complained that "establishing a good working relationship" (1) was the most difficult and challenging aspect of outsourcing.

Today's increasing cost pressures are also increasing demands on individuals and departments to produce more without sacrificing quality. This is aggravating the problem, and creating an environment where managers are being asked not only to manage their own staff more effectively, but to also manage their external outsourcing partners. Unfortunately, as many researchers have found, successful scientists do not always have the skills required to also be successful managers. As outsourcing expands, so must the skill sets of the industry's managers, on both sides of the equation—client as well as contractor.

It is becoming increasingly apparent that each side needs to manage the relationship better. Today, it is still not uncommon for clients who outsource projects to attempt to pass them off to their outsourcing service providers with minimal guidance, and even less ongoing communication. Insufficient communication has been well documented as a managerial problem that leads to poor results.

At the centre of the problem are managerial functions that must exist for a successful commercial outcome. Among other factors, managers must be able to lead in a highly dynamic environment, and to create an organization where effective communication flows at all levels (2). For example, many biotech firms are started by biomedical scientists. In fact, academic entrepreneurs account for 43.1 percent of biotech founders, far greater than any other industry (3). There may be a correlation between this predominance of scientists in managerial roles, and the fact that only about five percent of biopharmaceutical organizations succeed.

SHIFT TO STRATEGIC OUTSOURCING

As companies shift to strategic outsourcing, the need for managerial expertise will increase. In our 7th Annual Report and Survey of Biopharmaceutical Manufacturing, we have identified how outsourcing is maturing and becoming an essential part of the modern company's R&D and manufacturing strategies (1). The Report also describes trends in outsourcing in this segment. At a time when companies face some tough economic challenges, understanding trends can help the speed at which the industry is adapting to new

realities in hiring, budgeting, and training. The results of the study provide a global view from executives at more than 327 biopharmaceutical and contract manufacturing organizations.

The trend toward expanding outsourcing has come of age, and will continue to expand. In fact, most companies having recognized the strategic necessity to use their internal resources more efficiently. This allows greater focus on core competencies. Biopharmaceutical manufacturing is an area where outsourcing has been proven to offer advantages beyond just cost effectiveness. Outsourcing, when done well, can improve efficiency while reducing overall costs. But even as outsourcing increases, the skills needed to manage these expanding relationships evolve more slowly.

Our study indicates that many companies are starting to use outsourcing proactively rather than on a tactical basis. Outsourced projects now cover all areas of R&D, manufacturing, testing and services. They are now beginning to be used not only to fill temporary gaps in capacity, but also to focus a company's skill base on core competencies, in addition to controlling costs.

Large pharmaceutical companies are modifying their outsourcing approach, and are working to determine which functions can realistically be outsourced. Factors extend beyond simply reducing costs and now include optimize speed, increase flexibility internal operations, and place internal employees in more challenging positions that add value to the organization. Thus, outsourcing decisions, while ultimately centered on financial return on investments, are increasingly being initiated by analysis of value of full-time-employee (FTE) activities, staff allocation, and hiring.

Manufacturers are evaluating and planning to outsource an increasing number of operations tasks to maintain productivity. This is especially true for current activities typically outsourced. In our global study, we tested 24 different areas of outsourcing today. We found, for example, that 25 percent of respondents to the study will be outsourcing significantly more "Fill/finish operations" over the next 24 months than is currently done (Figure 1). Following are "validation services" and "product characterization testing" (24, and 23 percent of respondents, respectively) indicated this is where the greatest changes will occur in their outsourcing. Other areas of substantial growth include toxicity testing and downstream production operations, (where 18 and 14 percent of facilities, respectively, will see substantial changes).

Virtually all areas of R&D and manufacturing are now being considered as options for outsourcing and the impact of this is being felt on a global basis, with emerging markets ranking

favourably alongside established markets as outsourcing destinations.

The rise of outsourcing has resulted in many companies establishing centralized contracting groups to handle the complex and time-consuming business of selecting and managing partners. This allows a greater consistency in evaluating the progress on projects and reduces start-up times. As the use of outsourcing partners becomes more embedded into the strategy of companies, effective management of the contract by pharmaceutical companies will become a more critical issue.

