



Cost Cutting Becomes the Pharma Industry's Mantra

Green Technology Gains in Importance

The pharmaceutical industry, including drug companies and contract manufacturers, is under pressure to bring down costs, particularly in manufacturing, due to an increased focus on emerging markets, “genericization” of pharmaceutical products, and indirect consequences of the global economic downturn, industry experts say. Companies are introducing “green” technologies and processes, and expanding the outsourcing of production, as part of the cost-cutting effort. “Pharmaceutical companies around the world are pressured to lower costs, not only due to the current global economic slowdown, but also due to continuing pricing pressure, the pro-generic agenda, and the drying research and development pipeline,” says Supratim Majumdar, industry analyst/health-care practice, South Asia and Middle East at Frost & Sullivan (Kolkata, India).

The pharmaceutical industry has not been directly hit by the global recession, but “governments across the globe are under pressure to reduce health-care costs and are therefore promoting generics,” says Enrico Polastro, v.p. and senior industry specialist at Arthur D. Little Benelux (Brussels). “Pharmaceutical companies are discovering emerging markets and there is much more emphasis now on these markets, where people cannot afford to pay high prices for drugs.”

Recent examples of the growing focus on emerging markets include Pfizer’s decision last May to enter into licensing agreements with two pharma companies in India, which also significantly expanded Pfizer’s portfolio of generic medicines. GlaxoSmithKline formed an alliance with Dr. Reddy’s Laboratories (Hyderabad, India) last June to develop, manufacture, and sell selected products in several emerging markets.

Developed markets face stagnant or negative growth, but major emerging markets such as Russia, India, China, and Brazil, as well as other Latin American countries, are seeing strong growth, Frost & Sullivan says. “Based on the strong emphasis by global pharma companies on emerging markets, it is evident that the future of the industry now lies in these markets,” Majumdar says.

Saltigo, the custom synthesis and manufacturing services subsidiary of Lanxess, says there is optimism among its customers about the potential opportunity in emerging markets. “At the moment our impression is that they are still formulating strategies on how best to develop these markets, which require more attention to distribution channels and regionalized manufacturing capacity,” says Andreas Stolle, head of the pharma business line at Saltigo. “Affordability of products in these markets represents one of the largest hurdles to quickly develop sales. Our expectation is that this pricing barrier may be best overcome by the industry making further acquisitions or joint ventures in regions that already have a good manufacturing platform along with the necessary low-cost structures,” Stolle says.

Developed as well as emerging markets are going through a genericization phase, in which pricing plays a vital role because generics are a low-priced but volume-driven business, Frost & Sullivan says. This has made it necessary to bring down manufacturing costs.

Aesica Pharmaceuticals (Newcastle upon

Tyne, U.K.), a supplier of active pharmaceutical ingredients (API), formulations, and custom synthesis to the pharma and biotechnology industries, says it and other contract manufacturers have been impacted by the increased focus on emerging countries. "The big pharma companies are looking at emerging markets, which makes it necessary for costs to be lower, and they pass the cost challenge on to contract manufacturers," says Adam Sims, commercial director at Aesica. Pharma companies, when trying to reduce their costs, will "squeeze their suppliers," Polastro says.

Lonza, however, says that the sharper focus on emerging markets has not put any additional pressure on Lonza to lower costs. "Contract manufacturing organizations have always been under pressure to find innovative production methods to reduce costs when producing APIs for customers, irrespective of the end market," says Janet White, head of sales and business development at Lonza Custom Manufacturing. "In these [emerging] markets, it is crucial that all drug development costs are given appropriate scrutiny," White says.

API and pharma intermediates producer Hikal (Mumbai) says it has been under pressure to lower costs, but the company cites different reasons. "One of the main reasons for the pressure is that very few new products are being developed or approved," says Jai Hiremath, vice chairman and managing director at Hikal. "Pharma companies are therefore trying to prolong the life of their old products, and stay competitive by entering generic markets," he says.

Increased outsourcing of manufacturing to low-cost destinations is one method pharma companies are using to cut down on manufacturing costs. "It gives pharma companies a cost reduction of about 30%-40%," Majumdar says.

AstraZeneca is one of many major pharma companies that intend to outsource more. The company plans to outsource all manufacturing of APIs within 5-10 years and is implementing changes to its global manufacturing and supply chain operations as part of a program to improve efficiency. AstraZeneca announced in November 2008 that it would permanently close pharma manufacturing plants at Destelbergen, Belgium; Porrino, Spain; and Umea, Sweden, and that it would further invest in its Wuxi, China plant to support the company's growth in the Asia/Pacific region.

