

Who's judging drugs?

Whether a new drug makes it to market could ride on data from doctors under disciplinary measures.

By KRIS HUNDLEY, Times Staff Writer
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You might think that when pharmaceutical companies hire a doctor to test new drugs, they automatically would reject someone disciplined for "gross or repeated malpractice." You would be wrong.

Consider the case of Dr. William J. Espinoza.

Just hours after the Coral Gables surgeon performed a liposuction and tummy tuck on Osmarlyn Acosta, the 36-year-old single mother was dead.

Acosta's family said Espinoza sent her home too soon after the outpatient procedure and dismissed their concerns about her unresponsiveness and profuse bleeding. They complained to the state Department of Health, which determined that Espinoza's behavior "ultimately led to Acosta's death."

The state issued an emergency order in March 2006, restricting Espinoza from performing office surgeries. Regulators said his practice "fell below the standard of care and his failure to maintain adequate medical records presented an immediate and serious danger to the health, safety and welfare of the public."

Espinoza proceeded to ignore the state's order and operated on a patient the following month. The Board of Medicine temporarily suspended his license, put him on two years' probation and fined him \$15,000.

The board cited the 69-year-old doctor for failing to keep adequate medical records or practice medicine "with that level of care, skill and treatment which is recognized by a reasonably prudent similar physician as being acceptable."

But such criticism did not interfere with Espinoza's ability to conduct drug studies for pharmaceutical companies. After Acosta's death, the doctor registered with the U.S. Food and Drug Administration to run four clinical trials. At least one of them was conducted while Espinoza's license was suspended.

Acosta's daughter, Banesa Bernal of Miami, was shocked to hear Espinoza had been testing new drugs for pharmaceutical companies.

"I was told they took his license away," she said. "How can they give him a job like that?"

The answer: There is nothing to stop doctors from being disciplined by state regulators one day and hired to test new drugs on the public the next.

Espinoza signed up to conduct a diabetes trial four days after the state punished him for the "unacceptable" medical practices that led to Acosta's death.

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Most new drugs used to be tested on people through university medical centers. But drug companies wanted to speed the process and began moving the work out into the community, offering drug studies as a sideline to physicians' regular practices.

Now most pre-approval drug data is gathered by neighborhood docs, who usually recruit subjects from their patient case load. Doctors can earn more than \$1,000 per patient, depending on the length and scope of the trial.

The drug companies that recruit these "clinical investigators" and FDA officials who review their data depend on them to follow protocol, accurately record results and protect patient safety. The data they produce determine whether the FDA ultimately accepts or rejects a new compound.

"The integrity of the investigator is the linchpin," said Arthur Caplan, professor of bioethics at the University of Pennsylvania. "If they are not trustworthy or have failed to comply with licensing requirements, that spells huge potential troubles to studies."

But as Espinoza's case shows, drug companies can miss serious black marks on a doctor's record. It wasn't until he fessed up about the state's action against him that his supervisor removed him from the diabetes trial.

A *St. Petersburg Times* analysis of public databases identified several doctors who have conducted clinical trials despite run-ins with the Florida Board of Medicine. They include:

- Dr. Serge Vilvar, a family practitioner and psychiatrist in North Miami Beach, had his medical license suspended for giving \$3-million worth of unnecessary infusion therapy to more than a dozen patients with HIV or hepatitis C. He has done a dozen clinical trials, two after the Health Department initiated disciplinary action.
- Dr. Abbey Strauss, a psychiatrist in Boca Raton, was fined \$15,000 for prescribing OxyContin and other controlled substances to a patient "inappropriately or in excessive or inappropriate quantities." He has conducted 46 trials, two since the state's disciplinary action.
- Dr. Sergio Mather, an internist in Fort Myers, was fined \$5,000 for failing to keep legible medical records or appropriately treat a patient later diagnosed with breast cancer. Though the patient blamed an inept technician in Mather's office, she received a \$750,000 settlement from the doctor's insurer. Mather has run six trials since being disciplined.
- Dr. James Mark Zachary, a urologist in North Pinellas, was fined \$10,000 for failing to train and supervise a subordinate who left two women burned from off-label use of a prescription medicine and laser treatments. Zachary registered for two drug studies while he was also medical director for a cosmetic clinic that shared a Clearwater office complex with his practice.

