Bio-Growth Slowing?

A new report details bio-outsourcing trends in 2012

By Eric Langer, BioPlan Associates

Outsourcing has been a major trend in recent years, and the broad industry developments continue to favor increased biopharma outsourcing. However, our *9th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production*[1] confirms a number of trends related to outsourcing. This year's survey was based on responses from 302 biopharmaceutical industry professionals from 29 countries. Overall, the study indicates
that outsourcing continues to increase, but spending is leveling off, and industry attitudes and the execution of outsourcing appear to increasingly be more sophisticated, strategic and better planned (as opposed to being areas for reflexive cost-cutting).

Trends include the continued and accelerating emphasis of large international Big Bio/Pharma companies (those collectively responsible for ≥90% of industry R&D and sales (see www.top1000bio.com[2])), on increasing involvement in development of biopharmaceuticals, and the coming of biosimilars. Already, ≥40% of the overall pharmaceutical R&D pipeline is reported to involve biologics (vs. small molecule drugs), and this expected to eventually reach 50%. Compared to drugs, biologics offer more specificity and reduced toxicities; associated with this, they have a higher success rate in clinical trials and attaining approvals, have higher sales per unit (the products cost much more), often with fewer sales involved, and higher profit margins.

Biosimilars

Biosimilars are finally coming to the U.S. market, with FDA having issued its first guidelines in early 2012[3]. This event means the bio-outsourcing industry landscape will likely change. Contract manufacturer organizations (CMOs) will be among the recipients of benefits from biosimilars (and the related category of biobetters). In coming years, as data and market exclusivities and patents expire on the majority of the first decades' worth (1980s-1990s) of recombinant proteins, we can expect multiple — perhaps, five to 10 or even more — biosimilar (and biobetter) versions of every successful established product to enter the U.S. and world markets. Many manufacturers may shift their legacy off-patent products to CMOs, while devoting in-house manufacturing capacity to newer, innovative, higher-profit products. Many dozens of new biosimilar developers will require manufacturing capacity for a growing number of products. Because most biosimilar developers are smaller companies, they often lack manufacturing infrastructure and expertise, and with biosimilar markets being relatively small (compared to the established products they target), a large proportion of biosimilar developers will find benefit in the use of CMO services. There are relatively few CMOs with actual *commercial* bio-manufacturing experience, but that will increase. Biosimilars will also result in growth in use of other outsourced services, including analytical data and bioassays, with this perhaps starting to be evident in our survey data.

Standardizing

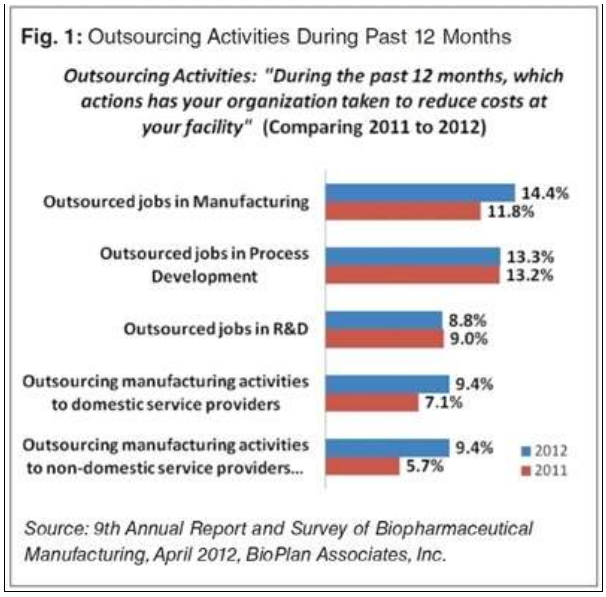
Standardization of manufacturing is another trend supporting outsourcing. Particularly within larger companies, as more biopharma manufacturing is performed to support worldwide markets, companies are working to standardize their products and manufacturing processes on a worldwide basis. This includes having second- or even third-source facilities either actively manufacturing or serving as back-ups. In some cases, it can be more cost-effective to hire and transfer a process to a CMO as an additional or backup manufacturer.

