

The Fight of His Life

Locked in a bitter dispute over how he can use the fruits of his research, Bob Shafer is asking the same question the courts are now grappling with: Just what can be patented, anyway? By Joe Mullin

Bob Shafer is one unhappy doctor.

An expert in bioinformatics—the science of using computers to enhance medical treatment and decision making—Shafer has learned more in the past year about how the country’s patent system works than most medical researchers will ever know, and certainly more than he ever wanted to know. His newfound knowledge has come at a steep personal cost: Waging a battle to wipe out a pair of patents that he believes threaten to destroy his life’s work, Shafer has racked up more than \$100,000 in legal bills while putting himself at odds with Stanford University, where he is an associate professor of medicine and pathology.

The cause Shafer is staking his career, reputation, and retirement nest egg on is the HIV Drug Resistance Database, a highly regarded free resource that he developed, Stanford hosts, and doctors and scientists around the world rely on. Shafer says he’s fighting for more than the survival of his creation—he’s fighting for the future of bioinformatics research itself. It’s something he and many colleagues believe is imperiled by a European company’s move to assert a patent claim against Stanford over the database. “They are saying that if you want to use computers to help doctors make medical decisions, you have to give us money,” Shafer says of the company, Advanced Biological Laboratories, S.A. “They could go after users. It’s a slippery slope.”

PHOTOGRAPHY BY MICHAEL SEXTON



Bob Shafer, on the Stanford University campus. He sees ABL's patents as a threat to his HIV database.

Meanwhile, what started as a patent dispute has turned into something else. In December, ABL sued both Shafer and Stanford for breach of contract—and Shafer alone for defamation—for failing to fulfill an agreement meant to resolve the original conflict. In April, ABL settled with Stanford, but its defamation suit against Shafer continues.

The standoff among Stanford, Shafer, and ABL is unique in its details, but it comes at a time when the outer boundaries of what constitutes patentable subject matter are in flux, following the decision in *In re Bilski* issued last December by the U.S. Court of Appeals for the Federal Circuit. The dispute also comes as another closely watched case—one that raises the specter of a future face-off between the medical establishment and the patent bar—makes its way to the nation's top patent court. The rules of this game are being rewritten on the fly.

Bob Shafer is 51 years old and slightly built. He speaks in a monotone staccato, and when he talks, he tends to delve so deeply into details that a conversation's starting point can soon become a distant memory.

Shafer arrived at Stanford nearly 20 years ago, and launched the HIVdb online in 1998. Since then, the database has built a following among HIV researchers and practitioners around the world, attracting some 50,000 unique visitors a month. Those who use it generally fall into three categories: academic researchers, commercial and noncommercial laboratories, and doctors.

The database allows users to enter genetic information for viruses from individual patients or groups of patients, and to retrieve drug resistance information, which can then be used to help devise treatment regimens. Such information is critical to HIV research and drug development, as well as to treating individual patients. HIVdb is especially popular in the developing world—not least because it's freely available to anyone with an Internet connection. In some developing countries, medical practitioners have heard of Stanford University mainly through their interactions with HIVdb.

"Fantastic" is how Mark Wainberg, a professor of molecular biology at McGill University in Montreal, and a former president of the International AIDS Society–USA, describes the database: "It provides the ability to interpret what can sometimes be very complicated patterns of resistance."

The threat to this renowned resource emerged in January 2007. That's when ABL, a medical software company based in Luxembourg, first claimed, via an e-mail sent to Stanford lawyers, that the database infringed the company's

patents. Though ABL's cofounder and CEO, a French doctor named Chalom Sayada, won't discuss specifics of the alleged infringement, the company did buttress its initial e-mail to Stanford with an accompanying Excel spreadsheet that detailed how HIVdb met each claim.

ABL acquired the patents—which describe a way of doctors using databases to diagnose and treat diseases—as part of its 2004 purchase of a failing North Carolina medical software company, TherapyEdge. Today, Sayada says, ABL markets TherapyEdge software in Europe, where it's mainly used as a diagnostic tool, and in the developing world, where it helps doctors and hospitals manage patient care. Sayada has also launched a side business in patent licensing. To date, the ABL patents have just one public licensee: Viralliance, which took its license after Sayada sued Viralliance's parent company in 2007.

Sayada now insists that the database's "commercial" users—those who would seek to develop money-making products by using HIVdb—are the only true targets of ABL's patents. "We respect the science done by Dr. Shafer, and we respect the database as a tool," he says. "Our goal is not to be overwhelming, or prevent scientific research."

ABL wasn't taking that position in early 2007, though, which is why Stanford was concerned about a possible patent infringement suit. The university called in Shantanu Basu, a lawyer from Morrison & Foerster, one of several firms that regularly act as outside counsel to Stanford on patent matters.

After grilling Shafer about HIVdb's workings and analyzing ABL's claims, Basu (now with Mintz, Levin, Cohn, Ferris, Glovsky and Popeo) said the database did not infringe the patents, which had been issued in 2000 and 2001. In fact,

Shafer says, Stanford's lawyers said it was unlikely that the patents—which read as they covered the basic concept of creating software to help physicians make treatment decisions—would be issued today: "They told me," he says, "these are ridiculous patents, and could easily be invalidated."

Still, worried about getting mired in litigation in the plaintiff-friendly Eastern District of Texas, Stanford moved to invalidate the patents by filing a declaratory judgment suit in California in October 2007. Several months later, after the opening salvos of litigation, the two sides reached a settlement: ABL agreed not to sue Stanford for patent infringement; Stanford agreed to put a prominent disclaimer on the HIVdb, informing those who used it that, depending on the nature of their work, they might need a patent license from ABL.