Diane Lubrano was one of the women scarred by the unsupervised medical treatment in 2004, which resulted in a felony charge against the untrained employee. Lubrano, 56, said she doesn't think Zachary should have been doing clinical trials, where supervision of subordinates is critical.

"It seemed like he was simply lending his medical license number to the cosmetic clinic and getting paid for it," said Lubrano, who never met Zachary. "So I question whether or not he was just running clinical trials for the money."

Zachary registered for his last drug study in May 2005, before the state's disciplinary action but several months after the arrest of the cosmetic clinic employee. According to an arrest affidavit, Zachary told Health Department investigators he knew the worker had no medical training.

Other than Strauss, none of the doctors named above responded to phone calls or certified letters requesting their comments for this story. In settlements with the state, each doctor "neither admitted nor denied" the state's allegations.

Strauss said the judge in his case decided the patient improved under his care but still recommended a fine due to the quantity of pain medications prescribed. "I would have appealed the fine, but I couldn't afford it."

Strauss said that when he applies to do a clinical trial, drug companies have begun to question him about the state's disciplinary action. "They're afraid," he said. "I can't deny what's out there, but it taints you as bad."

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A doctor's background and skills are crucial to the conduct of a clinical trial, said David Rothman, head of Columbia University's Institute on Medicine as a Profession.

"If this is a doctor you wouldn't trust to examine you, would you trust his data?" he said. "These are truly scandals waiting to happen."

Nor are state licensing boards known for being tough on doctors, Rothman said. So when a board does take action, drug companies should pay close attention.

"State medical boards are generally very passive and very slow-moving," he said. "Nobody should think they are an effective tool of regulation."

Drug companies say they recruit only the best doctors to perform clinical trials. The industry's trade association says investigators are selected based on their "qualifications, training, research or clinical expertise."

Drug companies submit doctors' resumes to the FDA when they apply to conduct a new drug study. Doctors fill out a separate questionnaire for the pharmaceutical company that asks if they have been the subject of a state licensing hearing or if such action is pending.

But drug companies overlooked or were not aware of the state's complaint against Vilvar. He was fined \$50,000, suspended and put on probation after the Health Department found that the unnecessary infusions he gave HIV patients in 2002 and 2003 amounted to "gross or repeated malpractice."

State regulators said Vilvar, who earned his medical degree in Haiti, administered the same dosage of immune globulin to at least 14 patients regardless of their condition. They criticized his medical records as being illegible and "grossly inadequate to document how the patients' serious medical conditions were being addressed other than through the ineffective therapy."

Vilvar billed Medicare and Medicaid \$3-million for the infusion treatments. When Medicaid questioned the treatments, the doctor reportedly refused to provide the necessary documentation. He was terminated as a Medicaid provider.

Vilvar registered to conduct the first of a dozen clinical trials in 2004. The state filed its initial complaint against him in May 2006.

In August and December 2006, he registered for clinical trials. By February, Vilvar's license had been suspended. The status of Vilvar's latest drug study is not known.

Dr. Mark Lamet of Hollywood always tells drug companies about his history with Florida regulators, according to his attorney. That hasn't stopped companies from hiring him for 10 studies since state inspectors found numerous deficiencies at his surgery center in 2002.

Among the state's complaints was that Lamet did not adequately evaluate or inform patients about the risk or choices of anesthesia. Lamet signed a settlement and was fined \$10,000 in June 2005.

His lawyer, Bruce Lamb of Tampa, said the informed consent issue was quickly corrected and the state fined the doctor because his landlord's back-up power generator did not meet Florida's requirements.

Drug companies hire Lamet despite the incident, Lamb said, because the allegations "are completely unrelated to his participation in clinical trials."

Lamet, who declined to comment, was recruiting patients in early August for a new treatment for colitis.

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The FDA, charged with protecting the public, acknowledges that it seldom checks up on doctors doing trials.

Dr. Rachel Behrman, deputy director of the FDA's Office of Medical Policy, said that during a study, the agency relies on the drug company to verify a doctor's qualifications and monitor his activities. With some 60,000 trials taking place worldwide, the FDA inspects, at most, 1 percent of the sites.

Behrman said that the agency can disqualify or restrict an investigator if problems arise.

But the case of the last Florida doctor to be subject to restrictions illustrates how time-consuming the process can be.

Dr. Jacques R. Caldwell had conducted more than 150 trials over two decades before FDA inspectors visited his research site in Gainesville in 2002 and noted serious problems.

