
Pharmaceutical Makers Look For Ingredients Closer To Home

By Gordon Graff

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Has the mounting wave of outsourcing manufacturing of ingredients to Asia by U.S. pharmaceutical manufacturers run its course? While there are no hard and fast statistics to prove this, circumstantial evidence suggests that importing active drug ingredients from Asia has lost its allure for at least some U.S.-based companies.

Safety and security of the supply chain probably head the list of reasons why some U.S. drug makers are re-evaluating foreign sourcing, especially in light of last year's illnesses and deaths linked to tainted heparin imported from China. But escalating costs of manufacturing in Asia, plus a host of logistical issues, are convincing some U.S.-based pharma players that it may be best to manufacture their critical ingredients closer to home, at least in the early stages of drug development.

For the past decade, outsourcing of pharma ingredients has shifted steadily from the U.S. to Asia. But now "the pendulum is beginning to swing the other way," says Helena Champion, a principal at Drug Quality Assurance, a Winchester, Mass. consulting firm. "Certainly it was very attractive to have all those savings" from outsourcing to China or India, she adds. "However, the reality of the tremendous costs required to monitor quality at remote manufacturing locations abroad is just hitting home," she continues. When these costs are factored in, says Champion, expectations of a huge economic windfall from foreign sourcing "are not that realistic."

When it comes to the production of active pharmaceutical ingredients (APIs), "we are seeing more work coming back to the U.S. from Asia due to safety and compliance issues," says Stephen Munk, president and CEO of Detroit-based Ash Stevens, a contract drug development firm. Ash Stevens recently announced a \$6 million expansion of its API manufacturing facility in Riverview, Mich. Explaining the U.S. expansion, Munk acknowledges that "cost effectiveness is important" to his customers, but so is quality and the ability to deliver finished products reliably.

"The difficulty of communicating across many time zones" is a concern for customers, who "demand prompt communication and solutions to any issues that come up," Munk adds. "Being close to our customer base allows us to respond to these situations more quickly."

Another company that is cutting a larger profile on the U.S. API manufacturing scene is

Cambridge Major Laboratories, which does developmental and commercial chemical synthesis work for pharmaceutical and biotechnology clients. Earlier this year, the firm dedicated a new API production facility at its Germantown, Wis. headquarters. The unit is a large one, with an installed capacity of 18,000 gal., and is GMP (good manufacturing practices) certified, meaning that it meets government standards for handling sensitive drug materials.

Why expand in the U.S. when so much contract manufacturing for pharma is still going abroad? Cambridge Major's president and CEO, Michael Major, says more and more U.S.-based drug companies—his customers—are seeking "solid, robust API manufacturing capabilities within the U.S." These customers, he notes, are tired of the hassles of foreign outsourcing.

"They want to have guarantees that there will be no hidden costs, like constant foreign travel or hiring translators," says Major. "Also, they don't want to worry about whether their suppliers conform to GMP standards, or whether there are IP [intellectual property] issues."

Chemical giant Sigma-Aldrich Fine Chemicals (SAFC) has also been beefing up its U.S. presence in API manufacturing. The company is adding API manufacturing capacity in Verona, Wis., and is enlarging its viral products production capacity in Carlsbad, Calif. But Dave Feldker, vice president of SAFC Pharma, says these expansions are near existing facilities, so expanding at those U.S. locations is simply a case of not wanting to spread the company's "core competencies" around the world.

"If we had something that was a core competency in Asia, we would expand there," Feldker comments. In fact, he says SAFC has "strategic plans to expand in Asia" as the need arises.

Indeed, it is possible to oversell the case that production of pharmaceutical chemicals is migrating en masse back to the U.S. "The heparin affair of last year heightened concerns about overseas sourcing of pharma ingredients," says Bhaskar Venepalli, president of CiVentiChem, a Research Triangle Park, N.C. contract research firm that does custom syntheses for drug development clients. "But there is no wholesale rush to return sourcing to the U.S. because of the economic advantages of Asian sourcing, principally in China and India."

