U.S. Not Told of 2 Deaths During Study of Heart Drug

By Stephanie Stahl
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The Scios unit of Johnson & Johnson yesterday added to the questions already clouding its heart failure medication Natrecor, saying the company had failed to tell federal regulators about the deaths of two patients in a clinical trial of the drug.

The two deaths were also omitted from a report of the trial published in October in The Journal of Emergency Medicine, the company said. That article reported 6 deaths within 30 days among 237 patients given Natrecor or other treatment in hospital emergency rooms in 2001 and early 2002. Five of those deaths were of people who had taken Natrecor.

The two additional deaths raised the total to seven among Natrecor patients, although Scios said yesterday that the difference did not change the safety assumptions about the drug.

Neither Scios nor Dr. W. Franklin Peacock 4th of the Cleveland Clinic, the principal investigator in the study, disclosed yesterday how the deaths had been omitted from the results, but said they had learned only recently that the deaths occurred within the 30-day study period. A final analysis of the results is under way and will be submitted to the Food and Drug Administration, said Mark Wolfe, a Scios spokesman. He said he did not yet know the causes of the two additional deaths.

But a spokeswoman for the Cleveland Clinic, Eileen Sheil, said that Dr. Peacock strongly believed that the deaths had been accidental and not related to problems with Natrecor.

Natrecor, which the F.D.A. approved in August 2001 for use in acutely ill heart-failure patients, became a big seller for Scios. Sales were helped by use of the product in less severely ill patients, known as off-label use, sometimes in outpatient clinics in cardiologists' offices.

After achieving sales of $400 million in 2004, though, Natrecor's growth failed to meet forecasts last year after questions arose about its safety and whether it was effective enough to justify a cost of about $500 a treatment, compared with much cheaper alternatives. The Justice Department is also investigating whether Scios promoted the drug for unapproved uses. And the government recently announced that Medicare and Medicaid would no longer cover the drug's outpatient use.

Scios consistently defended Natrecor's safety. But the failure of researchers to accurately collect and report the death data in the Natrecor trial comes amid questions elsewhere in the medical industry about the accuracy of studies of drugs and medical devices.

"When you're talking deaths in clinical trials, mistakes are not an option," said Dr. Arthur Caplan, a medical ethicist at the University of Pennsylvania. "It's just an area where we have to have absolute, foolproof reporting in place."

Last month, the drug maker Merck was accused of misrepresenting the results of a clinical trial of the painkiller Vioxx to minimize its heart risks. The study was published in November 2000, almost four years before Merck stopped selling the drug amid safety concerns.

The Vioxx accusation came from Dr. Gregory D. Curfman, the editor of The New England Journal of Medicine, who said the authors of a Vioxx study had deleted data about strokes, heart attacks and other vascular problems suffered by some patients. Merck has denied mishandling the data submitted for publication.

While the findings of the Natrecor study were presented earlier at medical conferences, it was not until October that the complete results were published in The Journal of Emergency Medicine. At that time, Dr. Peacock and colleagues, who included a Scios executive, reported that five Natrecor patients had died within 30 days. The deaths included those from causes clearly not related to Natrecor use, including an accident, the study reported.

In the meantime, Scios had undertaken a retrospective review of the study to look at mortality in patients up to 180 days after treatment. It was during that review, according to the Scios spokesman, Mr. Wolfe, that the two additional deaths among Natrecor patients within the 30-day period were discovered. When the company learned of those deaths, it notified the F.D.A. and Dr. Peacock, Mr. Wolfe said.

Ms. Sheil, the spokeswoman for the Cleveland Clinic, said Dr. Peacock learned of the additional deaths in September and notified The Journal of Emergency Medicine, but the article had already been published. Its authors say they will update it once the analysis by Scios is completed, sometime in the next few months.