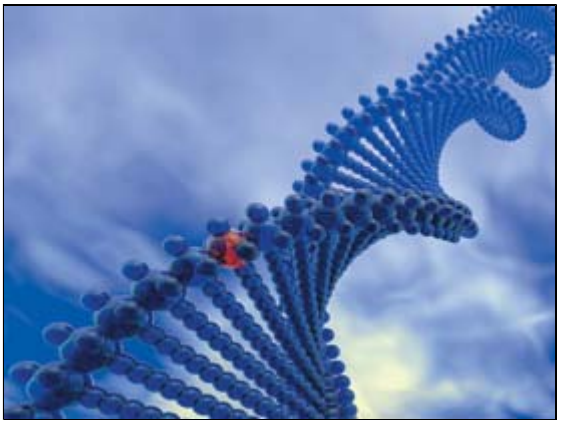
Bio-Capacity in 2012

The outlook is bright for CMOs

By Eric S. Langer

Outsourcing to CMOs is increasing on all fronts, regardless of expression system, and this trend looks like it will continue to benefit CMOs at least through 2012. This is according to the results of the just-released *5th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production*. In a survey of 434 biomanufacturers and CMOs in 32 countries, this year's study assessed critical industry factors, including: Capacity Utilization, Current Capacity Constraints, Future Capacity Expansion, Use of Disposables, Downstream Purification, Quality Issues, Hiring and Employment, Suppliers to Biopharmaceutical Manufacturing, and other areas.



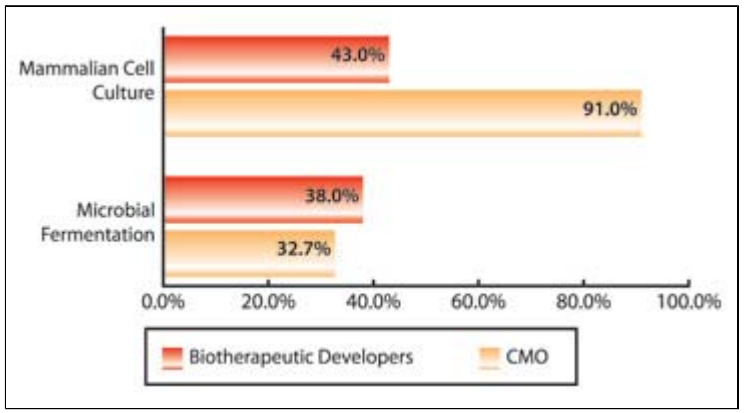
Future Capacity Expansions by 2012

We compared CMOs' planned capacity expansions with the five-year expansion plans of biopharmaceutical companies. During the next year the CMO industry will be working to substantially increase production capacity, especially in mammalian cell culture. CMOs believe their facilities will increase production capacity by an average of 91%, total, in the next five years. In comparison, biotherapeutic developers expect a total increase in production capacity averaging 43% during the same time period. As recently as last year, when we asked respondents to project their capacity out five years, CMOs were less bullish. This suggests the rate of increase may be growing for CMOs. For biotherapeutic developers, however, that rate appears to be declining slightly. Last year they were projecting a 50% 'five-year' increase for mammalian cell culture capacity, compared to a 43% total increase through the period 2007-2012.

This correlates with general indications of continued growth among CMOs. The mammalian system numbers are significantly higher for CMOs than for biotherapeutics developers, especially when compared with other expression systems. This suggests that the industry has grown comfortable with the outsourcing of mammalian cell culture activities. This is not unexpected, as it is the most mature segment of work at CMOs. Most of the established CMOs offer mammalian production capacity.

However, other factors may be at work. According to Geoff Hodges, vice president, Process Development and Technology, at Xcellerex, Inc. (Marlborough, MA), "A possible disturbing alternative is that some CMOs may be out of touch with the trends in the industry and have overestimated the amount of mammalian capacity [that will be] required."

Figure 1: Planned future capacity expansions: 5-year estimates, 2008 through 2012; Biotherapeutic Developers vs. CMOs



US vs. European Capacity Expansions by 2012

Both European biotherapeutic developers and CMOs are planning significantly more expansion in all systems than their U.S. counterparts are. For mammalian cell culture, respondents indicated a 30% difference; five-year expansion plans call for a total increase of 36.4% in the U.S., vs. a total of 66.1% in Europe.

