

**Custom Chemicals**

By Ann Thayer

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**After struggling through 2009, contract manufacturers are honing their strategies and hoping for a better 2010**

“It is much harder to be in this business today than it was five or 10 years ago,” admits **Hovione** Chief Executive Officer Guy Villax. Although Villax believes that having a clear strategy is increasingly fundamental to success, he admits that “it’s quite tough and requires much better thinking to come up with the value proposition that you present to your customers.”

After having been through the economic ringer of 2009, custom chemical firms are reshaping their strategies, but the clarity they need to move decisively ahead is lacking. Villax and other executives describe the “flux” that pervades customers’ and even their own firms. This volatility and the resulting marketplace uncertainty have been clouding their view. Nevertheless, most anticipate that business will improve, and some even see glimmers of hope.

Hovione took the risk last year of buying a former Pfizer plant in Cork, Ireland, to get the large-scale capacity it wants (**C&EN, June 8, 2009, page 30**). “We need to have the right assets in the right places to address the different needs of customers,” Villax says. He adds that the company’s value proposition arises from doing drug development in Portugal, making clinical trial materials in the U.S., launching products from Ireland, and conducting low-cost work in China.

Villax expects Hovione’s sales to be up 10–13% when its fiscal year ends in March. Producing generic drugs, especially for emerging-market customers, is contributing to the growth. Like most custom chemical manufacturers, however, it experienced a decline in early-stage projects. “It forces you to rethink what your chemists will be doing,” he says. “We put a lot of ours to work in the plants to improve existing processes.”

**Carbogen Amcis** rethought things as well and has restructured its Swiss operations. Despite less early-stage work, the company saw a considerable uptick in late-stage projects. As a result, “we were able to do some internal juggling of both personnel and assets to boost the late stage, but we still had to make some cuts overall,” says Rhona McIntyre, Carbogen’s commercial director.

Several factors contributed to the drop in early-stage projects. During 2009, small biotech and emerging pharma firms had limited access to capital. They tried to conserve what cash they had and make strong cases to investors for new funding.

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“They needed to show progress in their highest value assets in the development cycle,” McIntyre says, so they emphasized one or two advanced projects and dropped or postponed others.

Major pharma companies continued to cut their R&D budgets and are generating fewer drug candidates. Focused on costs, they too killed a lot of projects in early-phase development. “The R&D platform across the pharma industry overall has shrunk,” McIntyre says. “How or when that is going to come back to the level we have seen before is a question.”

Meanwhile, mergers have reduced the number of big companies, which will mean stiffer competition for pharmaceutical chemical suppliers. A sense of dread pervades the supply side as everyone waits for the major drug companies to sort out their merged operations. Evaluating R&D programs to determine which have value is expected to be a long and drawn-out process.

While the assessment is under way, projects have been put on hold. “They aren’t outsourcing anything on those projects, whereas before they were pushing them quite heavily,” says David Feldker, vice president for **SAFC Pharma**, part of Sigma-Aldrich’s fine chemicals business. Although suppliers anticipate that big pharma will eventually outsource more, for now the stalled projects are clouding the market.

Big pharma customers have also tried to control their cash flow through their own supply-chain strategies and how much product they buy. “The pharma companies are trying to limit the amount of inventory that they are carrying to the greatest degree possible,” says Mark B. Hassenplug, pharmaceutical market leader at **Ernst & Young**.

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This phenomenon is showing up on the bottom lines of some leading custom chemical firms. California-based

**Ampac Fine Chemicals** was hit last year when sales volumes of its largest antiviral product fell 82%. Although the decrease was partially offset by other products, Ampac’s fine chemicals revenues for the fiscal year ending in September 2009 declined 23% to \$95.5 million.

**In April 2009**, India’s **Piramal Pharma Solutions** pointed to changes in inventory holding patterns as a reason to discontinue operations at its Huddersfield, England, site. For the nine months ending on Dec. 31, 2009, sales from Piramal’s assets

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outside India fell 29% while those from operations in India rose 28%, for a 12% decline overall.

