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Germ Watch

Clinic Infections Put a Sterilizer Of Lab Devices Under Microscope

Maker of Widely Used System Defends Its Effectiveness After Bacterial Outbreaks

Word of a Probe by the FDA

BY PAUL DAVIES

PITTSBURGH -- Two years ago, the chairman of medicine at Allegheny General Hospital here wrote to more than 500 former patients warning that they might have been exposed to deadly bacteria during a simple test at the hospital.

The warning was too late for Earl Foster. He had his lungs examined at the hospital with an endoscope, a tubular device with a tiny camera and light. Days later, he died of pneumonia, which the hospital and a coroner linked to bacteria from the endoscope. In all, 16 patients who had such procedures picked up the bacteria, and nine died, according to the hospital. It didn't attribute the other eight deaths to the infection.

After a two-month investigation, the hospital told the Food and Drug Administration that water filters in a device used to sterilize the endoscopes can lead to bacteria in the rinse water, and this was the "probable cause" of the outbreak.

The maker of the sterilizing device, Steris Corp., denies it is to blame. It says its own inquiry concluded the hospital might not have followed proper cleaning and disinfection procedures in using its sterilizer, called the System 1. The company says the product's effectiveness has been confirmed repeatedly through studies and millions of sterilizations, "and has never been directly linked with any incidences of infection when used according to the directions."

The FDA, which cleared the sterilizer 16 years ago, challenged it twice after that, in 1999 and in 2001, eventually resolving the issues. But Steris said in a corporate filing for its June 30 quarter

that it was being investigated by the FDA and the U.S. Justice Department. Steris says it hasn't been contacted by investigators but will cooperate, and that as far as it knows the investigation is continuing.

The probe apparently sprang from a fired Steris executive's assertion, in Ohio state court in Cleveland, that sterilizer failure has led to injuries or death and that Steris "engaged in a persistent pattern of destroying evidence." The wrongful-termination suit was quickly settled, and the executive, Larry Joslyn, declines to comment. Steris says that the executive hadn't worked with the System 1, that it believes his claims about the product were meritless, and that it isn't aware of any document destruction.

The disputes about Steris underscore a persistent issue facing hospitals and outpatient clinics that use endoscopes for surgery or examinations. They do more than 10 million such procedures a year, including routine exams. Guidelines urging people over 50 to get colonoscopies have increased the number. But every year or so a facility reports an infectious outbreak among a cluster of patients who had endoscopic procedures.

Tracing the cause is always hard. Hospitals' inquiries almost always point to improper cleaning of endoscopes or misuse of attachments in the cleaning process. In two cases, including Allegheny General's, inquiries by hospitals or doctors have turned up bacteria in the Steris sterilizer's water rinse, which ought not to have any. Steris doesn't make endoscopes, just the sterilizing system.

Steris says reports it has gotten represent "one potential (not actual) incident for every 5.2 million uses of System 1."

Complicating the matter are some conflicting recommendations about how to carry out the sterilizing process -- including one suggestion that federal health officials put forward, but Steris rejects.

Moreover, some scientists who have studied the issue caution that instruments that work perfectly in a laboratory setting can be less reliable in the real world of a bustling hospital.

Endoscopes cost \$10,000 to \$70,000, and financial pressures drive hospitals to quickly clean and reuse those they own. A busy hospital might use one such instrument in as many as 10 patients in a day. That puts a premium on speed, and here Steris has a big advantage. It can reprocess an endoscope in just 30 minutes, by using liquid chemicals to kill germs. Competing methods, such as ethylene oxide gas, take up to 24 hours.

Although other firms make speedy cleaning systems, the FDA permits them to claim only "high-level disinfecting," not full sterility, as Steris can. The result is that Steris dominates the market for quick cleaning of endoscopes used in surgery, where full sterility is essential. For routine screening such as colonoscopy, its system is also widely used but not as dominant. In all, Steris says, the System 1 is used 35,000 times a day, by more than 5,000 U.S. medical facilities.