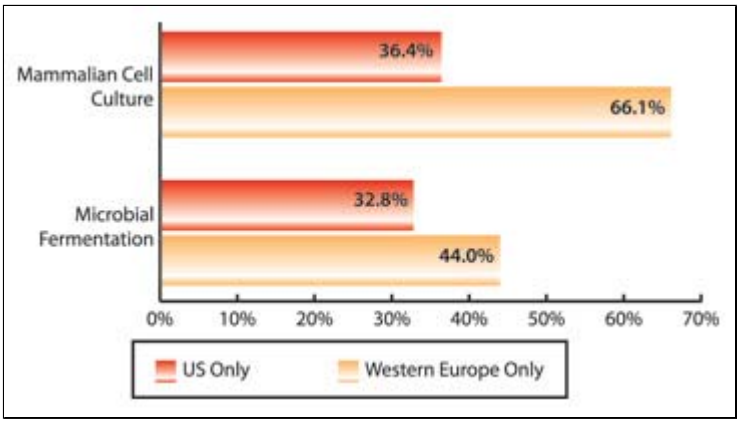
Some of this expansion may possibly not take place in Europe at all, if the biotech industry in overseas locations can succeed in attracting this growth as outsourced capacity. This may result in a net shift to Asia, including countries like India, China,

Singapore, Korea, and others. However, according to Xcellerex's Dr. Hodge, this trend has not yet been established: "As a CMO we still see a fair amount of interest in CMO capacity from companies in or near Europe and have not observed a notable shift in interest from outside the US."

Large-scale Capacity Expansions

More than 22% of all respondents (CMOs and biotherapeutic developers combined) using mammalian cell culture systems are projecting to at least double their production capacity by 2012. In comparison, 13% of respondents using microbial fermentation systems expect expansions of greater than 100%. These projections have remained relatively constant over the past three years. For microbial fermentation, the numbers were 14.3% and 12% (2006 and 2005, respectively). Beyond the standard systems, we also identified trends in insect cell systems that indicate these may also see significant capacity expansion.

Figure 2: Planned future capacity expansions: 5-year estimates, 2008 through 2012; U.S. vs. Western Europe



Future Capacity Constraints

This year, we evaluated 20 unique factors that create capacity constraints. Respondents were asked to identify the major factors that may impact their organization's production capacity during the next five years. The factor expected to produce the greatest constraint was "Physical capacity of downstream purification equipment," indicated by 29.6% of respondents. This was a shift from 2005 and 2006 when "Inability to hire new, experienced technical and production staff" topped the list, with more than 30% of respondents indicating it would be the major factor in production capacity constraints. In 2007 the hiring concern proved to decline in importance somewhat, to the second biggest constraint, as indicated by 27.9% of respondents. This 'hiring' factor has continued to decline in importance from 2003 when more than 52% of respondents felt that the lack of experienced production staff would be the major capacity bottleneck. Third on the list of factors was "Lack of financing for production expansion," with 22.4% of respondents. Other factors evaluated include:

- Physical capacity of fermentation/bioreactor equipment
- Inability to hire new, experienced technical and production staff
- Inability to retain experienced technical and production staff
- Costs associated with downstream purification
- Inability to optimize my overall system, given my current technology and resources
- Inability to hire new, experienced scientific staff
- Inability to retain experienced scientific staff
- Inability to optimize the yield expected using my current technology
- Inability for new technologies to achieve claimed performance
- Quality control/process monitoring issues
- Inability to meet international regulatory requirements in a timely manner
- Production problems with downstream purification
- Inability to obtain raw materials required for production
- Inability to meet domestic regulatory requirements in a timely manner
- Lack of regulatory staff