Pfizer says that cost is always a concern in the industry. Pfizer is in the process

of reducing its number of manufacturing sites from about 100, to 41. "Many of the manufacturing sites came to Pfizer through acquisitions and so there were sites with overlapping functions," says Tony Maddaluna, v.p./strategy and supply network transformation at Pfizer Global Manufacturing. "Optimization of facilities was therefore necessary based on the existing and projected demand."

Pfizer expects the process of cutting the number of production plants in the pharma industry to speed up, and it anticipates greater outsourcing. "I believe this [reduction in manufacturing plants] will be necessary as we see most of the major pharma companies move away from the old prevalent philosophy of 'we make what we sell,'" Maddaluna says. "This will result in a need for both consolidation of capacity industry-wide and for creative solutions, which may include co-manufacturing." Pfizer says that although controlling costs is the key to competitiveness, assuring quality and supply is an imperative.

Some pharma players, including DSM Pharmaceutical Products, a DSM subsidiary, do not expect a major increase in outsourcing but forecast structural changes in the contract-manufacturing sector. "The amount of outsourcing in the pharmaceutical industry is likely to remain the same in the near future," says Ronald Gebhard, director/R&D at DSM Pharmaceutical Products. "But there will be more consolidation among suppliers and contract manufacturers, and this will help increase critical mass," he says.

Dishman Pharmaceuticals & Chemicals (Ahmedabad, India), a producer of APIs, intermediates, and fine chemicals, also says that the number of suppliers is unlikely to grow substantially but that suppliers will grow in importance, particularly in Asia. "The breadth of services offered by Asian API producers is now expanding into areas such as biopharmaceuticals, formulation, and clinical research with ever improving levels of service and quality, and this trend will continue over the next five years," says David Andrews, sales director at Dishman Contract Research and Manufacturing Services. "Dishman believes the number of suppliers will probably not grow significantly but we will grow in importance to the industry and the capabilities, in terms of complexity of chemistries offered, will continue to improve," Andrews says.

The use of better manufacturing processes, including green technology, is also



STOLLE: Affordability in emerging markets represents a big hurdle.



SIMS: Cost challenge passed on to contract manufacturers.



WHITE: All drug development costs must be scrutinized.

helping pharma companies and contract manufacturers to cut costs and stay competitive. Pfizer says that multiple initiatives involving operational excellence and lean manufacturing, as well as several green programs across the company's manufacturing and supply network, are paying off. "Pfizer Global Manufacturing is constantly looking for ways to manage processes more efficiently and effectively," Maddaluna says. "Lean manufacturing, process analytical technology, and green chemistry have all yielded, and continue to yield, cost savings. Our green efforts alone, currently comprising 4,000 ongoing projects at 80 Pfizer facilities have yielded \$110 million in cost savings over the past five years alone," Maddaluna says. Total cost savings achieved through these efforts in the next five years will be \$300 million-\$400 million, Maddaluna says.

DSM says it is trying to bring down its manufacturing costs through process intensification. "By developing process intensification technologies, we are able to offer shorter and more efficient scale-up of pharmaceutical chemicals, speed up development, and drive down material costs," Gebhard says. An integrated approach using biotechnology, chemistry, and process technology is the best way to achieve sustainable manufacturing, DSM says.

DSM's "green chemistry tool box" includes route scouting with enzymes and the use of micro-reactor technologies for commercial-scale production. The tool box involves chemocatalysis and biocatalysis, process intensification, and the proactive management of learning curves to increase

yield and reduce waste. "Our experience with various processes and applications has provided us with insights to increase our range of materials, refine scale-up, and best manage the safe handling of these processes," Gebhard says. DSM says it has scaled up more than 30 industrial enzymatic processes, possibly the highest number implemented by any one company. "More pharma firms will have to use green technology in the future," Gebhard says.

Newreka Green Synth Technologies (Mumbai), a provider of "green chemistry solutions" to firms making pharmaceuticals, specialty and fine chemicals, agchems, and dyes and pigments has seen a rise in its number of pharma customers in the past 2-3 years. "The number of pharma customers has been increasing mainly because of competition, pressure from regulatory bodies, and demand from customers," says Nitesh Mehta, founder director of Newreka.

The pharmaceutical market has become more competitive and, to sustain an edge over their competitors, most manufac-



MADDALUNA: Consolidation of manufacturing is inevitable.