Caldwell failed to evaluate subjects' adverse reactions to drugs, enrolled patients who should have been excluded and submitted data he knew to be false, the FDA's inspectors alleged. Caldwell also signed physical exams and lab reports "on dates that you were not physically present" in Gainesville.

More than two years later, the FDA began disqualification proceedings against Caldwell, who had conducted 10 more trials in the interim.

In May 2006, Caldwell, who has since moved to Maryland, agreed to three years of restrictions, "without admitting wrongdoing."

Caldwell's brother Michael, a lawyer in Atlanta, said the FDA's allegations were "gross exaggerations." He blamed two subordinates for all the problems.

Caldwell himself called in the regulators, the brother said, otherwise the FDA never would have uncovered the problems.

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Inadequate oversight of clinical trials means that unethical practitioners can easily escape detection, said Caplan, the bioethics professor.

"We do many more unannounced inspections of animal studies than we do of human studies," he said. "If an investigator wants to work around the rules, they can."

Because the public's health is riding on a clinical investigator's integrity, Caplan said, doctors who have had their medical license suspended should be automatically disqualified from such work.

"That's a privilege," he said. "Not some sort of economic right."

But the FDA's Behrman wasn't so sure when she was asked whether a doctor should be allowed to conduct a drug study while under suspension or probation by the state.

"That's a very complicated question," she said. "We're going to want to look at it. It may not be appropriate."

Times researcher Carolyn Edds contributed to this report. Kris Hundley can be reached at hundley@sptimes.com or (727) 892-2996.

Docs in trouble? No problem

Here are some doctors who got in trouble with the Florida Department of Health and then were picked by drug companies to conduct clinical trials -- with no objection from the FDA.

Dr. William J. Espinoza, Coral Gables and Hialeah

Complaint: After outpatient tummy-tuck and liposuction resulted in a patient's death, the state Department of Health issued an Emergency Restriction Order against Espinoza's license in March 2006, ordering him to cease performing office surgeries. He violated the order the next month, performing a non-emergency procedure.

Discipline: Reprimand, \$15,000 fine, 78-day suspension, two years' probation

Number of clinical trials: Four, including one during suspension

Dr. Mark Lamet, Hollywood

Complaint: State inspection of Lamet's surgical center found deficiencies in several areas, including informed consent agreements and lack of backup power.

Discipline: \$10,000 fine

Number of clinical trials: 51, including three after health department complaint

Dr. Sergio Mather, Fort Myers

Complaint: Allegedly failed to practice medicine "with that level of care, skill and treatment which is recognized by a reasonably prudent similar physician" based on failure to diagnose patient's breast cancer.

Discipline: \$5,000 fine

Number of clinical trials: 44, including six after disciplinary action

Dr. Abbey Strauss, Boca Raton

Complaint: Allegedly prescribed controlled substances, including OxyContin, "without medical justification, in quantities which endangered the patient's health and were not in the best interest of the patient."

Discipline: \$15,000 fine

Number of clinical trials: 46, including three after health department complaint

Dr. Serge Vilvar, North Miami Beach

Complaint: Allegations of gross or repeated malpractice for giving \$3-million worth of unnecessary infusion treatments to at least 14 HIV or Hepatitis C patients.

Discipline: Reprimand, \$50,000 fine, 6-month suspension, 1-year probation, permanently restricted license; terminated as Medicaid provider

Number of clinical trials: 12, including two after health department complaint; one trial under way while license suspended

Dr. James Mark Zachary, Safety Harbor

Complaint: Allegedly failed to provide "direct supervision and control" to an employee of a cosmetic institute where he was medical director, resulting in facial burns to two patients from unsupervised laser treatments.

Discipline: \$10,000 fine

Number of clinical trials: Six, including three after incidents that led to disciplinary action

About this story

We searched the FDA's database of clinical investigators for Florida physicians who have registered to do drug studies (www.accessdata.fda.gov/scripts/cder/bmis/index.cfm). Then we checked for disciplinary proceedings under each doctor's profile with the Florida Department of Health (www2.doh.state.fl.us/IRM00profiling/searchform.asp).

The *Times'* analysis focused on doctors who were approved to conduct trials after the state disciplined them.

The FDA database does not include details about the nature of the clinical trial or the drug company sponsoring the trial.