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Capacity Utilization &Capacity Constraints

Trends and differences in the U.S. & Western Europe

By Eric S. Langer

The biopharmaceutical industry is responding to the global funding crisis by retrenching on some long-term projects. In other industries the economic situation has created across-the-board budget crunches. But healthcare and biopharmaceuticals have thus far been insulated to some degree from the short-term impacts. Especially for mammalian cell culture, the trend this year has surprisingly consistent in terms of capacity utilization, which, over the past three years, has held steady at 63% for mammalian systems. Global utilization for microbial systems has dropped from 62% to 55%.

Photo of EasyLyo vials courtesy of SGD group.

There are, however, some sharp differences between U.S. and European capacity utilization rates, as well as the causes of capacity bottlenecks. We discuss these trends based on data from my company's 6th Annual Report and Survey of Biopharma-ceutical Manufacturing1. In this, we evaluated global capacity utilization, among other trends. The study provides a worldview from executives at 446 biopharmaceutical manufacturers and contract manufacturing organizations (CMOs) in 35 countries.

Relevance of Capacity Utilization

Capacity utilization information is important for planners and investors as they determine whether capacity will be available for the production of pipeline drugs that may be reaching approval. In 2003, the biopharmaceutical industry's utilization rates exceeded 76% for mammalian systems. This was a capacity-crunch period that led to facility build-outs by both biotherapeutic developers and contract manufacturers. The resulting expanded capacity brought the utilization rate down so that by 2006 it appeared that a stable capacity utilization rate would be around 63%.

This is also an important number when compared with overall U.S. industrial production. In February 2008 for all U.S. industries, the capacity utilization rate was to 80.7%2. By February 2009, that rate had fallen nearly 10 points to 70.9%3. Yet in the biomanufacturing sector, capacity utilization has remained relatively flat. Overall U.S. industrial production fell 1.4% in February 2009 and has now declined for 10 of the past 12 months. Overall U.S. output in February was 11.2% below its year-earlier level and was the lowest level since April 2002. This rate matches the historical low, reached in December 1982.

The biopharma segment tends to aggressively avoid unanticipated high production demands that can create a capacity crunch. Despite this, we have seen a narrowing of the capacity utilization gap, which has moved from an 18-point spread between U.S. total industrial vs. biopharma capacity utilization rates last year, to an 8-point gap this year. This excess, 'flex,' or buffer capacity is important in this business because the opportunity costs associated with not getting a company's product to market can be devastating.

On the other hand, the cost of an idle biomanufacturing facility, as well as costly excess capacity, is also actively avoided. So predicting industry capacity becomes a high-stakes game. Today, smoothed-out biopharmaceutical industry utilization rates are due primarily to improved planning by manufacturers and the lack of major blockbuster drugs that might absorb substantial industry capacity. The leveling-off in biomanufacturing capacity suggests that companies are using their existing capacity more efficiently, and are planning more effectively for shifts in capacity demand.

Study Results

In our study, respondents indicated their capacity utilization for various production systems. Below are the average responses. Capacity utilization has remained flat for mammalian cell culture systems (at 63%), and is relatively flat for microbial fermentation, as well (at around 55%).

Since 2003, capacity for mammalian cell culture systems has dropped significantly, from 76.4% in 2003 to 63.2% this year. However, capacity utilization has flattened out in the past four years, and change has amounted to a 2.8-point decrease since 2005. Microbial fermentation capacity declined as well from 71.0% in 2003 to 53.8% in 2007 (CAGR –13.0%). But since 2005, the decrease has slowed to 2.9% annually.

Capacity Utilization Changes Since 2003

Mammalian cell culture: 63.2% in 2008. Capacity use seems to have stabilized at approximately this level over the past few years, down from 76.4% in 2003.