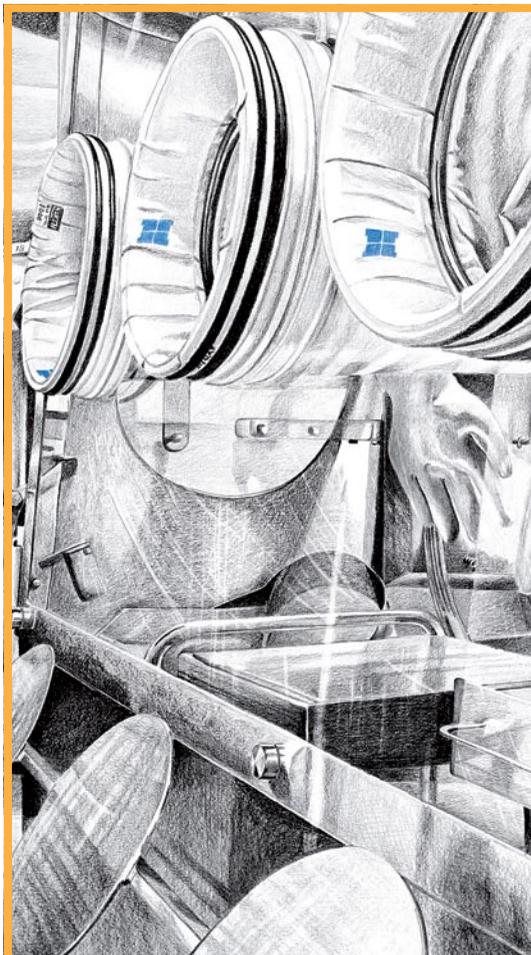
ANDREWS: Asian suppliers will grow in importance.

turers are on the lookout for innovation to enhance their process efficiencies further, Newreka says. The pharma industry generates more effluents than any other industrial sector. Regulatory bodies are demanding that pharmaceutical companies re-evaluate their process chemistries and find ways to reduce effluent. Big pharma companies, despite initiating green chemistry programs within their organizations and their manufacturing sites, say they cannot achieve sustainability until their suppliers in all regions follow sustainable manufacturing practices. This is causing big pharma companies increasingly to prefer suppliers with greener processes and that treat and dispose of their waste

responsibly, Newreka says. More pharmaceutical companies "will start using green technologies as this not only takes care of the environmental pollution problems but also helps to improve the economics of the product, making the manufacturer more competent in the long run," Mehta says.

Dishman has this year strengthened the "ozonolysis center of excellence" that the company established at its Bavla, India site. Ozonolysis is the reaction of ozone with organic compounds, dissolved in a solvent, to form ozonides. Many compounds that have high commercial value can be synthesized via ozonolysis. Most commercial applications of ozonolysis are in the pharmaceutical, and flavors and fragrance industries, Dishman says. As well as being a green process, ozonolysis is economic because it only produces the exact amount used and does not generate waste.

Pharma companies are implementing a range of initiatives that will improve their manufacturing processes, lower costs, and also benefit the environment. Sigma-Aldrich Fine Chemicals (SAFC) says that it



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SAFC launched the vendor auditing services program earlier this year to trace and assure the quality of raw materials and intermediates. The service conducts audits worldwide and helps reduce inefficiencies.

Aesica says there is an ongoing initia-

tive at the company's Queenborough, U.K. formulation plant to introduce further automation by 2010 and reduce costs. AstraZeneca says it has launched several initiatives to improve its manufacturing and supply processes, and is introducing lean ways of operating at its manufacturing facilities worldwide. At the company's Macclesfield, U.K. site, AstraZeneca take gas from the national grid and converts it into electricity and steam, which are used at the site. Some electricity is exported back to the grid, making the company a

net exporter of electricity from this site. AstraZeneca has also introduced a new concept for transporting the company's products in Europe, by co-loading its product into vehicles with products from competitor pharma companies, significantly reducing costs and environmental impact.

Process chemistries have to be reviewed at the lab scale, and companies need to tackle low yields and high solvent usage, says Girish Malhotra, president of Epcot International (Pepper Pike, OH), a consulting firm for manufacturing and technology simplification. "There is significant opportunity for process-yield improvement and reduction of solvent consumption at the API stage," he says. "Progress here will significantly reduce total manufacturing costs and energy consumption, and reduce waste handling and associated costs, as well as environmental impact. On a global scale the savings from such an effort would be in billions of dollars," Malhotra says.

—DEEPTI RAMESH

too is seeking to reduce costs and improve quality through process improvement and specific initiatives in supply chain and purchasing. "Part of our business strategy is to continue to develop process improvements and, in some cases, technologies that improve manufacturing and quality, and help manage costs more efficiently," says Gilles Cottier, president of SAFC. "We have introduced products and services that help control costs or reduce overall cost of ownership, such as our vendor audit services for pharma and biopharma customers."

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