Steris was founded in 1985 by a microbiologist and a mechanical engineer. It got FDA approval for the System 1 in 1988 through a method that didn't

require clinical trials: by simply convincing the FDA its system was "substantially equivalent" to existing sterilization methods. After that approval, the Mentor, Ohio, company quickly began winning hospitals' and clinics' business. Publicly held since 1992, it has about \$1 billion in annual revenue, of which \$150 million to \$200 million comes from the System 1, by analysts' estimates.

When Steris has faced criticism of the device, it has defended it staunchly, including at times by hinting at legal action.

Six years after it hit the market, it faced a challenge from an independent agency that evaluates medical devices, ECRI Inc. A bioengineer there, Lawrence Muscarella, concluded that the System 1 couldn't guarantee sterility in endoscopes that are flexible, a common kind especially hard to sterilize. He proposed rating it "not recommended -- conditionally acceptable." ECRI sent Steris a copy of the proposed rating for feedback.

Steris met with ECRI. It says it provided information to clarify how the system works. But Steris also sent a letter to ECRI saying that publishing the negative rating would be "willful and malicious disregard of the facts." ECRI later rated the device "conditionally acceptable," omitting the "not recommended" part.

Dr. Muscarella contends ECRI caved in to pressure from Steris. ECRI founder Joel Noble says Steris raised legitimate technical arguments that prompted the change. He says he believes the System 1 works fine and that the occasional infectious outbreaks among endoscopic-exam patients may be due to the design of the endoscopes themselves.

Months later, ECRI fired Dr. Muscarella. He sued for defamation and reached a settlement that included an apology by ECRI for false statements. He now works for a competing maker of disinfectant systems.

A microbiologist at the Centers for Disease Control and Prevention also criticized the System 1, and also faced challenge. It happened when a medical journal published a study by one of the founders of Steris in 1993. The study said a "biological indicator" -- basically, a test strip -- used to check the effectiveness of steam and gas sterilizers could also be used in a liquid one, such as Steris's.

The journal, *Infection Control and Hospital Epidemiology*, asked CDC

employee Walter Bond to respond to the study. The microbiologist wrote that scientific principles for monitoring steam and gas sterilizers can't be applied to ones using liquids. Steris officials flew to Atlanta to meet with the CDC and demand a retraction, according to people familiar with the matter. The CDC refused. Mr. Bond declined to comment.

Steris says outbreaks can result if hospital workers sterilizing endoscopes don't use proper attachments. Tubes called "channel connectors" must be properly hooked up to the instruments to help flush sterilizing fluid through them.

Reports filed by hospitals with the FDA seem to confirm that in the bustle of daily hospital care, things aren't always done exactly by the book. One such "incident report" to the FDA, for instance, said that hospital workers had "jerry-rigged" parts of these connectors.

Michelle Alfa, a microbiologist Steris hired this year to study its system, says that mistakes or misunderstandings can result from conditions in the hospital setting -- operating rooms get busy, there's employee turnover, and instructions get passed from worker to worker. "Steris tends to take a lot of flak because of the sterilization claims, but the complexity of the endoscopes makes it difficult to guarantee that they are sterilized," she says, adding: "It is a wonder there are not more outbreaks."

At New York Hospital Queens in 1998, bacteria colonized 18 patients who'd had endoscopic lung exams. One person, who already had pulmonary disease, got infected and died. The hospital concluded the System 1 worked fine. It partly blamed "conflicting recommendations" from Steris and the endoscope's maker.

There are at least two such conflicts. The FDA and CDC in 1999 suggested that hospitals "consider" adding a final step to the sterilization process: flushing an endoscope with alcohol and then air-drying it. The problem is, following this nonmandatory advisory would violate Steris's own directions for how to proceed. Steris says that endoscopes cleaned with its system should not be air-dried.

In a further legal bind for hospitals: Steris says it guarantees sterility only when the channel connectors it supplies are used in the process. But endoscope makers stand by the instruments only if connectors they make are used.

In September 1999, 13 patients at Los Angeles County-USC Medical Center were infected with bacteria after lung exams with endoscopes cleaned with the

System 1. The Los Angeles County Health Services Department concluded the instruments hadn't been cleaned in a timely fashion or -- echoing the FDA and CDC advisory -- properly dried.

It also said bacteria were found in the System 1. Although these weren't the same bacteria as in the patient outbreak, the chief of acute communicable disease control at the department, Laurene Mascola, said: "You shouldn't find bacteria in a sterile solution -- period."

