

HIV/AIDS

Tangled Patent Dispute Over 'Free' Drug-Resistance Database

A patent dispute among a small European biotechnology company, Stanford University, and one of its HIV/AIDS researchers has triggered a defamation lawsuit, raised issues of academic freedom, and led some observers to call it a battle out of *Don Quixote*.

At the center of the dispute are U.S. patents owned by Advanced Biological Laboratories (ABL) S.A. in Luxembourg that involve computer methods to guide treatment of patients with HIV infection and other diseases. In early 2007, ABL notified Stanford that its popular Internet-accessible HIV Drug Resistance Database (HIVdb) possibly infringed two of the company's patents. The HIVdb helps clini-



Standing firm. Stanford's Robert Shafer rejects ABL's assertion that it has patent rights over the popular database (right) he posts on the Web.

cians, researchers, and drug developers around the world make sense of the complex array of mutations the virus has developed to dodge specific treatments. "It's a tremendous tool that takes full advantage of the power of the Web and marrying sequencing and clinical data," says HIV/AIDS clinician Daniel Kuritzkes of Brigham and Women's Hospital in Cambridge, Massachusetts. "I use it every time I'm in the clinic."

Robert Shafer, an infectious-disease specialist at Stanford who began building the database 10 years ago and receives support from the U.S. National Institutes of Health and unrestricted grants from industry, was outraged by ABL's claims. "It's so blatantly wrong," says Shafer. He claims the patents are overly broad and vague and notes that the European Patent Office "refused" a similar application in 2006.

Shafer says at first he saw eye to eye with Stanford's attorneys, who in October 2007 filed for "declaratory relief," essentially asking a judge to prevent litigation from moving forward. Stanford also told ABL that it might file reexamination requests with the U.S. Patent and Trademark Office (USPTO), which can correct or invalidate issued patents.

The company and the university continued to negotiate and in March 2008 reached a settlement—without Shafer's input. The "immunity agreement" states that ABL would not file patent-infringement claims against any party that used the database for noncommercial purposes. But only people affiliated with Stanford had the right to pursue commercial activities with the database; anyone else who used it "in activities for a fee or otherwise in exchange for monetary con-

sideration" remained subject to ABL's patents. As part of the agreement, Stanford pledged to post a notice on the HIVdb that said as much.

Shafer says telling him what to post on his Web site violates academic freedom and he balked, noting that many companies

use the HIVdb to develop drugs or to support their own commercial tests that help clinicians make treatment decisions. The agreement, says Shafer, "gives ABL a green light to go and sue other people. It makes Stanford complicit and makes me seem complicit."

Five months passed before the Web site posted a notice, which said, in part, "Stanford does not represent that use of this database would not infringe patent rights of other persons or entities." To ABL's dismay, this was not the agreed-upon language, and the notice made no mention of the company.

Shafer hired his own counsel and on 10 October 2008 filed reexamination requests with USPTO on the two patents. Twelve days later, he posted a notice on the Web site that mentioned the company's patent rights but noted that he had filed the reexamination petitions. Shafer also included a disclaimer that said he "considers these patents to be harmful to research on the use of computers in medicine and is concerned that the recent litigation resulting from these patents is harmful to the care of persons with HIV infection."

On 1 December, ABL sued both Stanford and Shafer for breach of contract and defamation. Chalom Sayada, a co-founder of ABL who has led the company's negotiations with Stanford, says he has "a very deep and sincere respect" for Shafer's scientific work and the HIVdb. And he stresses that ABL has attempted to solve these issues amicably.

Sayada, a geneticist who has served as CEO of several other biotechs, strongly objects to Shafer's allegation that the patents have harmed research and patients. "We are not aiming to prevent research," he says. "And we obviously are not looking to harm or prevent the care of anybody." He adds that clinicians, even though they charge their patients fees, are free to use the HIVdb without paying licensing fees to ABL. "We try to be realistic," he says.

Sayada contends that Stanford's and Shafer's actions have hurt ABL's business. "People are speaking very badly about my company," says Sayada. And he says USPTO's patent reexamination is the proper venue to resolve the debate. "Anything beyond this is mere politics, and I'm not sure who benefits."

Sayada thinks Stanford made a "big mistake" by not involving Shafer during the original agreement negotiations. Stanford counsel Patrick Dunkley sees this as a misstep, too. Although the university owns the database and "had the complete authority to enter into the agreement without consulting with ▶

Professor Shafer,” says Dunkley, “in hindsight, it probably would have been more prudent to have involved him.”

Shafer, who says he has spent more than \$100,000 of his own money pursuing the patent reexaminations and defending himself against ABL’s suit, contends that Stanford set a bad precedent by caving in to ABL’s threats. “The university didn’t back down at all,” retorts Dunkley. “What the university did was protect the rights of the research community, and upon achieving its objective, there was no ongoing fight to have.”

Shafer has peppered many colleagues with e-mails about the dispute and about restrictive patents in general. This has alienated some colleagues who see his impassioned battle against allegedly harmful patents as tilting at windmills. But he has also attracted some strong support. “As a faculty member who does work precisely in this area, I was surprised and concerned that the university took the position it took rather than trying to contest the patent,” says Mark Musen, a Stanford researcher who specializes in biomedical informatics.

USPTO is expected to rule on the patent reexamination requests within the next few months. Stanford and Shafer have until the middle of March to respond to ABL’s lawsuits. ABL’s Sayada has attempted to engage Shafer in an informal mediation with leading HIV/AIDS researchers, but Shafer vows to fight to the end. “I’m not doing it out of spite,” says Shafer. “It’s a way of a vindication to say, ‘Look, you guys were scared, but I fought this and was able to win this.’ I want to show Stanford should have taken a stand.”

-JON COHEN