Downstream Production Impacts Overall Capacity

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INFO

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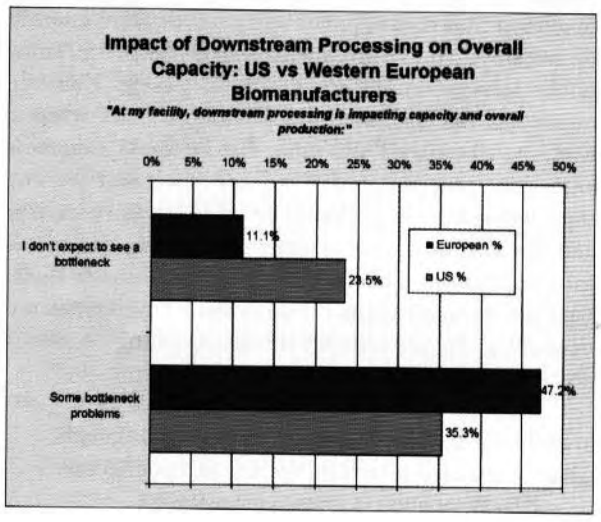
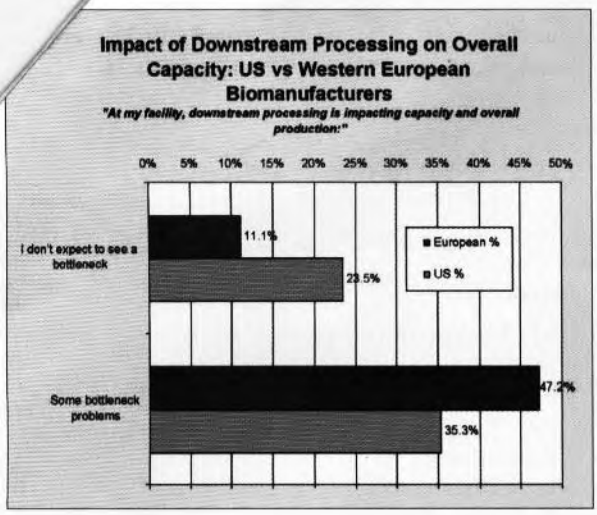
Although only about 5% of biomanufacturers on either side of the Atlantic today are experiencing serious bottlenecks from downstream purification, over 47% of Europeans are seeing «some» bottleneck problems. This compares with 35% of US biomanufacturers who are experiencing more than just a minor squeeze (See Fig 1).

Where is the Pinch?

Downstream purification covers a broad range of technologies and systems. When evaluating specifically where these downstream bottlenecks are occurring we found, as expected, that most are associated with chromatography columns. Here, as well, European respondents are feeling the pinch more acutely. Over 23% of European respondents were experiencing «Severe» or «Significant» constraints as a result of chromatography column bottlenecks. This compares with 18.7% of their US counterparts. Similarly, depth filtration steps were causing overall capacity constraints among 16.7% of European manufacturers, compared with 10.4% of US producers. In ultrafiltration steps, the bottlenecks were seen as less acute both in Europe and in the US.

When we asked respondents to comment on their downstream bottlenecks, we found a broad range of reasons. The increasing upstream yields, especially in monoclonals, are driving biomanufacturers to require ever-larger downstream scales. This has resulted in chromatography steps that are slowing overall facility throughput. Many respondents also indicated that poor scalability of individual process steps was also creating major problems, as was the lack of availability of trained staff in these production areas. The problems have been compounded by factors such as costs of protein A.





Downstream Processing vs Other Factors Impacting Capacity

To put downstream processing factors in context, we also evaluated 19 other factors that are creating capacity constraints in biomanufacturing. We then compared US and Western European responses from biotherapeutic developers and CMOs. A few of these are shown in Figure 3. 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. In the US, this factor was indicated by nearly 25.1% of respondents (second only to physical capacity of downstream purification equipment). However, in comparison, 37.1% of European facilities indicated hiring staff would cause capacity problems within 5 years. In the US, lack of financing for production expansion was expected to be causing relatively fewer capacity problems (19.4% in the US vs. 30% in Europe). Although Europeans are expecting physical capacity of downstream purification equipment to be a larger problem (37.1% vs. 28.9% in the US), both regions found this factor to be at the top of their list of factors creating capacity constraints in 2012. Overall, relatively more US facilities indicated that they are unlikely to see capacity constraints in 2012 (24.6% in the US vs 15.7% in Western Europe).

