Plant in China under scrutiny

Initial testing finds irregularities with blood thinner heparin made at the facility

By Don Lee and Ricardo Alonso-Zaldivar
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CHANGZHOU, CHINA — The maker of a blood thinner suspected in four U.S. deaths and allergic reactions in 350 people said Tuesday that its investigation was focusing more closely on whether something went awry during the processing of ingredients in China.

Baxter Healthcare Corp. spokeswoman Erin Gardiner said testing had detected irregularities in samples of the drug, heparin, that were processed in China from raw material extracted in China. No such irregularities were detected in heparin made from raw materials from China but processed at a supplier's plant in Wisconsin. Gardiner stressed that the findings were preliminary and that the company had reached no final conclusions about what caused the adverse reactions among patients.

Baxter has said that a Chinese plant here, Changzhou SPL, was the source of much of the active ingredient in its heparin. The U.S. Food and Drug Administration said it never inspected the factory because the agency mixed up the company with another one that has a similar name. Changzhou SPL apparently wasn't examined by Chinese drug regulators either, because it isn't licensed as a pharmaceutical manufacturer with the Chinese government.

Such bureaucratic oversights are of growing concern in the U.S., given that China accounts for about 22% of the foreign factories producing drugs for the American market -- more than any other single country. Yet facilities in China accounted for only 6% of the overseas inspections conducted by the FDA from 2002 to 2007.

A report by the Government Accountability Office last fall found that the FDA conducted 88 inspections in China during the five-year period, from a low of nine in 2003 to 21 in 2005. That means the vast majority of the 714 Chinese facilities involved in making drugs for the U.S. market were not inspected. By contrast, Italy, with 150 manufacturing facilities, underwent 131 inspections over the five years.

The FDA has said it would inspect the Chinese factory that was the source of Baxter's heparin this week but didn't specify when.

Heparin is derived from pig intestines, and China has come to dominate the global market thanks to its abundant supply of swine and low labor costs. The country exported more than $100 million worth of heparin ingredients last year, according to various estimates.

Changzhou SPL -- a joint venture that is 55% owned by a Wisconsin company and 45%

by a Chinese partner -- was China's sixth-largest exporter of heparin ingredients last year by volume. On Tuesday, Changzhou SPL maintained its silence. Employees and guards at the plant, located amid farmlands on the edge of this dusty city west of Shanghai, refused to comment.

But about 10 miles to the north, another leading maker of heparin ingredients welcomed a reporter to tour its facility and ask questions. Managers at Changzhou Qianhong Bio-pharma Co., China's second-largest exporter of heparin, provided copies of certificates from regulators in China and Europe, its primary export market. They showed fingerprint scanners at entrances, labs and clean rooms.

Chen Honglei, Qianhong's export manager and an 18-year industry veteran, said that he hadn't been inside Changzhou SPL's operations but that the production processes at the major heparin ingredient manufacturers in China were similar. He added that SPL had an experienced team led by Wang Yan, who came from SPL's American owner, Scientific Protein Laboratories of Waunakee, Wis., which has been making heparin's active ingredient in the U.S. for three decades.

Changzhou SPL "is quite well known. It enjoys a good reputation," Chen said.

Yet like most everybody else in the industry, Chen was puzzled why that plant wasn't licensed with the Chinese drug regulatory agency. According to China's State Food and Drug Administration database, 32 companies are registered to produce heparin compounds.

"That company is not a pharmaceutical manufacturer, so it has no license," State FDA spokesman Shen Chen said of Changzhou SPL. He declined to comment further. The agency has yet to release any information on the matter.

Licensed pharmaceutical plants in China say Chinese regulators have typically visited at least once a year, although that has increased in recent months as China's drug and food safety practices came under global scrutiny after recalls and product scares involving Chinese-made medicine, toys and pet food. Changzhou Qianhong, for example, said it was inspected three times last year, twice unannounced.

Usually the FDA will make an on-site visit before a new foreign drug or active ingredient maker is allowed in, but the mistake with Changzhou SPL has drawn fire from members of Congress. Changzhou SPL started operations in 2004.

The FDA says it is aware of only one other Chinese company that ships the active ingredient for heparin to U.S. pharmaceutical makers that produce and sell the finished drug. That company, Shenzhen Hepalink Pharmaceutical Co., said the FDA inspected its facility several years ago before issuing a certificate for sales to the U.S.

Shenzhen Hepalink, China's largest exporter of active ingredients for heparin, is a supplier to Baxter's Illinois rival, APP Pharmaceuticals Inc.

Chinese producers of heparin ingredients have been exporting to Europe for two decades and to the U.S. for several years. Shipments have grown briskly, although the volume shrank last year because a shortage of pigs led to a sharp increase in prices. Intestines from about 3,500 pigs are needed to make about 2.2 pounds of active ingredient for injectable heparin.

There are no squealing pigs at Changzhou Qianhong's sprawling facility. Rather, shipments of extracted ingredients in granule form come into Qianhong's operation, where impurities are removed.

Jiang Wenqun, Qianhong's deputy general manager, said the company spent about $17 million to build a 22,000-square-foot active ingredient plant, which began operations four years ago. The private firm, which employs about 260 people and also makes finished heparin and other compounds, has been exporting since 1991. Last year, she said, its revenue surpassed $42 million, with a little more than half of that coming from heparin exports.

Managers at Qianhong said the investigation of the Baxter drug hasn't hurt sales, although their European clients have called asking about the matter. "I'm not worried," said Chen, Qianhong's export manager. "After all, this is a very old product. We've been producing it for decades."

don.lee@latimes.com

ricardo.alonso-zaldivar@latimes.com

Lee reported from Changzhou and Alonso-Zaldivar from Washington.