A Steris spokesman, Aidan Gormley, said that the hospital "didn't use the proper culturing technique" when collecting samples and that the outbreak was due to failure to hook up connectors properly.

The FDA sent Steris a warning letter in late 1999 saying it had found a variety of "serious regulatory problems" with the System 1. It ordered Steris to take prompt corrective action. The letter said there had been at least a half-dozen infectious outbreaks in which Steris had failed to investigate adequately and report the cause to the FDA. It said "the violations...may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems."

Two years later, the FDA sent another letter to Steris raising concerns about bacterial outbreaks surrounding use of the System 1. "The association of the Steris System 1 processor with patient infections usually caused by waterborne organisms leads us to question the ability of the processor to provide sterile water rinse," wrote the FDA's consumer safety officer, adding: "We believe that the processor may not be functioning as it is labeled."

An FDA compliance official, Timothy Ulatowski, said this fall that the agency remained confident in the System 1. The FDA says matters raised in its 1999 and 2001 letters have been resolved. However, an FDA spokeswoman said yesterday that the FDA has other issues relating to Steris outstanding. It isn't clear whether they relate to the FDA probe that Steris disclosed. The FDA declines to comment on the investigation.

In the outbreak at Allegheny General Hospital in Pittsburgh in 2002, the FDA investigated but never came to a conclusion about the cause.

When the hospital itself was investigating, the CDC recommended testing the sterilizing system's rinse water for germs. Told that a Steris technician had removed the filters, making such a test

invalid, the CDC suggested the hospital send in the rinse water from another System 1. When it did so, the CDC reported back that the water contained bacteria "TNTC" -- "too numerous to count."

Steris says the test couldn't have been valid because "it is not possible to obtain a water sample from System 1 without compromising the sterility of the process." The hospital maintains it collected the sample using sterile techniques.

The hospital, in its report blaming the Steris sterilizer, theorized that filters may break down over time and let germs through. Dr. Alfa, the scientist Steris hired to study its system, also raises this possibility in an interview, but calls the System 1 "effective when used according to the manufacturer's recommendations." Steris says filters aren't a problem because a built-in diagnostic test checks their integrity.

Allegheny General's chairman of medicine, Richard Shannon, signed the letter the the FDA blaming the System 1 and spoke about it publicly. Steris says it told the hospital that he had made "threatening and libelous" statements and that the hospital and Dr. Shannon could be held responsible. Steris says this letter was a normal practice to protect itself.

Among those who became ill during the outbreak was Jerry Forsythe, 63. He had arrived at the hospital in a coma in August 2002, after a motorcycle crash. Doctors used an endoscope to peer inside his lungs to see the extent of his injuries.

In October, having regained consciousness, Mr. Forsythe was moved to a rehabilitation hospital. Doctors expected him to be home by Christmas 2002. But the lung infection slowed him down. Ten months after his crash he died, with pneumonia ruled a contributing factor. His wife and daughter are among about 20 people who are suing the hospital and Steris.

The widow of Mr. Foster, who died of pneumonia at 58 after a lung exam, received a payment from the hospital, according to a person familiar with the situation. Mrs. Foster, an employee of Allegheny General, declined to comment, as did the hospital. Steris wouldn't say whether it reached a settlement with her.

The hospital stopped using the System 1 in its pulmonary lab, site of the outbreak, which involved a resistant bacterium called *pseudomonas aeruginosa*. Instead, it's using a system

approved by the FDA in the category of high-level disinfection, not sterilization, and is adding an alcohol rinse and air drying.

Yet despite having blamed the Steris System 1 for a bacterial outbreak, Allegheny General continues to use the system with some of its equipment. The hospital says it "has implemented safety protocols...that are in addition to those recommended by Steris."

Earlier this year, Steris hired a former FDA official, Gerald Faich, to determine if there was a statistical connection between the System 1 and patient infections. Steris says he concluded it "functions well in practice and reinforces the consistent achievement of sterility by the device." In an interview, Dr. Faich says that in view of how frequently the System 1 is used -- millions of times a year -- if it really were defective, hospitals would have more bacterial outbreaks than they do.