Merck sought to trim Vioxx risk

By Thomas Ginsberg
Inquirer Staff Writer
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Three years before Merck & Co. Inc. conceded that its pain-reliever Vioxx had safety problems, the company tried to patent a way to reduce heart-attack risks for users of the drug.

Merck's 2001 patent application and internal discussions about it raise new questions about the drug maker's actions around Vioxx, which was withdrawn in September after company-sponsored studies showed it caused heart attacks and strokes.

Merck discussed and pursued the patent while it was publicly denying that Vioxx could cause heart attacks and strokes. It never followed through on the patent application, a Merck attorney said.

The recall has rattled the drug industry, prompted calls for changes in the federal drug-safety system, socked Merck's fortunes, and sent millions of patients worldwide scrambling for new treatments.

More than 2,000 Vioxx users so far have filed product-liability and fraud lawsuits against Merck, alleging it long knew about the risks but did not warn patients or regulators. Equity analysts have estimated that damages could reach billions of dollars if Merck loses.

Merck denied the allegations yesterday, saying it recalled Vioxx as soon as reliable studies proved a conclusive link to heart attacks and strokes.

In response to questions from The Inquirer yesterday, Merck attorneys said in a statement that the patent application proves only that the company sought to help Vioxx users who had switched off aspirin, which is known to help prevent heart attacks by acting as a blood-thinner.

"This patent application has nothing to do with Merck's firm belief in the cardiovascular safety of Vioxx," Kent Jarrell, a spokesman from Merck's outside law firm, Hughes Hubbard & Reed, said in a statement.

Plaintiffs' attorneys, however, contend that an internal Merck document proves that Merck executives sought the invention to counter Vioxx's tendency to cause blood clots, according to a ruling released Friday by New Jersey Superior Court Judge Carol E. Higbee.

The internal document, titled "Confidential Memorandum of Invention," is a memo between company executives and their patent lawyers. Higbee ruled Friday that because Merck inadvertently gave it to plaintiffs' lawyers, the company can take it back under attorney-client privilege.

In the 2000 internal document, according to a copy obtained by the Associated Press, Merck executives stated that the way in which Vioxx reduces pain might also increase cardiovascular problems. They raised the idea of seeking a patent for a method of combining Vioxx with another agent to lessen the risk.

Plaintiffs' attorneys say the memo and subsequent patent application prove Merck knew that Vioxx could cause heart attacks and strokes. Merck says the evidence merely shows Merck was concerned about Vioxx users already at risk for heart attacks.

While siding with Merck in the procedural ruling, Higbee made clear that she considers the patent issue potentially crucial to the case.

"The court recognizes this is a serious and important point of contention," wrote Higbee, whose court is in Atlantic City. "Merck is ordered to produce any and all information regarding the invention that is not otherwise privileged."

Garret Fitzgerald, a University of Pennsylvania scientist and Vioxx critic whom Merck once paid to study the drug, said the patent application was nearly identical to a fix he had proposed privately to Merck in 2000.

"Quite frankly, you should be fired if you were not thinking about doing this," Fitzgerald said in a telephone interview yesterday.

The patent application, dated May 14, 2001, and obtained from the U.S. Patent and Trademark Office, lists its top inventor as Edward M. Scolnick, former president of Merck Research Laboratories. Scolnick also was involved in writing the confidential internal memo, according to Higbee's ruling.

In the application, Merck sought to patent the idea of supplementing Vioxx with a substance which, like aspirin, would protect against cardiovascular problems caused by blood clots.

Vioxx, known as a COX-2 inhibitor, was developed to relieve pain without causing the gastrointestinal problems of aspirin and other traditional pain relievers. Aspirin, however, is known to help cut the risk of heart attacks by preventing clots, known as "thromboembolic events."

"The present invention concerns a method for treating patients with COX-2-mediated conditions, and who are also at risk of developing thromboembolic events," the application said.

It staked a claim on the idea of adding, either directly to Vioxx or as a supplemental medication, a compound known as "thromboxane synthase inhibitor," which mimics aspirin's cardioprotective action.

"For patients who are taking COX-2 selective inhibitors and who may benefit from the cardiovascular protective effect of aspirin, there remains a need for a cardiovascular protective treatment that does not expose them to increased risk for gastrointestinal side effects," the application said.

The application did not explicitly blame Vioxx for the blood clots. Instead, it asserted that people at risk of blood clots would not be getting the benefit of the older painkillers.

The patent also did not limit its scope to Vioxx. It mentioned all COX-2 inhibitors and many possible aspirin-like compounds.

Fitzgerald, the Penn professor, said he had told Merck in 2000 that the French pharmaceutical firm Servier was developing a "thromboxane synthase inhibitor" that might counteract the Vioxx-related health risks, no matter how they were caused.

It was unclear whether Merck and Servier discussed the idea. Servier's media office did not return a phone call from The Inquirer at closing hours yesterday Paris time.

A Food and Drug Administration official estimated last year that Vioxx caused 139,000 fatal and nonfatal heart attacks and strokes since its 1999 launch.

Since the recall, however, FDA advisers have concluded that Vioxx is safe enough to be used with a special warning. Merck has not said whether it would relaunch Vioxx.

Merck has its headquarters in Whitehouse Station, N.J. Much of Vioxx's global marketing, sales, legal and eventual recall work was done from its 10,000-worker complex in West Point, Montgomery County.