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GE's Own Safety Team Urged Company to Restrict MRI Drug

by [Jeff Gerth](#), ProPublica - April 15, 2010 5:50 pm EDT



GE healthcare event in NYC (Daniel Acker/Bloomberg)

GE Healthcare ignored the advice of its own safety experts to “proactively” restrict use of its imaging drug, Omniscan, after reports in Europe linked the drug to a potentially crippling disease, according to a newly unsealed order in a lawsuit against the company.

The recommendation came at a May 2006 meeting convened by the company's vice president for drug safety. But instead of immediately alerting doctors to stop using the drug in high-risk patients, GE spent the next year arguing that approach wasn't necessary, even as some government and radiological experts favored such a ban.

GE publicly took the position that its drug was no more dangerous than those of its competitors and argued against putting an exclusive warning on the drug's label. It wasn't until September 2007, after pressure from federal drug regulators, that GE and manufacturers of similar drugs revised their labels to warn that patients with serious kidney impairment have a greater risk of [nephrogenic systemic fibrosis](#) [1], or NSF.

The order by a Chicago judge became public this week in one of the approximately 500 lawsuits filed by NSF patients against GE. It provides the first public glimpse at internal documents and other evidence the company has successfully fought to keep sealed.

Plaintiffs' lawyers say the May 10, 2006, meeting is pivotal because many patients were exposed to Omniscan afterward. According to the judge's order, an “action” item at the end of the meeting

minutes stated, [“We should proactively propose to restrict the use of Omniscan in patients with severely impaired renal function.”](#) [2]

The order also references previously sealed evidence indicating doctors and the U.S. Food and Drug Administration [had not seen internal company](#) [2] research that raised questions about Omniscan’s propensity to break down chemically, releasing the potentially toxic metal gadolinium into the body.

Cook County Circuit Judge Deborah Mary Dooling said the evidence she reviewed was sufficient to add a claim of punitive damages, which could have greatly increased GE’s financial exposure. But with a trial set for April 20, the parties reached a confidential settlement.

[\(Document Viewer: Read the judge's order](#) [3])

Jeff DeMarrais, a spokesman for GE Healthcare, said Thursday that by the time of the May 2006 meeting, the company had already issued a “global safety alert” to regulators. A few weeks later, GE also [sent a letter](#) [4] to doctors about the NSF cases stating that a “causal relationship” between NSF and imaging drugs “has not been established.”

“The company promptly and proactively engaged with regulatory agencies worldwide consistent with Dr. Flaten’s recommendation,” he said, referring to Dr. Hugo Flaten, the vice president of Global Pharmacovigilance, who led the internal meeting.

DeMarrais also said GE has been dismissed from 140 Omniscan cases without any payment and that it has settled “a number of cases,” mostly in state courts. A substantial majority of the cases against GE are in federal courts.

He declined to say how many NSF patients had been exposed to Omniscan after the May 2006 meeting. “It is difficult to put an exact number on this,” DeMarrais said in an email.

Imaging agents such as Omniscan have become an essential part of medical diagnostics, with millions of doses safely administered worldwide each year. Patients are injected with the drugs, which make it easier to read MRI scans. Omniscan belongs to a class that use gadolinium as the key ingredient. Healthy kidneys normally filter out the metal.

Concern about Omniscan first surfaced that April when researchers in Denmark and Austria published studies saying 25 patients, all of them with severely impaired kidneys, had contracted NSF after undergoing magnetic resonance scans with Omniscan. The disease can cause a painful hardening of skin around joints and can affect internal organs.

A few of GE’s competitors also have been sued by NSF patients. But some doctors and drug safety experts, including key medical reviewers inside the FDA, have singled out Omniscan as riskier, in part because of studies suggesting it is less chemically stable. Research by GE Healthcare and other manufacturers is ongoing into the causes of NSF and the possible role of gadolinium, a key ingredient in all the drugs.

