PREFERRED CONTRACTS

Custom manufacturers of pharmaceutical actives and intermediates VIE FOR A POSITION in new big pharma supply chains

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PHARMACEUTICAL fine chemicals manufacturers heading to Frankfurt later this month for CPhI, the conference on pharmaceutical ingredients, say business is looking up for the third year in a row. Having weathered a five-year downturn that saw the exit of several big chemical firms from the sector, they are optimistic about the opportunity for more business from emerging and biotech drug firms, as well as from major drug companies.

But the improved profitability may be more than a business cycle upswing. Industry watchers cite a fundamental shift in supply chain strategies among large pharmaceutical companies, characterized by plant closures and commitments to permanently higher levels of outsourced supply of both drug intermediates and active pharmaceutical ingredients (APIs). New approaches to managing manufacturing contracts are also emerging. Suppliers say they will be competing to get onto top-tier supplier lists as drug firms shift from spot contracting to the establishment of strategic global manufacturing networks.

“We definitely have a next chapter. Not a pendulum at all,” says Guy Villax, chief executive officer of Hovione, a pharmaceutical chemical manufacturer based in Lisbon, Portugal. “The drivers are fundamental changes in an industry where large pharma companies have finally faced the fact that they need to be efficient.”

Although the change results in part from the drug sector’s embrace of efficiency programs that other industries tackled in the 1990s, including manufacturing quality regimes such as Six Sigma, there are also drug industry-specific agents at work. New drug approvals are down and a raft of top-selling therapies is due to come off patent in the next few years. Major research-based drug companies are also launching generic drug businesses and scrambling to advance their interests in biotechnology.

These trends are converging to force drug companies to rethink their supply chains and develop leaner, more efficient manufacturing infrastructures that make heavy use of contract suppliers. “And the challenge for us is that the pharmaceutical companies will not lower their standards for the kind of manufacturing they have always done in-house,” Villax says. “The question is, Who will be able to meet these standards?”

Enrico T. Polastro, a Brussels-based fine chemicals analyst with Arthur D. Little, argues in a new report that the need to gain a competitive edge in the procurement of intermediates and APIs is causing a big shift toward outsourcing at large pharmaceutical companies.

“The thesis is that [full-scale in-house drug manufacturing is] adding little if any competitive advantage, while ... detrimentally impacting overall returns on investment,” Polastro writes in “Chemical Sourcing Within the Pharmaceutical Industry: Towards a New Model?” He continues, “Pharmaceutical companies tend to vastly outspend by a factor of two to four independent fine chemicals vendors in terms of investment outlay per unit of capacity.”

Polastro advocates an equilibrium—a balance of in-house capacity and outsourced supply that will allow drug companies ready access to a broad range of technologies and limit their exposure to setbacks that could idle dedicated facilities.

PFIZER SEeks such a balance. According to Anthony J. Maddaluna, vice president for strategy and supply network transformation for Pfizer Global Manufacturing, the company is acting to put in place what he calls a competitive global supply network. “Years ago, it was make what you sell and sell what you make,” he says. “The manufacturing divisions were devoted to the company.”

This is changing at Pfizer, with the emphasis shifting from producing new blockbuster drugs to managing a portfolio of existing products. “What we find as we move more into the established products arena is that we have to set up a really cost-
competitive strategic supply network,” he says. “Our initiatives include divesting sites.”

It also involves a redefinition of manufacturing as one facet in a supply chain encompassing purchasing, packaging, and distribution—and tied in to Pfizer’s drug development efforts, he says.

Pfizer’s factory count spiked with the acquisitions of Warner-Lambert and Pharmacia, according to Maddaluna. The company had 93 chemical and formulation plants after the 2003 purchase of Pharmacia, and the count rose to nearly 100 before a steady stream of divestments and closures that leaves the company with 55 plants today. Pfizer targets further reduction to 43 plants by 2010.

Maddaluna says the firm expects to increase outsourced production from 17% currently to 35% over the next five years. More than half of the contract production will be provided by companies Pfizer has sold its plants to, one of which is Pramati Healthcare, which purchased Pfizer’s Morpeth, England, plant in 2006. Although Pfizer is currently working with 165 contract firms and plans to increase the number to approximately 180, Maddaluna says it had been working with 300 contract vendors in 2001. Pfizer, he says, will work mostly with a roster of top-tier suppliers that collaborate as part of the company’s global supply chain.

It is a big change, even from just a couple of years ago, according to Maddaluna. “It’s transformational,” he says. “It truly takes us to a competitive global make-or-buy supply network.” The determination of where to make and where to buy, however, remains fluid. “We will look at everything. It is not just about cost; it’s about quality, supply reliability, and cost,” he says.

Merck & Co. has taken a similar approach with a rash of plant closures and a rethink of its supply chain. “In recent years, we have worked to concentrate our internal manufacturing capabilities on core competencies while better leveraging external capabilities,” says Bob Kanuga, executive director of external manufacturing operations. “As a consequence, some operations historically conducted internally have been shifted to external suppliers.”

Kanuga estimates that external suppliers will eventually provide up to 35% of Merck’s manufacturing. Currently, most of the outsourced supply comes from U.S. firms. Merck is also vetting contractors for...
their ability to operate as part of a global supply chain.