SAFC saw the impact from destocking earlier. In some cases, customers “cut too far back in 2008 and now don’t seem to be quite as conservative as we move into 2010,” Feldker says. With orders continuing to rise and projects advancing, SAFC is on track to report single-digit sales growth for 2009.

SAFC’s strategy has been to stick to its guns. Moving ahead with planned expansions, it is adding capacity for high-potency fermentation in Israel; high-potency active pharmaceutical ingredients (APIs) in Verona, Wis.; and late-stage viral products in Carlsbad, Calif. “The way things are lining up it looks like it was a good move,” Feldker says. “Commercial additions that we are putting in place generated enough interest that 2010 looks like it should be off to a decent start.”

Demand for highly potent compounds is a bright spot for SAFC, Carbogen, Piramal, and others. For example, Carbogen has announced plans to expand services in Switzerland, and late last month it opened a \$25 million large-scale high-potency facility in India with its parent, Dishman Pharmaceuticals & Chemicals. High-potency projects should offer double-digit growth, McIntyre says.

Similarly, **Ash Stevens** is investing aggressively to extend its high-potency capabilities, President Stephen A. Munk says. Between 2009 and 2010, the Detroit-based firm hopes to spend about \$6 million. “We’re doing it because we think there’s an opportunity,” he says.

The company recently started up a new isolated reactor bay with a hydrogenation cell and intends to build a \$3.5 million specialized warehouse for materials handling. “We actually are planning detailed engineering on another \$12 million worth of expansions that we hope to start in about a year.” Munk says. These plans would add vessels up to 1,000 gal, along with process development labs and other facilities.

Munk anticipates another strong year in 2010 after posting record sales of about \$20.5 million in 2009. A mix of approved and development-stage projects for a diverse client base helps keep Ash Stevens’ business balanced, he believes.

Balance and flexibility are two goals of **Lonza**’s recent restructuring moves. Its sales declined 8% in 2009 compared with 2008, while earnings plummeted 33%. Price declines, lower demand, and unexpected cancellations and postponements of large-scale projects late in the year were factors, CEO Stefan Borgas explained in a late-2009 conference call with analysts.

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In response, Lonza is reducing its fixed costs by 5%, or about \$70 million, over the next 18 to 24 months. The company has consolidated its business units and expects to see a 6% reduction in personnel.

Lonza will also close its exclusive synthesis plant in Conshohocken, Pa., by the fourth quarter and move small-molecule production to its site in Nansha, China. In biopharmaceuticals, where product approvals are looking less likely but clinical work continues, the company is adapting large-scale reactors in Portsmouth, N.H., to handle smaller batches.

The changes “will allow us to adapt our structures and processes to lower growth and to deal with this much higher volatility and much lower short-term visibility,” Borgas explained. “As systems get more flexible, our cost base becomes more manageable.”

Borgas expects the business environment to remain volatile for at least two or three years but sees good prospects for signing product development deals and filling capacity. Expansions that are under way will add large-scale capacity in Nansha and high-potency drug facilities in Visp, Switzerland.

In the end, he believes that Lonza’s sales will still grow, although maybe less consistently year to year. “Our life sciences growth strategy remains intact,” Borgas told analysts. “Lonza is not in a crisis. We are more careful than in the past but not less upbeat about our business and about our company in the long term.”

Coping with customer problems during the downturn presented new challenges for fine chemicals firms. With large drug companies that have commercial products, suppliers can use long-term contracts to keep their plants running near capacity. When it comes to smaller, cash-strapped customers, they have learned that they may have to construct more robust contracts or ones where payment is tied to success factors in product development.

“As these relationships develop, there is no doubt that they will build on what they have learned together, and we will see different arrangements constructed over time,” Ernst & Young’s Hassenplug says. The parties will have to consider whether they want traditional vendor-client relationships or more of a strategic partnership, he adds.

At the same time, to make sure that they won’t be left high and dry, customers are looking more carefully at the financial stability of fine chemicals suppliers. “Once folks go through a downturn like this and lose or have difficulty with their supplier, people move that concern up a notch in importance in their decision-making,” SAFC’s Feldker says. It’s one reason, he says, that some key customers are asking SAFC to handle

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everything from raw materials and intermediates through to the final API.