Contract manufacturing organizations (CMOs) are evaluating how current economic conditions will change the outsourcing landscape in the \$125 billion worldwide biopharmaceutical industry. This industry sub-sector is estimated by various sources at around \$2.5 billion, and growing. So the stakes are high, and current economic pressures are putting strains on both sides of the relationships between bio manufacturers and their CMO service suppliers.



Figure 1. Selected outsourcing activities projected to be done at "Significantly higher levels".

Source: 7th Annual Report and Survey of Biopharmaceutical Manufacturing; Other areas tested include: Downstream Process Development, Testing: Lot release, Media optimization, Cell line development, API biologics manufacturing, Contract manufacturing of biologics, Upstream Process Development, Regulatory services, Testing: Cell line stability, Environmental monitoring services, Design of Experiments (DoE), Testing: Host cell protein analysis, Plant maintenance services, Upstream Production Operations, GMP Training, Contract Research (laboratory), QbD Services.

IMPACT ON OUTSOURCING RELATIONSHIPS

Biopharmaceutical companies, both large and small, are becoming increasingly risk- and cost-averse, especially for high-risk, high-cost projects such as manufacturing. Biologics organizations are beginning to view their outsourcing more strategically and are necessarily considering their internal staff's project management skills. However, this is not easy to assess. Perhaps as a result of the growth in outsourcing, relationship problems in the Client-Contractor relationship continue to expand. For example, in this year's study we identified 11 critical issues that CMOs (Contractors) find are the most common mistakes made by their clients (bio manufacturers). Two of the critical "pain points" experienced by CMOs were "Clients don't plan their tech transfer process" and "Clients don't communicate with us effectively". Both of these require project, and relationship management, and demand superior managerial skills. In a high-stress environment these factors may be in short supply, and the success of the overall project can be put in jeopardy.

The most critical aspect was operational: "Clients want to contain cost by doing limited development runs, but still expect successful full scale manufacturing", mentioned by 78 percent of CMOs as either "Very Important" or "Important": (see Figure 2). This issue involves cost containment and time-to-project completion. It also suggests that the majority of bio manufacturers, who are under increasing cost and time

pressures, are pushing that stress onto their suppliers. The second relationship problem involves unrealistic expectations: "Clients don't build in sufficient time for the project (unrealistic timeframes)". This was mentioned by 46 percent as "Very Important"

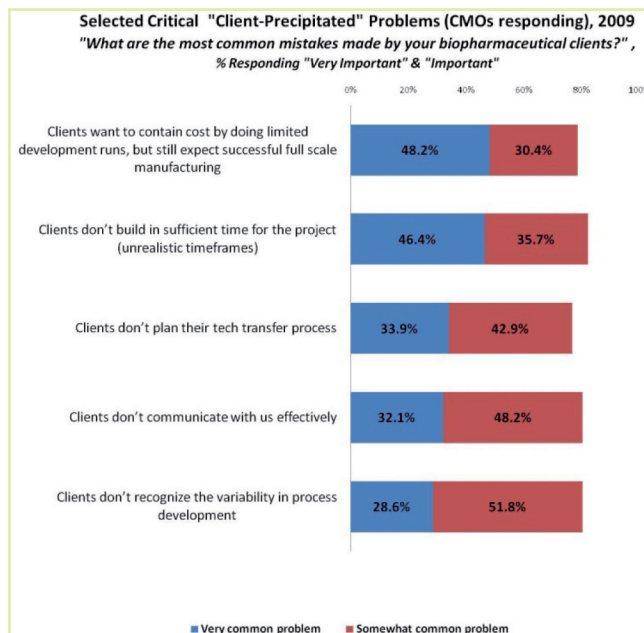


Figure 2. Selected critical problems from CMO's perspective. Source: 7th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity, April 2010, BioPlan Associates, Inc. Rockville, MD www.bioplanassociates.com.

OUTSOURCING PROBLEMS FACED BY BIOMANUFACTURERS

Bio manufacturers (clients) this year continue to be stressed over the issues that have concerned them the past 7 years that we have been measuring these factors. Now, however, relationship issues may now be spilling into operational concerns. For example, this year concerns about compliance with quality standards jumped dramatically to 64 percent from 59 percent last year (percent respondents indicating the factor as "Very Important"). The quality issues may be the result of worries about possible cost-cutting and service reductions on the part of CMO vendors. Biologics manufacturers may not yet be sufficiently confident in their outsourcing partners can guarantee quality standards.