This does not limit the supplier list to big-name, global contracting firms. In January, for example, Merck established a contracting relationship with the new owners of its former plant in Riverside, Pa., Cherokee Pharmaceuticals, a minority-owned firm. “No traditional pharmaceutical or chemical-based buyer emerged to take over the facilities there,” Kanuga says. Merck worked with a nontraditional buyer to help create what Merck claims is the only minority-owned API manufacturer in the U.S.

Despite the manufacturing scale-back, Kanuga says the company remains committed to significant in-house production. “Over the past 10 years, Merck has spent approximately $5 billion on the construction of new facilities and the renovation of existing facilities in the U.S.,” he says.

Roche has also gone through a series of plant sales and closures in Mexico, the U.S., and Europe, and currently manufactures at seven sites. “We aim to have a flexible manufacturing model in place that involves both in-house production and outsourcing,” says Annette Wals, a spokeswoman for Roche. “Roche selects its key suppliers on the basis of long-term procurement strategies. Today, whenever possible and of benefit, Roche strives for global contracts versus local contracting in the past.”

Although global “make or buy” supply decisions are geared toward more than simple cost-cutting, most drug companies say they have Chinese suppliers on their radar screens. Boehringer Ingelheim, for example, recently signed a contract agreement with Zhejiang Hisoar Pharmaceutical, which will begin production of intermediates at its plant in Chuanan, Zhejiang province, next year. Boehringer will process the Chinese intermediates into APIs at its own plants in Europe and the U.S.

Although Boehringer has done spot contracting with Chinese producers, the Hisoar agreement marks its first long-term contract—Hisoar will build dedicated capacity for its work with Boehringer. Roughly a third of Boehringer’s production is done on contract today.

Likewise, China and India will figure in AstraZeneca’s push to shift all intermediate and API manufacturing to third parties, according to Marc Jones, vice president of global external sourcing. But the firm will rely heavily on contractors in Europe and Japan in launching new APIs, he says.

“In the past, we have launched a product from our internal assets,” he says. “The big step for us is that, through working with a small handful of preferred contractors, we will actually launch those new products from their facilities.”

ALTHOUGH LOW-COST production is a consideration in what Jones characterizes as a uniquely aggressive move on AstraZeneca’s part, the main impetus to eliminate in-house pharmaceutical chemical production is risk management in commercializing new drugs. “Instead of us building our own assets,” he says, “it is better to access that mature supply base externally.”

According to Hovione’s Villax, pharmaceutical chemical suppliers will need to follow their customers in efficiency improvements if they expect to get into strategic partnerships with the big firms. “It will force everyone to be much leaner, more efficient,” he says. “It is a trend.”

Villax agrees that there is a transformation under way and that it will ultimately lead toward even more widespread outsourcing. “Look at the big carmakers. They design and market—nothing else. Maybe some assembly,” he says. Big pharma, according to Villax, will eventually develop drugs or license them, take care of regulatory matters, and market the products.

Villax says the fine chemicals industry will need to learn from the lean manufacturing practices of the auto industry as well. He notes that Hovione’s plant manager in Lisbon came from the French automotive firm Saureia and is implementing methods from that industry.
Roger Laforce, general manager of Fabbrica Italiana Sintetici (FIS), a pharmaceutical chemical maker based in Vicenza, Italy, agrees that drugmakers and their suppliers are taking a close look at auto industry practice. "It can be clearly seen," he says. "One of the first elements is that they are pursuing contracts using clear criteria of establishing a number of preferred suppliers. They are developing a tier." 

FIS does 60% of its custom manufacturing for major pharmaceutical companies and has long-standing relationships with Roche and other large pharmaceutical companies. "There is a steady flow of projects," Laforce says, adding that FIS works closely with key customers on managing their pipelines. Cost optimization is a major focus.

Raghu Ananthanarayanan, president of Piramal Pharma Solutions, says the pharmaceutical manufacturing shift has accelerated in recent years partly because of the headway made by outsourcing pioneers and partly because of the decline in new drug approvals and the impending loss of patent protection for many drugs in the market. "If they don't do it today, it will be too late," he says.

Ananthanarayanan says Piramal has begun working with large drug companies on "transition management," or developing means of streamlining and networking numerous plants. He says Piramal, in future acquisitions, will look at buying multiple sites from large drug companies.

**BIG SHIFTS** in manufacturing infrastructure have started only in the past two or three years, but many in the contract sector say they saw big changes coming and planned ahead for them. Ian Shott, CEO of Excelsyn, formed in 2004 with the acquisition of Great Lakes Chemical's fine chemicals business, says the transformation under way now is part of a 10-year trend in the drug industry.

"We set up Excelsyn against the context of substantial change expected in the industry," Shott says. He notes, however, that the drug industry is likely to continue to maintain control of technology and intellectual property (IP) in their relationships with contractors. "Pharma companies are expert at managing IP and leery of suppliers owning it," he says. "We have a lot of formal IP, but we try not to use that as a lever against our customers. Suppliers need to be sensitive." 

Suppliers agree that contract firms will need to continue anticipating change as drug companies find their balance in manufacturing. Success will hinge on keeping up with the science, as well as the business, of global supply chain collaboration. The level of sophistication is rising on both sides of the bargaining table, and doing business with major pharmaceutical companies will have little in common with the approach taken during the late-1990s boom in pharmaceutical fine chemicals.

"The world changes," Villax says. "The standards evolve. No one can go to sleep. The last eight years have been a mess, but it seems to me they will help to show what is the incorrect way and what is the right way to go about doing things."