GE denies that Omniscan is less stable. The company has maintained, and the FDA so far has agreed, that because “differential risk remains unproven” the various contrast agents on the market should be treated uniformly as a class.

Dr. Sidney M. Wolfe, who heads the health research arm of the consumer group Public Citizen, said he it was troubling that Omniscan research may have been withheld.

“I’m concerned, after reading the court order, and as a member of the FDA’s Drug Safety Advisory Committee, that there may be evidence pertinent to the safety of this drug that was not promptly or not completely sent to the FDA,” Wolfe said.

Last December, Wolfe and most other members of an FDA advisory panel, [recommended that the agency revise its policy and effectively ban](#) [5] use of Omniscan and one other contrast agent, Optimark, for patients with severe kidney disease.

The daylong hearing, and the accompanying submissions by GE and the FDA, did not reference some of the internal studies cited by the Judge Dooling, including a 1989 draft report by a GE Healthcare predecessor company, Nycomed, whose scientists were conducting toxicity studies before Omniscan was approved by the FDA in 1993.

According to judge’s [order](#) [6], the draft Nycomed report “concluded that Omniscan caused the highest retention of gadolinium in the liver as compared to other gadolinium contrast agents tested.” The finding “could be taken as an indication for the relative instability of [Omniscan],” Dooling wrote, quoting an exhibit in the case.

GE did not dispute that the draft report was never submitted to the FDA, Dooling’s order states, but said a final version of the Nycomed study dated May 28, 1991, “was submitted to the FDA with complete findings and conclusions.” The judge noted, however, that the final report “does not reference” findings in the 1989 draft.

DeMarrais said Thursday that GE “and its predecessors have fully and responsibly complied with their regulatory obligations in submitting data to the FDA.”

The FDA is still reviewing the advisory panel’s recommendation to restrict Omniscan and Optimark, according to Karen Riley, a spokeswoman for the agency.

In spring of 2007, the while FDA considered a labeling change for gadolinium-based imaging agents, [two medical reviewers](#) [7] at the agency [independently recommended](#) [8] that Omniscan be banned for patients with severe kidney disease.

An outside expert had the same opinion. Dr. Emanuel Kanal, head of a blue-ribbon panel on magnetic resonance safety for the American College of Radiology, said this week he was “surprised” to learn that GE insiders also had advised restricting the drug.

Judge Dooling’s order allowing a claim for punitive damages was signed April 2 and made public this week.

DeMarrais said the “order was a preliminary ruling under a unique Illinois procedural rule” and “did not mean that a claim for punitive damages would have been allowed to be submitted to a jury for consideration.”

But Tor Hoerman, the attorney for 57-year-old plaintiff Robbie Booker, differed. The judge “had an opportunity to analyze a lot of evidence, and chose to enter a rather detailed, fact-based order rather than a brief procedure-based order,” he said.

Dooling reasoned that there was a "reasonable likelihood" the plaintiffs might prove to a jury that GE engaged in willful misconduct, the standard for punitive damages. If the evidence were proved at trial, she wrote, the "jury could properly conclude" that GE Healthcare "[engaged](#) [6] in a course of action that showed an utter indifference to or conscious disregard for the safety" of patients with impaired kidneys.

Hoerman noted that Dooling’s opinion does not apply to the hundreds of federal NSF cases being coordinated by a judge in Cleveland. That judge, in a ruling last fall, allowed GE Healthcare to keep sealed, for the time being, internal corporate documents.

Last year, lawyers for the NSF plaintiffs estimated the litigation could cost the conglomerate \$1 billion. GE vigorously disputes this figure, saying it is grossly inflated and that its exposure is so small there is no need to disclose the lawsuits to investors.

Booker’s lawsuit says she had severe kidney disease for more than a decade and was diagnosed with NSF in October 2007. The disease left her completely disabled, profoundly disfigured and suffering from severe leg, arm and shoulder pain.

Booker says she received 11 injections of Omniscan, all but one of which took place before 2007.