Mergers

Outsourcing trends are also being driven by corporate mergers and acquisitions, which tend to be directed to improving R&D pipelines rather than cost-savings from facility consolidations and lay-offs. Associated with this, many large companies are now directing more attention to acquiring smaller companies and in-licensing candidate products. Partnering has intensified as large pharma and biopharma companies execute strategic initiatives toward better R&D and products, with most established biologics facing patent cliffs and increased competition from biosimilars, biobetters and other off-patent follow-on products.

Slowing and Becoming More Strategic

Outsourcing, including R&D and contract manufacturing, continues to be a major trend. However, our study data indicate that the rate of outsourcing is slowing, with prior increases in funding of outsourcing tending to level off. With this phenomenon, it appears that contract manufacturing will not be the primary manufacturing approach in the future, as it would be if prior high growth in outsourcing of manufacturing were to continue without slowing.



Companies of all sizes that formerly outsourced a majority of feasible processes are now taking a more rational approach — carefully evaluating and weighing options, including looking at outsourcing from a longer-term and strategic perspective. There appears to be a slowing of what often seemed to cost-directed cuts: downsizing, lay-offs and closing and divestment of in-house corporate capabilities. Perhaps, this longer-term outlook is enabled by improved economic conditions. We note that our survey data show 70% of biopharma companies outsourcing at least some activity.

Outsourcing to emerging markets continues, including Asia and Eastern Europe, but is slowing and reaching its limits, with outsourcing of R&D outpacing that of manufacturing. Eventually, bio-manufacturing will start to be significantly outsourced to lesser-developed countries, although it will likely be many years, perhaps a decade, before a significant number of U.S./EU biologics are manufactured in developing countries. No major trend has yet developed of companies outsourcing clinical or commercial manufacturing to lesser-developed countries. At the moment, developing countries lack the needed critical mass of facilities, knowledgeable and cGMP-experienced staff, information and quality systems, institutional know-how, business culture and ethics required for full U.S./EU cGMP biopharma manufacture. We can expect increased use of developing country-based CROs and also CMOs, but primarily to support pre-commercial R&D and product testing.

Industry Outsourcing Budget Trends

This year, we see evidence of slowing in outsourcing budgets, albeit with further increases planned. This includes responses showing a current leveling-off of outsourcing budgets. For 2012, the average reported outsourcing budget change was down a miniscule (within margin of error) 0.4%, with other increases and decreases in the past few years remaining within +/- 1.5%. By this measure, recent years' budget increases for outsourcing have leveled off or stalled. When asked to identify actions taken in the past year to reduce costs, an increased percentage, 14.5% (vs. 11.8% last year), cited outsourcing of jobs in manufacturing (while process development and R&D outsourcing remained steady); 9.4% cited outsourcing of manufacturing to domestic CMOs, up from 7.1% last year; and 9.4% cited outsourcing of manufacturing to foreign CMOs, up from 5.7% last year. Overall, outsourcing of manufacturing to domestic and non-domestic service providers (offshoring) involved only a small percentage of respondents (9.4%), indicating that there is still much capability for industry to expand its outsourcing of manufacturing to CMOs.

Outsourcing budgets my not have increased this year, but companies broadly expect to increase their future outsourcing, including for manufacturing. This year among respondents manufacturing using mammalian cell culture, 47% indicated they performed all their production "in-house," meaning that 53% outsource some product manufacturing. During the past few years, the percentage of developers doing all of their mammalian cell production "in-house" has shifted down slightly from 55.6% in 2006 to 57% in 2010, to 45% last year and 47% this year.