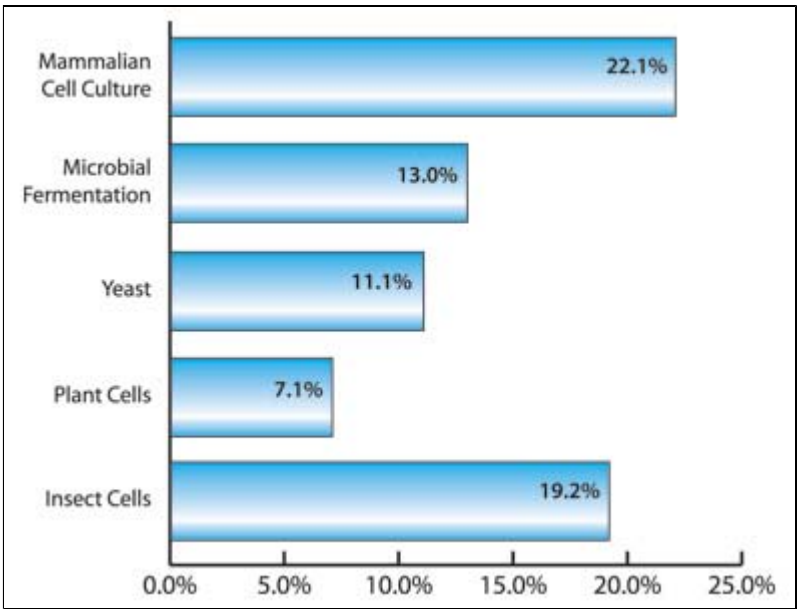
Only 22.7% of respondents indicated that "We are unlikely to see capacity constraints in 2012."

Future Capacity Constraints: CMOs

In 2006, CMOs appeared to be more concerned about manufacturing process performance and costs. In this year's survey, CMOs projected that they will face three severe capacity constraint factors in 2012: Hiring production staff, hiring scientific staff, and funding. Topping the CMO list at 46.4% of CMO respondents was hiring new, experienced technical and production staff. While 32.1% of CMOs said that hiring new experienced scientific staff would be

Figure 3: Percent of respondents projecting production increases greater than 100% by 2012

the second critical constraint. Lack of funding for production expansion tied for second place on the CMO's list of capacity constraints in 2012. In previous years CMOs indicated they were going to be capacity constrained by a lack of physical capacity for fermentation equipment and a lack of financing for expansion.



In comparison, for biopharmaceutical developers, in 2007, concerns about the physical capacity of equipment, as well as hiring, topped the list.

Future Capacity Constraints: U.S. vs. Western Europe

We also compared responses from biotherapeutic manufacturers (both drug innovators and CMOs) in the U.S. and Western Europe. There were significant differences in perception of how future factors may create capacity constraints by 2012. The greatest difference was seen in their perspective on hiring new, experienced technical and production staff. The "Inability to hire new, experienced technical and production staff" was indicated by nearly 37.1% of European facilities compared with 25.4% of U.S. respondents. In Europe, lack of financing for production expansion would be causing relatively greater capacity problems (30% in Europe vs 19.6% in the U.S.). Although Europeans are expecting physical capacity of downstream purification equipment to be a larger problem, both regions found this factor to be at the top of their list of factors creating capacity constraints in 2012. In addition, relatively fewer European facilities indicated that they are unlikely to see capacity constraints in 2012 (15.7% in Europe vs. 24.9% in the U.S.).

Perhaps as a corollary to their optimism about the future, CMOs are generally experiencing greater capacity constraints today, and they expect these constraints to continue in the future. This may be due partly to the growing tendency for biotherapeutic developers to outsource more of their production requirements. Biotherapeutic developers and CMOs both predict that the physical capacity of downstream purification equipment will be the greatest constraint on capacity. There continues to be a need for the improved efficiencies and productivity of existing downstream equipment. In addition, both CMOs and biotherapeutic developers must develop long-term solutions to their hiring problems if they are to avoid ongoing shortages of experienced technical and production staff. This may be particularly true among European manufacturers. CMOs feel that increased training and education in regulatory, technical and scientific areas would also be important to avoiding future capacity constraints.

Survey Methodology: *5th Annual Biopharmaceutical Manufacturing Capacity and Production Study Coverage*, the fifth in the series of annual evaluations by BioPlan Associates, Inc., yields a composite view from 434 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations in 32 countries. The methodology also encompassed an additional 126 direct suppliers of materials, services and equipment to this industry. This year's survey includes analysis from eight industry experts, and covers issues such 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. For more information, visit www.bioplanassociates.com.

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