

Manufacturers Must Cooperate To Compete

The biomanufacturing industry faces a Catch-22

By Eric Langer
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IN THE PAST DECADE, PHARMACEUTICAL industry advances have resulted in more blockbuster drugs hitting the market covering a greater variety of disease conditions than ever. Biopharmaceutical manufacturers have not had the same levels of success. While advances in drug development have increased, the technology and capacity developments of manufacturers have held steady or made only modest increases.

The American Society for Microbiology's venture arm, ASM Resources, got to the heart of the matter in a survey of top biopharmaceutical manufacturers. The survey found that the manufacturers' two biggest challenges were increasing production efficiency (46%) and complying with FDA regulations (45%). Taken separately, these results are not surprising, given the major pharmaceutical company's desire to produce more products faster and mitigate the omnipresence of the FDA. However, ASMR found that the two concerns were interrelated and may actually give rise to one another. Other factors important to the industry included manufacturing standards (29%), the costs involved with production scale-up (28%), and knowledge of emerging technologies (23%). See Table 1 on page XX for more information.

Broadly speaking, biopharmaceutical manufacturing technology has not changed in more than a decade. In order to increase production efficiencies, novel technologies are required. However, manufacturers are caught in a Catch-22 situation because novel technology development is cost prohibitive given the lack of clarity in FDA guidelines, but FDA guide-

lines cannot be further defined until novel technologies are proposed and scrutinized by the FDA.

This paradoxical situation has put the industry in something of a state of dormancy. However, pharmaceutical R&D has managed to gain FDA approval for hundreds of patent protected prescription drugs in the last 10 years. Why have they been successful while the manufacturing industry not? The answer may in part be industry complacency.

It's clear that FDA regulations slow the process of getting a product to the marketplace. Manufacturers know this but seem largely unwilling to take the risk of proposing novel technologies that may ultimately meet with FDA compliance. This level of risk aversion is counter-intuitive when a mere percentage increase in production capacity could result in millions of dollars in added revenues that could more than cover the costs of novel technology development.

For far too long, manufacturers have pointed the finger at FDA regulations for holding back the industry from reaching its potential. On the other hand, the biggest challenge faced by the industry, according to the ASMR survey, was increasing

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production capacity. Since the FDA is unlikely to reduce regulatory pressures anytime soon, the industry should refocus its efforts on developing novel technologies with FDA regulations in mind.

According to the FDA, guidelines do exist; it's simply a matter of applying these guidelines to novel technologies in the development stage. Paul Richards, FDA spokesperson representing The Center for Biologics Evaluation and Research (CBER), said that the FDA will also actively assist any

regulations, thus saving time and money and reducing risk.

"Manufacturers have to pool their collective knowledge of the FDA," said ASMR's Wesley Russ. "The FDA's outreach programs are a good start but the manufacturers need to apply what they know about FDA compliance, the guidelines that exist along with good science and engineering," continued Mr. Russ.

However, the ASMR Survey still ranks FDA compliance as one of the biggest challenges facing the industry. This is not surprising, even with stepped-up FDA efforts to coordinate with manufacturers. Despite the FDA's best efforts, it is still bound by existing guidelines that do not always apply to novel applications. The reality of the situation is that it is virtually impossible for the FDA to be predictive about a novel technology until a sponsor proposes it. Only then can the FDA begin testing.

If the biomanufacturers were like professional sports teams, it would be easy to go out and sign the industry's best to be on their squad. In fact, some of the larger manufacturers will recruit from among the brightest minds in the industry. But this is expensive and vests too much knowledge in individuals rather than organizations. Another solution would be to invest more into R&D. This is also problematic for several reasons, the first being that R&D budgets are already huge and probably do not have enough room to expand to the size required to facilitate the growth needed in the manufacturing sector. Another reason not to place the entire burden on R&D budgets is that these costs get passed on to consumers in the form of higher drug prices and this is already a political time bomb with which the industry is struggling.

A better resolution is for the industry to benchmark and share information more openly. The industry currently is very secretive about what it does for one obvious reason—competition. But sharing knowledge and setting benchmarks is not tantamount to giving away the secret recipe. In fact, lifting the kimono a little could be

good for competition. As Mr. Russ put it, "Biomufacturing is still in its infancy, crawling along at a snail's pace. Right now no one has a competitive edge because they are all doing different things. By opening up a little, the industry might be able to speed up and become more competitive."

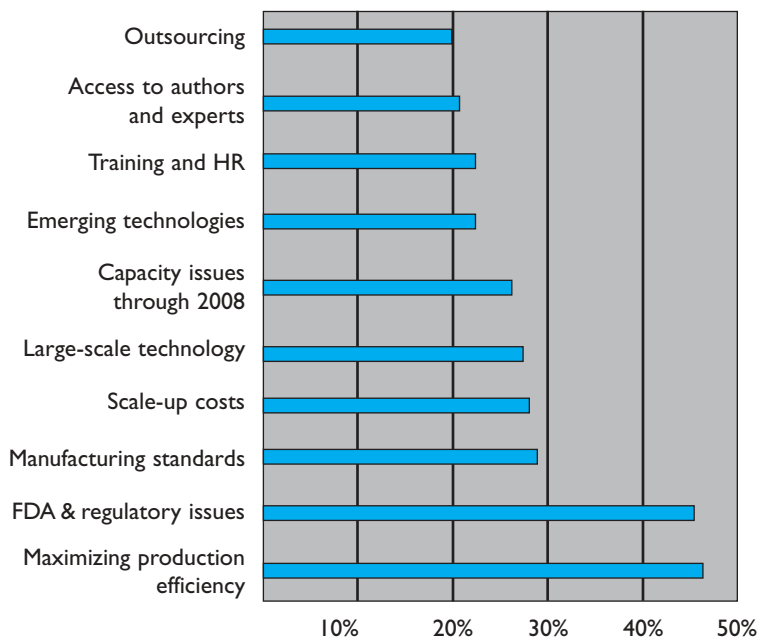
Benchmark

There have been few recent novel technology implementations among manufacturers and attempted developments are little heard. According to Mr. Russ, the industry needs to document the steps it takes toward advancing manufacturing facilities so those who follow do not repeat mistakes and have metrics against which to measure. This alone could speed development across the industry.

