



Current Trends in Biomanufacturing

The limited effectiveness of some existing drugs and demand for new therapeutic candidates for complex diseases has spurred the development of the biopharmaceuticals market. However, there is a lack of process innovation in biopharmaceutical manufacture to capitalize on the new leads and therapeutic candidates generated by biopharmaceutical R&D.

At present, the major obstacle in manufacturing biopharmaceuticals is inefficient downstream processing technologies. Historically, there has been a lack of technical progress in downstream processing compared with upstream technologies such as high-throughput screening.

The global downstream processing market has been hindered by a dearth of investment from big pharmaceutical, biopharmaceutical and contract research organizations (CROs) alike. This has resulted in downstream processing becoming a long-standing technology bottleneck, which has a negative impact on throughput and time scale in biopharmaceutical manufacturing.

The development of strategies to improve downstream processing efficiency relative to upstream phases of biopharmaceutical production remains one of the most relevant challenges facing biopharmaceutical companies worldwide. The efficiency of downstream

processing technologies must be improved; already, a number of positive steps are being taken.

Widely anticipated changes in investment patterns are expected to focus more on the establishment of new downstream processing facilities. There is a particular emphasis on new and emerging technologies that allow higher throughputs and shorter processing times, such as affinity chromatography in protein separation. The integration of different separation sciences to reduce the number of individual steps in the downstream processing stages promises to significantly reduce downstream processing time scales.

Another encouraging trend has been the increasing prominence of contract manufacturing organizations (CMOs). Outsourcing the manufacturing process can help drug discovery companies to avoid the high initial investment costs of establishing an in-house bioprocessing facility and avoiding excessive risk by investing significantly in facilities for the production

Phil Webster

is a research analyst at Frost & Sullivan Healthcare Practice, UK.

of a compound that may not achieve market success.

CMO firms that focus on innovative technologies and integrated bioprocessing solutions are expected to succeed in the global market place.

A recent analysis by Frost & Sullivan estimates that the world biopharmaceutical downstream processing CMO market generated \$3.85 billion in 2003 and is projected to accumulate an impressive \$9.2 billion by 2010 (Figure 1).

Investment and Innovation

In biopharmaceutical manufacturing, process development accounts for 30% of costs, upstream processing for 20%. However, the highest outlay in biopharmaceutical manufacturing is attributed to downstream processing, which is responsible for a massive 40% of the total costs incurred. These expenses are attributable to initial facilities outlay, as well as losses in profit occurring through slow manufacturing times.

Downstream Processing

Downstream processing is the major snag in modern biopharmaceutical manufacture and innovative solutions are strengthening the growing appeal of CMOs.

Instead of pumping money into their own downstream processing

facilities, biopharmaceutical companies are outsourcing their processing activities. They are also using CROs to source key intermediates and active ingredients.

Outsourcing to a CMO is viewed as a way to achieve the best cost savings and technical innovation. CMOs are investing heavily in developing their facilities and improving their technologies. The distribution of CMOs is influenced by the location of major biopharmaceutical R&D clients, with North America and Western Europe, the principal regions of CMO activity.

Although the US has the largest biopharmaceutical discovery industry, it has a relative shortfall in large-scale bioprocessing facilities to cope with escalating demand. Germany and the UK are leading regions for CMOs in Europe. Key CMOs in Europe include the UK-based Lonza Biologics Ltd, German-based Boehringer Ingelheim GmbH (Austria/Germany), Sartorius BBI Systems and Celonic. Other important CMOs are The Dow Chemical Company, Sigma-Aldrich, Co., Laureate Pharma L.L.P. and ProMetic Life Sciences, Inc.

Key Technology Trends

There has been considerable pressure to reduce the cost of downstream processing and cut the bottlenecks in the

biopharmaceutical production process. To boost production efficiency, increased volumetric throughput of apparatus and automated systems are being invested in. Examples of this are, the development of software solutions and higher throughput methods, such as membrane-based chromatography systems, is in line with efforts to create new specialized downstream processing apparatus.

In addition to increasing throughput times, mounting investment in automated systems also aims to reduce human resources and process development costs as well as boosting yield.

Rising competition for benchmark apparatus and consumables in the biopharmaceuticals market has been compelling participants to develop original technologies to outperform existing systems.

Other promising new downstream processing technologies include perfusion chromatography, plasmid DNA purification, protein crystallization and membrane affinity chromatography (Figure 2).

Another significant trend has been the availability of integrated technology systems such as a one-stop solution. Here, a single company offers each individual component of the downstream system including provision of instrumentation and

Figure 1 Biopharmaceutical downstream processing CMO market (world), 2003–2010.