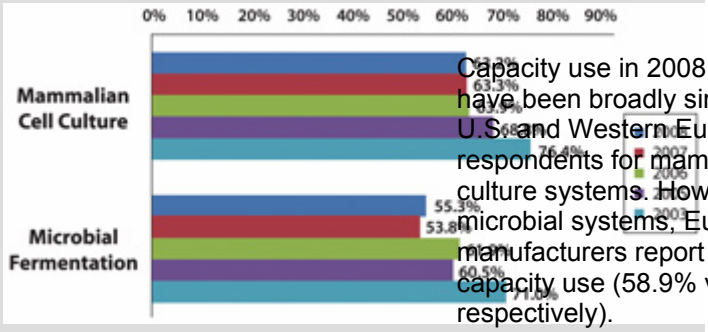
Microbial fermentation: 55.3% in 2008. Again, there are signs of a stabilization after a period of higher capacity use (71%) in 2003.

Yeast, plant and insect cells: For these systems, capacity utilization has fluctuated, and part of the variability in these numbers is a result of the relatively small data set for this system. However, the study data shows that of these three, since 2005, only capacity utilization for yeast systems appears to be on the rise.

Capacity Utilization, by System: 2003-2008

Capacity Utilization: Average Production as % of Operating Capacity, by System: 2003-2008

"My organization is currently operating at or around the indicated % of production capacity for each of the following:"



Average Growth Rate in Capacity Utilization: 2005-2008

Globally, capacity utilization changes in the past three years have generally been small (2-3%) for mammalian and microbial systems. For the less common systems, such as plant and insect, the decline has been greater. Yeast systems have shown a modest gain on capacity utilization. However, there are relatively few users of yeast systems, so these numbers may vary based on fluctuations at a relatively small number of facilities.

Change in Capacity Utilization, CAGR: 2005-2008

Change in Capacity Utilization:

% of Operating Capacity, by System, CAGR:2005-2008

- **Mammalian Cell Culture:**-2.8%
- **Microbial Fermentation:** -2.9%
- **Yeast:**+3.4%
- **Plant Cells:**-9.7%
- **Insect Cells:**-8.6%

Capacity Utilization: U.S. vs. Western European Manufacturers

Capacity use in 2008 appears to have been broadly similar between U.S. and Western European respondents for mammalian cell culture systems. However, for microbial systems, European manufacturers report higher capacity use (58.9% vs. 49.9%, respectively).

The differences between U.S. and European capacity utilization for microbial systems, according to Scott M. Wheelwright, president of Strategic Manufacturing World-wide, Inc., "Most likely reflects less overall fermentation capacity in Europe, compared to cell culture, and the move in the U.S. from products made microbially to products made in cell culture."

Some of these capacity differences between U.S. and European manufacturers may not be seen at larger CMOs. "We are not seeing distinct differences between Europe and the U.S. with regard to capacity utilization for microbial fermentation processes," said Dr. Christopher Dale, Head of Microbial Technology at Lonza (Hopkinton, MA). "The differential seen in the study may be experienced more at smaller companies, which may have lower overall capacity."

Capacity Utilization by System, U.S. vs. Western Europe

Average Production as %of Operating Capacity, by System, U.S. vs. Western Europe: 2008

"My organization is currently operating at or around the indicated % of production capacity for each of the following:"