"Nearly every industry has a tradition of benchmarking,

Table I

Percent of Respondents Ranking Factor Critically Important



Source: ASMR/BioPlan Associates Survey 2002

firm developing a new product that could potentially save or improve the quality of life, as early on in the research stages as possible. In fact, CBER has developed an industry outreach arm called The Manufacturers Assistance and Technical Training Branch (MATTB), which is devoted to informing the industry and trade associations about the status of CBER policies and initiatives.

While some argue that the FDA is understaffed and unable to interact with the volumes of sponsors who could potentially propose novel technologies, the industry should take advantage of the opportunity to interact with FDA on this level. This, combined with the industry's decades of experience in obtaining FDA compliance, should be deployed before a prototype is ever developed. In this way, manufacturers can have a very good idea of what they need to do in order to comply with FDA

except biomanufacturing," said Mr. Russ. "In fact, in the automobile industry, benchmarking is a catalyst for innovation and excellence."

ASMR feels so strongly about benchmarking that it has begun to pool together industry experts to create a clearinghouse of information on biomanufacturing. In the future ASMR may serve as the coordinator for cross pollination of best practices. However, the organization has high hopes that manufacturers large and small will take the initiative to document their own R&D and begin to share this information with their peers at industry forums and possibly through technology transfer where business arrangements can be made.

"As companies begin to share their innovations, the industry will probably identify considerable synergies that will spark further discovery," said Mr. Russ.

Share Technology Advances

In the pharmaceutical industry patent protections are worth their weight in gold and even more. This is not necessarily the case when it comes to biomanufacturers. Not every patent will result in millions of dollars in revenue nor will every patent give a company the competitive edge. The fact is that the industry could benefit from understanding which technological advances have been successful and which have not. In addition to advancing the state of the industry by sharing advances in technology more openly, there will inevitably be opportunities for the sale of intellectual property and licensing, both of which are positive for the industry.

Identify Federal Labs & University Research Centers

Commercial biomanufacturers should also embrace the economies of wealth offered by federal labs and university research centers. The combined knowledge that comes from federal labs and the research environments of universities, alongside the commercialization and marketing skills of private industry, make for a one-two-three punch that most assuredly will bring positive results for the industry. This is especially the case when it comes to complying with FDA regulations. Before any prototypes are ever produced, experts from these three areas can troubleshoot and rework technology to be FDA compliant and increase efficiency. In fact, biomanufacturers have a great opportunity to influence the direction of these two potential partners by engaging them. This level of sharing holds the most potential for advances in the industry.

Ed Sybert, director, Technology Advancement Program of the University of Maryland, is a firm believer in the private sector engaging universities and federal labs. He argues that the federal labs already have a mandate to transfer their knowledge to private industry and that by engaging them their job is made that much easier. As for the university labs, from where Sybert hails, he believes that the universities offer some of the best testing environments available. Universities already have the equipment and the interest in developing novel technologies in a virtually risk-free environment. The private sector should engage both of these enti-

ties as a way to pull their collective capabilities and guide them toward developing market driven applications. As Mr. Sybert put it, "No one knows what the market wants better than the private sector."

What Does This Mean for CMOs?

The results of the ASMR survey should raise a red flag for contract manufacturers. It's a confirmation that biopharmaceutical companies are closely scrutinizing their own manufacturing capabilities and will do the same with outside contractors. This may be nothing new to contract manufacturers but since the state of the industry has remained static for so long it's only a matter of time before the other shoe falls and the demand for greater production efficiencies becomes a primary criteria on RFPs.

So what should a contract manufacturer be doing to keep existing contracts and win new ones? The first priority is to bone up on FDA guidelines in order to adopt novel technologies quickly and ensure that they are compliant. These days every publicly held entity is pressured by shareholders to increase revenues. In the pharmaceutical industry that means either increasing capacity or decreasing FDA compliance times. Biomanufacturers will bear the brunt of scrutiny in both of these instances and need to be prepared. A second priority is to stay on top of the latest advances in the industry. In fact, this second priority presents an opportunity for a forward-thinking manufacturer to actively promote advances it has made in order to occupy a "thought leadership" position among industry peers. This would strengthen the industry through knowledge sharing and increase that company's bottom line over time.

What's a Pharmaceutical Company To Do?

It might seem that the obvious action for a pharmaceutical company to take would be to focus on ensuring that contractors increase efficiencies. Surely, the pharmaceutical companies should scrutinize contractors, but they should also cooperate with contractors more closely to ensure that compliance guidelines are understood and met. They can do this through knowledge transfer where applicable and also by identifying areas where contractors should begin developing novel technologies independently. Pharmaceutical companies should consider sharing intellectual property and patents as well as entering into exclusive partnerships with manufacturers who have compliant novel technology or those who have the incentive and the capability to develop it cost effectively.

Produce or Perish

Despite the slow economies of 2001-2002 the pharmaceutical industry remains strong. There will continue to be advances in drug development that will require outsourced manufacturing. However, biomanufacturing advances are not occurring as rapidly as new drug development has. It may ultimately be in manufacturers' best interests to share best practices and cooperate with federal labs and university research in order to develop the novel technologies required to meet the demands of pharmaceutical companies. ■