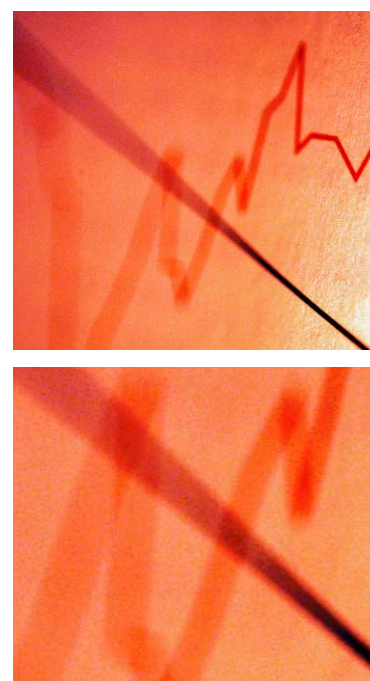
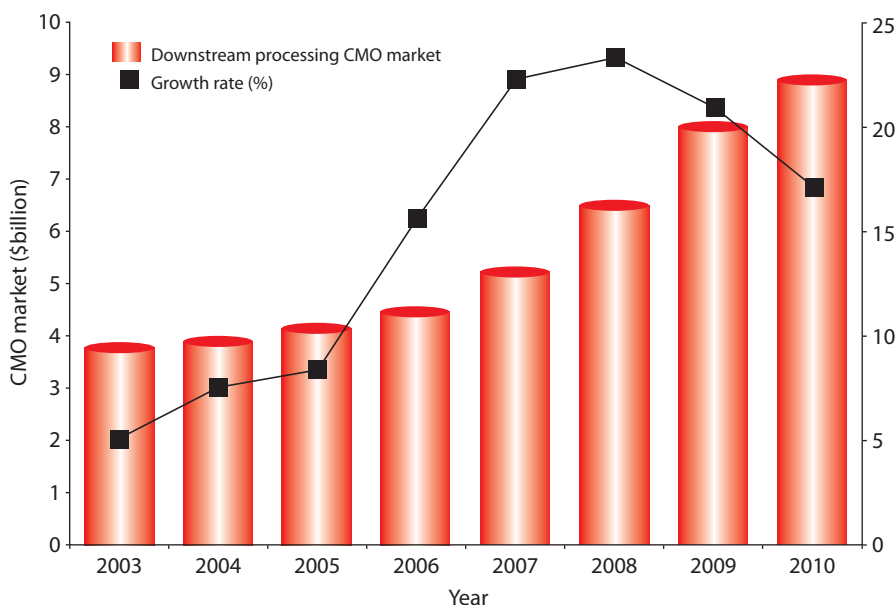
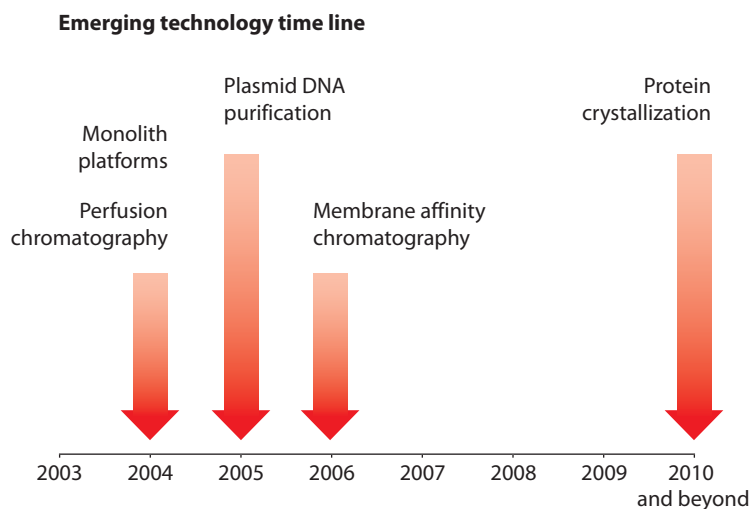


Figure 2 Analysis of emerging technologies: biopharmaceutical downstream processing market (world), 2003–2010.



consumables, validation, training services and technical support. Leading competitors in the field of integrated solutions include Amersham Biosciences, Millipore Corporation and Sartorius BBI Systems.

The advantage of integrated solutions is that they boost product recovery and avoid the 5–30% loss that typically accompanies each discrete step in the conventional production process. They also help to prevent the high cost of media and

apparatus, and long cycle times. The provision of training services and technical support reduces employment costs, which make up the bulk of process development costs.

Challenges Remain

Even as the prognosis for the biopharmaceutical downstream processing market is upbeat, challenges still remain.

Inherent in the market psyche is the lingering reluctance of large

European biopharmaceutical companies to adopt new technologies owing to quality control, safety and restructuring issues.

In other cases, despite their best intentions, more forward-thinking participants have to contend with the fact that the initial outlay required for setting up new downstream processing technologies is extremely high.

To prevent high installation and development costs, companies could resort to outsourcing downstream processing to CMOs with specialized equipment and expertise.

This is particularly prudent if a company is developing a product that falls outside its normal area of research, where investment in a whole new facility for a small number of new products would be inefficient.

At the same time, however, the development of integrated systems from technology providers may encourage big biopharmaceutical manufacturers to invest in-house, bypassing the need for CMOs. As more biomanufacturing facilities open, there are also concerns that the CMO market is approaching saturation point. This means that CMOs must be innovative and at the forefront of technology to remain competitive and sustain market growth.

Among other potential strategies, companies could invest in process automation that would reduce the cost of human resources. Instrumentation capable of high through flow from large-scale bioreactors would also enable companies to effectively clamp down on high expenditures.

Traditional downstream processing equipment has so far been scaled-up analytical laboratory equipment and is relatively inefficient. Moving forward, companies should initiate R&D investments in independent separation and purification products with high throughput capabilities.

Increasingly aggressive competition for benchmark apparatus and consumables presents both challenges and opportunities for market participants.

Developing innovative technologies, which outperform existing systems, and forging tactical alliances with other technology providers to offer end users enhanced integrated bioprocessing solutions serve as another strategic route to success. ■