Mammalian Cell Culture

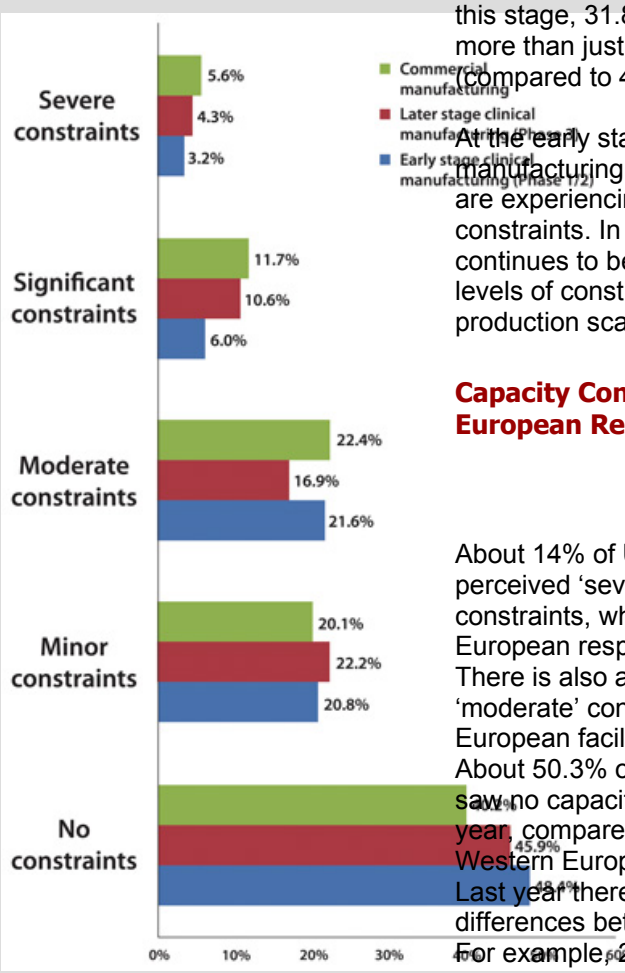
U.S.: 66.1%/W. Europe: 67.1%

Microbial Fermentation

U.S.: 49.9%/W. Europe: 58.9%

Capacity Constraints, by Stage of Production

"I believe our facility is experiencing production capacity constraints today."



Current Capacity Constraints

To assess the potential opportunity for facility growth in the industry, we first evaluated the severity of capacity constraints today. We found that 17.3% of respondents were experiencing 'Severe' or 'Significant' constraints at the commercial manufacturing level (compared to 20.7% in 2007). We found that 39.7% were experiencing more than just 'minor constraints' (compared to 48.3% in 2007). Clearly, there is more available capacity this year than last, at the commercial scale.

In addition, at "Later-stage clinical manufacturing" (Phase III), 14.9% of respondents were experiencing severe or significant constraints. This compares to 17% last year. At this stage, 31.8% were experiencing more than just 'minor constraints' (compared to 41.8% last year).

At the early stage clinical manufacturing a smaller percentage are experiencing capacity constraints. In general, there continues to be relatively consistent levels of constraint in earlier phase production scales.

Capacity Constraints: U.S. vs. European Respondents

About 14% of U.S. respondents perceived 'severe' or 'significant' constraints, while 11% of Western European respondents did so. There is also a trend toward 'moderate' constraints at Western European facilities (26% vs. 14%). About 50.3% of U.S. respondents saw no capacity constraints this year, compared to 40.5% of Western European respondents. Last year there were fewer differences between the two groups. For example, 25.6% of Western European respondents last year indicated that they were experiencing 'No constraints.'

Capacity Constraints: U.S. vs. Europe

Severe Constraints

U.S.: 5.2%/W. Europe:2.4%

Significant Constraints

U.S.: 9.1%/W. Europe: 8.6%

Moderate Constraints

U.S.: 14.3%/W. Europe: 25.7%

Minor Constraints

U.S.: 21.0%/W. Europe: 22.9%

No Constraints

U.S.: 50.3%/W. Europe: 40.5%

Expected Capacity Constraints by 2013: U.S. vs Western Europe

Western European respondents were about twice as likely as U.S. respondents to report expectations of 'moderate' constraints (29.9% vs. 15.2%), with correspondingly lower expectations of 'minor' or 'no' constraints. For 'significant' or 'severe' constraint expectations, the two groups were very similar (17% W.E. and 16% U.S.).

Survey Methodology: This sixth in the series of annual evaluations by BioPlan Associates, Inc. yields a composite view and trend analysis from 446 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations (CMOs) in 35 countries. The methodology also encompassed an additional 140 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.

This suggests that Western European biotherapeutic manufacturers and CMOs may be projecting either somewhat larger production demands, or slower capacity expansions that will lead to 'moderate' capacity constraints. U.S. biomanufacturers, on the other hand, appear to be expecting overall fewer capacity constraints. This

could be the result of a relatively greater built-up capacity in the U.S.

Factors Creating Future Capacity Constraints

We identified 19 different major factors likely to constrain respondents' production capacity over the next five years. This year, globally, the most frequently indicated factors were "Physical capacity of downstream purification equipment" (30.5%), "Costs associated with downstream purification" (26.9%), "Lack of financing for production expansion" (26.3%) and "Inability to hire new, experienced technical and production staff" (25.3%). Those who felt that they were "unlikely to see capacity constraints in five years" were in a minority (21.4%).