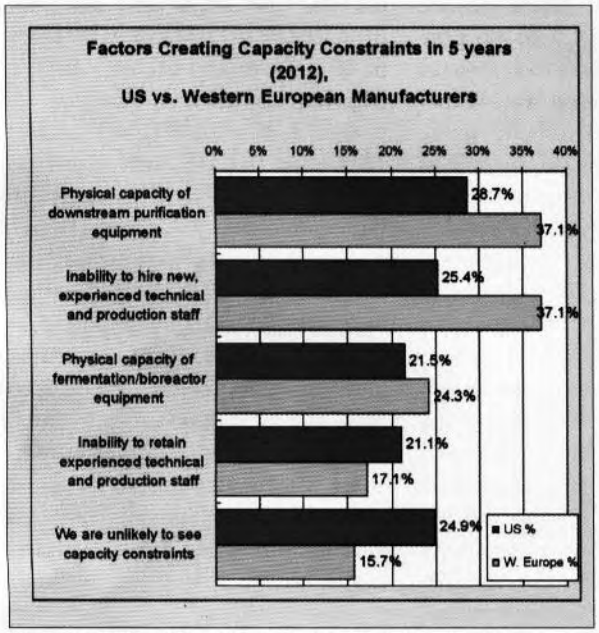


Figure 3: Abbreviated Capacity Constraint Factor List

Annual Trends: Factors Impacting Production Capacity

In 2005 and 2006 the major future production capacity problems were being generated by «Inability to hire new, experienced technical and production staff». Back then, this factor topped the list with over 30% of respondents worldwide indicating it would be a major factor in production capacity. In 2007 this hiring concern dropped in the ratings to second place (with 27.9% of respondents indicating). It is interesting to note that this number has continued to decline from 2003 when over 52% of respondents felt that lack of experienced production staff would be the major capacity bottleneck. And in 2005, 39.6% felt hiring would be the primary source of bottlenecks by 2010.

Today, «Physical capacity of downstream purification equipment» is predicted to be the greatest constraint (indicated by 29.6% of biomanufacturers and CMOs worldwide). In comparison, «Lack of financing for production expansion» rates fourth on the list, with 22.4% today. Back in 2006, «Physical capacity of fermentation/bioreactor equipment,» shared the spotlight with the, «Inability to hire new, experienced technical and production staff», with 21.4% of respondents' votes. This factor is fifth on the list in the current survey.

Downstream Purification Issues Facing the Industry

Today, downstream purification is clearly the area biomanufacturers and the industry recognize must be fixed to avoid future capacity constraints. Indeed, many vendors and biomanufacturers in the industry are evaluating options and developing improved downstream purification systems.

In this year's annual survey we first asked respondents to discuss the current downstream purification systems that are impacting their production. There was agreement that new routes to downstream purification technologies are needed to improve production processes, but the path has not been clearly identified. For example:

- Over 46% are now considering alternatives to protein A to reduce costs in new production projects.
- However, only 19% actually plan to move away from protein A for new production projects over the next 12 months.

Major Areas of Improvements for Downstream Processing

Whilst constraints caused by downstream processing is a hot topic, this concern has yet to be translated into broadly accepted commercialized innovations or products. Whether these innovations will come as stepwise, incremental improvements to current technologies, or be introduced as 'disruptive' technologies continues to be debated. Respondents to the survey were asked to identify areas where they believe major improvements in downstream purification will occur over the next five years (by 2012). Membrane technology was indicated as the area most likely to see major improvements for downstream purification. Following was the development of MAb fragments and the development of synthetic proteins. Interestingly, relatively few biomanufacturers and CMOs had opinions on these new downstream technologies. From this, we infer that the adoption rate for new technologies may be slow, as there may be a long learning curve for the industry. What is clear is that changes are very likely to occur in the way proteins are purified. Downstream innovation will likely drive these changes in an effort to lower costs and increase capacity compared with how current chromatography resins are being used. □

References

- 5th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, March 2008, BioPlan Associates, Inc.

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