But those economic advantages are getting slimmer. "The competition for labor in China is driving labor rates up," says Feldker, and "the cost of quality is also starting to drive pricing up in China and India." Overall, he adds, costs of pharma ingredients

out of Asia are still "probably slightly under" those sourced in the West, but tags for the Asian products "have almost doubled just in the past 18 months or so."

Beyond the selling prices for pharma chemicals, various other factors can increase the actual costs of sourcing in Asia. "Any small delay" in product deliveries "can easily wipe out cost savings associated with low-cost geographies," says Munk. Also, more than 25% of the cost of GMP work can be attributed to compliance with regulatory standards. So as Asian producers continue to harmonize their standards with the West, he says, their own costs will rise, further reducing their price advantage.

Even if pharma chemical buyers can still get a small edge on prices in Asia, that may not be the main reason they source there. "Some of the drug ingredients people want to buy have no source of manufacturing in the U.S.," says Ving Lee, CEO of Adesis, a New Castle, Del. firm that provides chemistry support services for early drug development. In that case, he notes, they have no choice but to buy the needed materials where they are available, which is often in Asia.

But when U.S. buyers do have a choice between domestic and overseas sourcing, they often select the U.S. or Europe for the more critical compounds. "From the customers' perspective," says Feldker, "generally speaking, the higher value pieces of the process they want closer to Western assets."

According to Major, North American clients in the early stages of drug development prefer to source at U.S. firms like his own, but when their products go commercial, they may later turn to China or India for sourcing.

In fact, the most successful pharma chemical firms have learned to leverage the best of U.S. and Asian sourcing, observes Paul Vogt, a vice president at SiGNa Chemistry, a pharmaceutical technology provider. Typically, he says, these firms have a "global presence," with facilities in the U.S., Europe and Asia, and the ability to deal with all the technological, financial, regulatory and intellectual property issues that arise in all three regions. So they may capitalize on the low costs in Asia, but make sure that their materials and procedures meet the safety requirements of U.S. regulators.

Regardless of where a compound comes from, purchasers must perform "due diligence" to make sure the chemical analyses and manufacturing data on the label are accurate, Champion emphasizes. (Inadequate auditing of shipments and mislabeling were widely blamed for the heparin fiasco.) "It's no longer enough to just trust your supplier," she says. Current U.S. laws for APIs "require that you be able to trace each shipment back to the plant it was manufactured in, no matter how remote."

Some larger pharma chemical suppliers, such as SAFC, have recently launched auditing services for their customers. And last June, a coalition of pharmaceutical and fine chemicals suppliers, as well as pharma trade groups, formed a global consortium called Rx-360. The aim of the group is to develop uniform standards for auditing pharmaceutical chemical shipments, disseminate analytical methods for spotting contamination and act as a clearinghouse for information about suspicious suppliers or practices.

Active pharmaceutical ingredient market at a glance

Pharmaceutical products market worldwide (2010, projected) ¹	\$825 billion
Growth of pharmaceutical products worldwide (2010, projected) ¹	4–6%
Average annual growth of pharmaceutical products worldwide (2009–2013) ¹	4–7%
Percent of drug firms planning to increase procurement spend in next 12 months (Global survey, 2009) ²	40%
Active Pharmaceutical Ingredient (API) market (2007, worldwide) ³	\$78 billion
Active Pharmaceutical Ingredient (API) market growth (North America, 2009) ⁴	2%
Projected API average annual market growth (2008–2020) ⁴	China — 32.2% India — 24.1%
Portion of API market that is outsourced (2009) ⁵	30%
API small-molecules average annual market growth ³	5–6%
API biologicals average annual market growth ³	12–15%
Contract-manufactured APIs, by revenues, consumed in generic drugs ³	2007 — 45% 2011, projected — 52%

¹Source: IMS Health Inc. ²Source: ICD Research ³Source: Frost & Sullivan ⁴Source: Global Markets Direct ⁵Source: Ferro Pfanstiehl Laboratories