We did, however, see some very significant differences in expectations regarding future capacity-constraint factors between U.S. and Western European manufacturers and CMOs. In particular, this year Western European respondents, compared to their U.S. counterparts, seemed much more concerned about downstream purification issues. These issues included:

- Concerns over *"Physical capacity of downstream purification equipment"* were noted by 42.3% of Western European respondents versus only 25.0% of U.S. respondents (Last year the figures were 37.1% and 28.7%).
- 26.3% of U.S. respondents foresaw capacity constraints arising from the *"Inability to **retain** experienced technical and production staff,"* whereas only 12.4% of European respondents did so.
- Similarly, 21.7% of U.S. respondents foresaw capacity constraints arising from the *"Inability to **retain** experienced scientific staff,"* whereas only 12.4% of European respondents did so. So employee retention issues in the U.S. are relaxing this year, while they have remained stable in Europe.
- However, hiring in Western Europe appears to be slightly more problematic than in the US. *"Inability to **hire** experienced technical and production staff,"* was indicated by 23% vs 26.8% of European respondents as a cause of capacity constraints.
- *"Inability to optimize my overall system, given my current technology and resources"* was a concern of 22.4% of U.S. respondents, vs. only 14.4% of Western European respondents. This suggests U.S. respondents may be more interested in novel technologies aimed at system optimization (perhaps better media formulations or expression systems).
- *"Production problems with downstream purification,"* although not a major issue for either group, appears to be a greater problem with European respondents.

This year, 23.7% of U.S. respondents, vs 20.6% of Western European respondents indicated that they were "Unlikely to see capacity constraints." This compares to 24.9% of U.S. respondents and 15.7% of Western Europeans last year.

Key Areas To Address To Avoid Capacity Constraints: U.S. vs Western Europe

We also wanted to understand how U.S. vs Western European respondents would recommend how to avoid capacity constraints. The primary areas of differences in how capacity constraints can be avoided are show below.

Western European respondents were more likely to want improvements in these areas:

1. Better downstream purification technologies (57.5% W. Europe, vs 42.8% in the U.S.)
2. Fund more research to maximize production efficiencies (33% W. Europe, vs 27.6% in the U.S.)

U.S. respondents were more likely to want improvements in these areas:

1. Regulatory standardization and streamlined approvals (38.8% in the U.S. vs 27.8% in W. Europe)
2. Reduced scale-up and early-stage costs (29.6% in the U.S. vs 21.6% in W. Europe)
3. Manufacturing standards and industry benchmarking (26.3% in the U.S. vs 16.5% in W. Europe)
4. Better training and education in technical areas (25% in the U.S. vs 10.3% in W. Europe)

This is generally similar to the patterns seen in last year's responses, where "Optimize downstream purification performance," was the top concern, with 45.5% of U.S. facilities versus 54.3% in Europe.

Industry Average Planned Production Increase by 2013

This year Western European

respondents projected they would see five-year capacity expansions for mammalian-cell systems of 62% on average, compared to 44% for U.S. respondents. However, compared to last year's expansion plans, Western European facilities have clearly scaled back. European respondents this year are planning for expansion of microbial systems with an average five-year capacity increase of 28%. That percentage has declined significantly from last year's projection of a 44% increase.

Despite the recognition by respondents of excess capacity today and in coming years, U.S. respondents, on average, indicated their expansion plans (for all common systems other than mammalian-cell systems) were greater than Western Europeans' projections. In summary, Western Europe has held to its plans for mammalian system expansion, but has significantly reduced its plans for additional microbial fermentation capacity, as well as for other systems.

References

1. 6th Annual Report and Survey of Biopharmaceutical Manufacturing and Production, April 2009 BioPlan Associates, Inc. Rockville, MD.
2. Source: U.S. Federal Reserve Statistical Release, Industrial Production Capacity and Utilization, March 17, 2008
3. Federal Reserve Statistics for February 2009, at http://www.federalreserve.gov/releases/g17/Current/

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