For microbial fermentation, 50.0% of this year's respondents indicated they performed all their production "in-house" (vs. 43.8% last year, 64.2% in 2010 and 58.1% in 2009). These and other data indicate an upcoming trend toward further outsourcing to CMOs. In contrast with these well-established manufacturing platforms, newer insect and plant cell culture platforms tend much more to be performed in-house.

When asked about outsourcing plans through the next five years (2017), overall results indicate a continuing trend towards greater outsourcing of manufacturing, with a majority of mammalian (58.2%) and even higher percentage of microbial systems user (72.2%; 59.6% last year) projecting some outsourcing by 2017. Microbial manufacturing is the area currently with the highest proportion now outsourced and is the highest future growth area for outsourcing.

Currently Outsourced Tasks

While manufacturing gets much of the attention due to it being a critical and, by far, the single highest outsourcing expense, industry outsourcing projects continue to be dominated by relatively lower value-added services, such as fill-finish, product characterization and other testing. Our study this year shows that the primary outsourced activity remains analytical testing/bioassays, with more than 80% of companies outsourcing at least some of this activity, followed by validation services (69.8%). Testing/product characterization (65.6%) and fill-finish (63.5%) are next on the list of 24 outsourcing activities. The area with the largest *growth* in response this year was analytical testing/bioassays, with biosimilar development perhaps contributing to this. At the other end of the scale, the lowest rates for outsourcing activity were for Design of Experiments,

downstream and upstream process development and operations, and QbD initiatives. These tasks are apparently considered core corporate capabilities not suitable to being outsourced.

Growth in the Future

When asked what activities will see "significantly higher" outsourcing in the next two years, 35.4% cited outsourcing of analytical testing/bioassays. This was up significantly in terms of the industry's perspective on the area's growth potential, from 18.3% last year. In addition, 32.3% noted validation services would be a hot growth area, up from 22.1% last year. Other areas of projected significant growth include fill-finish operations, manufacturing, cell line development, testing for lot release, and toxicity testing. When asked how their spending on outsourcing will change over the following 12 months, budgets for outsourcing at individual facilities will increase by 9.3% on average. Only 7.1% reported expecting any decrease in outsourcing!

However, outsourcing is not without its problems. Separately, when CMOs were asked to cite common mistakes made by clients, 86.1% responded, "Clients don't build in sufficient time for the project (unrealistic timeframes)," and, "Clients want to contain cost by limited development runs, but still expect successful full scale manufacturing." So, communications and infeasible performance expectations remain common problem areas when using CMOs.

The biopharma industry has survived the worldwide economic downturn of recent years and has even done rather well during this period. The biopharma industry has continued to grow at a steady pace and is now showing clear signs of further recovery and growth. Our survey data show that companies are now or are planning to spend and invest more in every budget area surveyed, including R&D and bioprocessing capacity, staff and other infrastructure. Larger and more established companies in particular are continuing to aggressively look for opportunities to cut costs and increase efficiency, with this continuing to benefit CMOs and CROs.

Sponsor companies are generally outsourcing more selectively and with more long-term strategic considerations. They are now much more knowledgeable, experienced and comfortable with managing outsourcing, including evaluating related impacts, and judging related cost-effectiveness and strategic value. Widespread layoffs and elimination of formerly essential facilities, with these functions outsourced, has slowed. New products and new markets, particularly internationally, continue to support market opportunity and potential for growth in outsourcing.

References

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Survey Methodology
The *2012 Ninth Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production* in the series of annual evaluations by BioPlan Associates, Inc. yields a composite view and trend analysis from 325 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations (CMOs) in 30 countries. The methodology also included over 150 direct suppliers of materials, services and equipment to this industry. This year's survey covers such issues as: new product needs, facility budget changes, current capacity, future capacity constraints, expansions, use of disposables, trends and budgets in disposables, trends in downstream purification, quality management and control, hiring issues, and employment. The quantitative trend analysis provides details and comparisons of production by biotherapeutic developers and CMOs. It also evaluates trends over time, and assesses differences in the world's major markets in the U.S. and Europe.