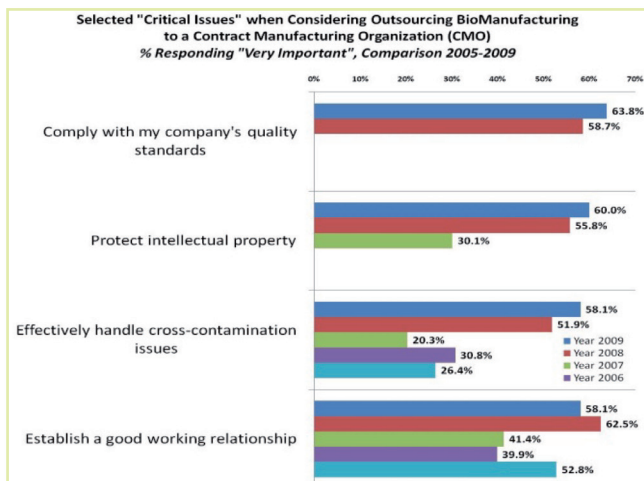


Figure 3. Selected "Critical Issues" when Outsourcing. Source: 7th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity, April 2010, BioPlan Associates, Inc. Rockville, MD www.bioplanassociates.com.

In addition, among the 25 factors we evaluated, "Protecting intellectual property" was also seen as critical by 60 percent of respondents this year. These IP concerns may be showing up due to increased interest in offshore (international) outsourcing. Worries about handling cross-contamination issues, again this year, jumped significantly, from 20 percent in 2007, to 52 percent last year, and 58 percent this year. The relationships trend between CMOs and clients have improved slightly this year; CMOs have moved the "Establishing a good working relationship" factor from 63 percent seeing it as "Very important" last year, to 58 percent this year.

ACTIVITIES BEING OUTSOURCED

Essentially all biopharmaceutical developers sooner or later use the services of CMOs, whether for manufacture of clinical or commercial supplies, or for testing, fill-finish or other outsourced activities. However, outsourcing today continues to be dominated by relatively lower value-added services, such as fill-finish and product characterization testing. The use of biopharma CMOs has become common, particularly for mammalian cell culture, but developers are continuing to keep some manufacturing in-house, i.e., relatively few are outsourcing all of their manufacturing needs. CMOs involved in manufacturing approved products for commercial sales are also increasing, as are the activities in which they are involved. Outsourcing activities today continue to consist of relatively lower value-added services, such as fill-finish and product characterization testing. Among the 24 areas of outsourcing testing in the study, we found that the primary outsourced activity today is product characterization testing, with biopharmaceutical companies outsourcing an average of 75.6 percent of this activity (See Figure 4). Toxicity testing (69.2 percent) and validation services (63.5 percent) were next on the list. At the other end of the scale, there appeared to be relatively low outsourcing activity, percentage-wise, for API biologics manufacturing and project management services. In some cases, CMOs are being asked to perform basic process design, scale-up, equipment selection, quality control testing and other key aspects, such as validation and support for regulatory approvals.



Figure 4. Selected results: percent outsourcing activities done today. Source: 7th Annual Report and Survey of Biopharmaceutical Manufacturing, www.bioplanassociates.com.

CMO INDUSTRY SHIFTS

Today, relationships between client companies and biopharma CMOs are maturing and improving. Companies are recognizing the increasing value offered by CMOs. And CMOs are understanding their clients' needs more insightfully. As a result, nearly one-half (48.2 percent) of surveyed biopharmaceutical manufacturers noted that they expect to

increase their budgets for biopharma CMO outsourcing. As more companies begin outsourcing, the need for effective project management will grow. Efficiency is an important aspect of outsourcing if it is to become a strategic foundation for biopharmaceutical companies. In times when there was less available capacity, CMOs with better technologies, expertise, and facilities, would have simply been too busy and pre-booked, to handle new clients.

Many of these shifts are the result of financial pressures. Outsourcing drivers are changing, and financial pressures are creating real concerns over hiring and staff allocation. Not only do outsourcing service providers need to justify the cost benefits, now they need to evaluate the impact of outsourcing on FTEs, staff allocations, and speed to project completion.