Similarly, customers are worried about quality and what it will cost them if it's not there, particularly in light of product contamination scares out of China. These concerns are expected to outlast the current economic troubles. "It's more of a systemic issue that is causing this," Feldker says. "It is truly a systemic breakdown of the supply chain in Asia."

Increasingly, large drug companies are taking the cost of quality into consideration when they construct their supply chains. "Whereas everybody was running over to Asia before in droves for the low cost, you really are seeing people take their foot off the accelerator because it could cost a lot more down the line if they don't have a very high quality supplier," Feldker says.

Ash Stevens' Munk agrees. "People are becoming increasingly leery of Asia," he says, because of product quality and safety problems in China and project management and timeline issues encountered in India. "There are some remarkably good companies there, and we certainly use India in particular, but also China, to buy raw materials," he says. "In today's world you have no choice but to be cost competitive yourself."

**For final** API production, however, Munk and other Western executives see drug companies turning to them for business. "I think there are a lot of opportunities for U.S. companies," Munk says. Relative to Asian firms, "what we can sell today is good project management skills, good regulatory compliance, and easy communication," he says.

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**Pfizer CentreSource** (PCS) has seen its steroid business based in Kalamazoo, Mich., benefit from changes in China. Consolidation driven by environmental concerns has led to one-tenth the number of Chinese suppliers of diosgenin, a raw material the Chinese use to make steroids, says Jeffrey W. Frazier, global marketing vice president for fine chemicals at PCS.

"This has stabilized supply and demand and has created more stable pricing throughout the steroid supply chain coming out of China," Frazier says. "China also wants to bolster its internal drug industry, and Chinese companies are looking to serve that market rather than solely be exporters."

Internally, PCS has optimized its large-scale production capabilities. "We've looked for ways to shorten processes, boost throughput, and get overall costs down," Frazier

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says. "We have also implemented a green chemistry option that is tremendously less stressful on the environment yet gives us the ability to produce material at the desired cost."

Similarly, the Pfizer Global Manufacturing facility in Kalamazoo has large-scale, regulatory-compliant fermentation capacity that it will be offering to select markets. "There is plenty of fermentation capacity for commodity products but not for products with high quality requirements, especially at the scale we can offer," PCS President Michael J. Kosko explains. The next step is finding projects that fit this niche offering.

Overall, Kosko is optimistic about business. "This past year has been a very successful year," he says. "We have been able to maintain and improve most of our market positions, so from a revenue and profit standpoint we met or exceeded our commitments to Pfizer Global Manufacturing and to Pfizer."

For U.S. companies competing with overseas firms, the weakness of the dollar puts them in a better situation, says Jeffrey M. Evans, a partner in the Syracuse, N.Y.-based consulting firm [Rondaxe](#). Although prices are relatively cheap in the U.S., capital isn't available to domestic buyers. "There's more interest in overseas companies acquiring U.S.-based operations," he says.

**Looking ahead**, some trends are expected to reverse. Many industry observers believe that it will only be a few years before Asian suppliers have addressed quality and environmental issues to become formidable competitors.

Large drug companies should eventually sort out their businesses and start to outsource more, fine chemicals executives expect, especially as many of them back away from manufacturing and sell their plants. At the same time, public scrutiny of drug prices will mean continued pressure on custom chemical firms to manufacture at the lowest possible cost.

Money from investors is expected to return to emerging drug and biotech firms, allowing them to restart development projects. "It's not the exuberance that we experienced a few years ago, but rather a deliberate engagement with the most promising clinical and preclinical assets," Evans says. "We should see opportunities with a higher than average chance of clinical and commercial success going forward, thanks to a more critical level of diligence by the investment community."

It will take several months, however, for that money to show up in the contract manufacturing industry, which means things should look better later in 2010. "I believe this will translate into a positive business climate for the more reputable firms in the service and supply industries," Evans says. "Marginal providers will continue to be

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stressed, however, and will need to continue to focus on enhancing the quality of their staff, capabilities, and services to remain competitive.”