Editorial

Pharmaceutical BIOPROCESSING

Pharm. Bioprocess.
(2013) 1(1), 7–9

Biomanufacturing: time for change?

»»"The biomanufacturing industry needs to innovate to compete with these new market entrants. It needs to seize opportunities when they arise and take risks on novel technologies that may disrupt the market as well as moving it forwards in small increments."««

Uwe Gottschalk
Sartorius-Stedim Biotech, Göttingen, Germany
Tel.: +49 551 308 2016
Fax: +49 551 308 3705
E-mail: uwe.gottschalk@sartorius-stedim.com

The biomanufacturing industry is heading for stormy weather. This may seem a rather blunt way to decry the lack of innovation in an industry that is forever caught between the need to standardize and the need to create value from new ideas, but there is now an urgent need to innovate in the industry as a whole to face the new market challenges, which are only just over the horizon.

Biomanufacturing was a new and unexplored territory 30 years ago. The first pioneers developed technologies that were suitable for a virgin market, focusing on product approvals rather than process efficiency and cost because their products were unique. Today's industry is so different that those pioneers could not have imagined how the environment would change. There is more competition, with hundreds of products in development, and there is also a rising wave of off-patent biopharmaceuticals that are attracting a new kind of player in the market, concerned only with the production of generics.

Albert Einstein is renowned for his creative and unorthodox approach to solving problems, but he also had rather a lot to say about innovation. He once proclaimed: *"If you do what you always did, you will always get what you always got"*. This encapsulates the problem facing established biomanufacturing companies, which are mired in traditional production technologies and trapped by inertia and the historical pressure from the regulators to keep things as they always were. But the new players are not playing by the same rules, and the regulators are not the inflexible custodians of tradition they used to be. Innovation is now encouraged and new actors are taking up this challenge. A good example is Samsung, which is currently staking its claim in the biomanufacturing arena. Samsung has recently commissioned a manufacturing plant in Korea that will be operational by mid-2013, with the intention of gaining regulatory approval by the end of the year. Samsung has sized up the market and is getting ready to launch its own range of generic biopharmaceuticals, focusing on lucrative monoclonal antibodies that are coming off patent. The president of Samsung Biologics, Tae-Han Kim, was recently quoted as saying *"Biopharmaceutical companies are good for sales, and biotech companies for innovation, but neither is good for manufacturing"*. This is a slap in the face for all of us working in the biomanufacturing industry because we are proud of our achievements, but Kim is right to hold the mirror up to us in this way. Indeed, biomanufacturing is a long way from industrialization and there is no wonder that other companies aspire to create value from the markets when established companies cannot.

The biomanufacturing industry needs to innovate to compete with these new market entrants. It needs to seize opportunities when they arise and take risks on novel technologies that may disrupt the market, as well as moving it forwards in small increments. The focus on platform technologies is a milestone achievement in process development, but this is only suitable when processes can be transferred to subsequent products such as monoclonal

FUTURE SCIENCE

10.4155/PBP.13.2 ISSN 2048-9145

antibodies. For the large number of non-antibody products winding their way through clinical development, out-of-the-box thinking may be a better strategy. Albert Einstein on innovation once again: *"We cannot solve problems by using the same kind of thinking we used when we created them"*. And so it is in the biomanufacturing industry, where increasingly it is becoming advantageous to set aside old standards and even reconsider technologies that were once abandoned. The increase in product titres and the need to find increasingly cost-efficient ways to process biological feed streams without increasing the fixed costs of manufacturing are driving the market in a new direction, and only innovative new biomanufacturing processes can turn the tide for established companies.

The industry needs to innovate in terms of enabling technologies, it needs to innovate during process development by building quality into the process early in development to avoid the need for refitting closer to the market, and it needs to avoid waste in terms of facility space, buffer usage, water usage, and lost time through cleaning and validation. If we fail to address this challenge then the pressures of R&D costs, manufacturing costs, regulatory compliance and the burgeoning generics market will force the industry into a corner with only the largest and most robust companies still able to operate in the market. The CEO of Merck, at a recent Goldman Sachs conference, addressed this issue by predicting further consolidation within the industry to reduce infrastructure redundancy. But despite this overcapacity, new projects are mushrooming. There is a trend towards the construction of smaller, more flexible facilities and decentralized manufacturing. What seems like a contradiction is a clear indication that new companies are leaving old standards behind to gain a competitive edge by building capacity that is more easily accessible, based on the most recent technologies and with a more favorable cost structure.

There is also hope on the horizon because of the many examples of innovation already in the supply chain, with signs that the large pharmaceutical companies are taking note. In terms of upstream production, there have been advances in the development of chemically defined cell-culture media and innovative strategies to increase product titres without higher process volumes. Cell line improvement has been achieved, for example, through more efficient automated selection methods and through genetic modification to increase yields, such as the recent development of RNA interference to inhibit genes that reduce productivity. In downstream processing, innovations have focused on bottlenecks, particularly virus clearance and chromatography when large feed stream volumes are required. Such innovations include next-generation resins and membranes, the use of flocculants and precipitation to reduce process volumes, and the use of disposable modules to replace some of the most expensive unit operations. Disposable chromatography media are becoming increasingly popular for flow-through purification steps, but are also emerging as robust replacements for certain bind-and-elute steps, for example in vaccine manufacturing.

"The industry needs to innovate … during process development by building quality into the process early in development to avoid the need for refitting closer to the market, and it needs to avoid waste in terms of facility space, buffer usage, water usage, and lost time through cleaning and validation."

Earlier in process development, innovations come in the form of fundamental changes in the regulatory framework, which demand quality in the process as well as the product. The quality-by-design initiative builds quality into the process so that the product is manufactured under strictly controlled tolerances (critical quality attributes), which are implemented throughout the product life cycle, thus allowing quality to be ensured by monitoring and controlling process parameters rather than testing batches of the product after manufacture. A key area of continual innovation is the integration of design spaces for individual steps to create a clear definition of design space for the entire process. Others include the improved understanding of the impact of raw material variability on design space and the development of high-throughput scale-down models that allow rapid process specification. Process analytical technology is an initiative involving the continual monitoring of process parameters to allow feedback control and the correction of off-specification processes. The ability to automate and regulate biomanufacturing in real time has led to the concept of continuous processing as a replacement for batch manufacturing, taking the lead from conventional pharmaceuticals and other industries.

The need to innovate in biomanufacturing is, therefore, a direct response to current trends in the biopharmaceutical industry, which is confronted with the prospect of a maturing

business model, new product types and also with the desire to penetrate lower-cost markets with a favorable climate for biosimilars. The biomanufacturing industry must rise to this challenge, in some cases by thinking the unthinkable and testing out novel technologies, and also revisiting old ones that may now find a comfortable place in the more accommodating regulatory framework. This emerging phenomenon is perhaps best expressed in another quote by Einstein: *"If at first the idea is not absurd, then there will be no hope for it".*

Financial & competing interests disclosure

U Gottschalk is an employee of Sartorius-Stedim Biotech. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

A translation and proof reading service was utilized in the production of this manuscript.