MORE RISK ANALYSIS ON OUTSOURCING ACTIVITIES AND RELATIONSHIPS

Although outsourcing is on the rise, the same reasons companies have always outsourced still apply, notably saving costs and time, increased flexibility, convenience, and relying on specialists with needed expertise and infrastructure in place. Bio manufacturers are evaluating their outsourcing relationships based on more rigorous risk analysis. Today, most expect to work more efficiently and establish CMO relationships that allow this. Companies are creating internal models to evaluate the thousands of different items involved in manufacturing and operations, and assessing risks of working with an external service provider. Some major companies today use a rating system to assess the risk of outsourcing. This approach can help funnel the decision making to a relatively few items that may ultimately be outsourced. As companies attempt to assess more than the monetary expenses, they are including the overall risks of working with a CMO. Using in-house rating systems, risks can be measured and weighed, quality standards can be compared, and decisions can be increasingly made on relationship management and overall probabilities of successful outcomes.

CONCLUSIONS

Clients are increasingly seeking to build relationships with their outsourcing partners, but the managerial component of that is still evolving. Until effective project management processes are in place, and the skills to manage external relationships are established on both sides of the fence, outsourcing may find the limiting factor is relationship management. Human factors in effective management are difficult to measure. And although milestones are increasingly being used to measure performance, soft factors such as relationship building and risk sharing are difficult to quantify. These are recognized as important for long-term success.

Establishing long-term relationships with CMOs may be more resource-intensive and costly in the near-term, but in the longer term this will allow companies to better manage their development plans and reduce internal expenses. As just about every company continues to cut costs, and lay off staff, they increasingly need to assure themselves of access to critical expertise no longer available in-house.

Even as pharmaceutical companies continue to define their own internal, core capabilities, they will likely establish more, deeper alliances, and expect to get more out of their provider relationships. Generally, the CMOs able to adapt to the changing economic situation are keeping busy, and demand is increasing, especially as adjustments to the new climate

take place. As larger companies continue to cut back and lay off staff, the need for greater external technical expertise and resources to support biopharmaceutical development will expand.

A few companies have gone to great extents to establish more intimate relationships with their service providers. Merck, for example, recently acquired Avecia, a major U.K. biopharma CMO, and Merck now also owns Diosynth, another major biopharma CMO, from Diosynth's earlier acquisition by Schering-Plough, which recently merged into Merck. In some cases of CMO acquisition by a bio/pharmaceutical company, the CMOs are being allowed to operate as largely independent subsidiaries. Fully integrating a CMO into a company could result in loss of many of their advantages, such as competitiveness, adaptability, expertise, speed and ingenuity. However, the benefits of closer relationships and access to CMOs core competence may outweigh these factors.

The BioPlan survey shows that industry outsourcing for biopharmaceutical manufacture is a long-term trend, with increases expected to continue as the industry adopts project management processes, and establishes the skills needed to manage external relationships. The industry and, particularly, client-contractor relationships will continue to mature and become more complex. The underlying reasons why companies want to outsource biopharmaceutical manufacture are changing as the biopharmaceutical industry

matures. With this change will come steady growth and greater value, and a more mature approach to managing the outsourcing relationship.

REFERENCES AND NOTES

1. 7th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, BioPlan Associates, Inc, Rockville, MD, 2010 Preliminary Data.
2. *How Scientist/Founders Lead Successful Biopharmaceutical Organizations: A Study of Three Companies*, Ph.D. Dissertation, 2008, Langer, L.J.
3. J. Zhang, N. Patel, *The dynamics of California's biotechnology industry* (2005).

Survey Methodology: This seventh in the series of annual evaluations by BioPlan Associates, Inc. yields a composite view and trend analysis from over 327 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations (CMOs) in 35 countries. The methodology also encompassed an additional 117 direct suppliers of materials, services and equipment to this industry. This year's survey covers such issues as: current capacity, future capacity constraints, expansions, use of disposables, trends and budgets in disposables, trends in downstream purification, quality management and control, hiring issues, employment and training. The quantitative trend analysis provides details and comparisons of production by biotherapeutic develops and CMOs. It also evaluates trends over time, and assesses differences in the world's major markets in the U.S. and Europe. 