"In medicine and in research, the word would be out that I sold out," Bob Shafer says.

One problem: Because Shafer wasn't required to sign the agreement with ABL—even though he maintains and controls every aspect of the database's operations—Stanford's lawyers never told him about the settlement's terms until after it was reached. Only then did he get an e-mail from the university's dean of medicine telling him to post the notice about ABL's patents. As he began to understand the details of the deal, Shafer grew distressed. "It goes against everything I believe in," Shafer says of the agreed-upon notice, which would inform all visitors that use of the HIVdb "does not imply any rights under any third party patents, including U.S. Patent Nos. 6,188,988 and 6,081,786, held by ABL, S.A. (www.ablsa.com)."

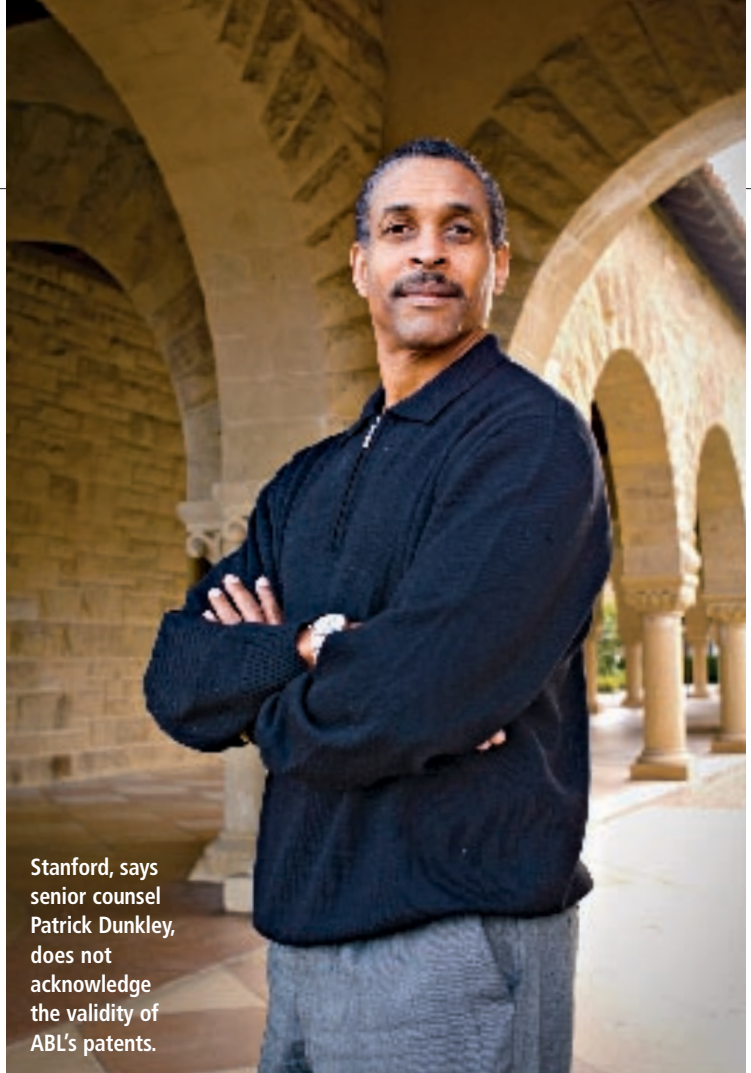
Posting such a notice, Shafer says, could lead doctors to think they owe money to ABL, and that the database—built mostly with taxpayer-funded National Institutes of Health grants—is no longer free. Anyone who charges a patient for the gene testing necessary before data can be processed through HIVdb, Shafer notes, is technically engaged in a commercial transaction—and thus a potential ABL target. "In medicine and in research," he says, "the word would be out that I sold out."

Shafer's Stanford colleagues were equally upset. "It's chilling to think there's a company that may have been able to get this patented," says Mark Musen, a biomedical informatics professor whose office sits near Shafer's. "I'm disappointed that the university's first reaction was not to fight this."

Shafer—under pressure from university administrators—ultimately did post a notice about ABL's patents, but he buried it on an obscure page of the HIVdb site where it is unlikely to be seen by many users. Shafer also appended his own language to the notice, claiming that ABL's patents are "obvious and broad."

Beyond that, Shafer noted that he has challenged the patents by filing two reexamination requests with the Patent and Trademark Office. Challenging a patent in a reexam—a lengthy process, but one that's far cheaper than going to court—boils down to one essential issue: whether there is a "substantial new question of patentability" the PTO missed in its initial review of the patent in question. (Shafer has hired patent lawyers at Day Casebeer Madrid Batchelder's Silicon Valley office to represent him for the reexams.)

Shafer's defiance prompted ABL to sue. "The quid pro quo for the license to Stanford was the posting that would direct commercial users of the Stanford database to ABL," says the company's lawyer, Edward Goldstein of Goldstein, Faucett & Prebeg, a Houston patent litigation boutique.



Stanford, says senior counsel Patrick Dunkley, does not acknowledge the validity of ABL's patents.

For his part, Sayada says: "We made a very generous offer to Stanford, and we reached an agreement." How does he characterize that agreement? "We believe they need a license, and they don't disagree." Regardless, Sayada says, once the agreement wasn't being followed, ABL had no choice but to take Stanford and Shafer to court.

Stanford administrators defend the university's original agreement with ABL as being in the best interest of science. "The intent of the agreement was to protect and preserve the ongoing use of the HIVdb Web site for the research community, in higher education or elsewhere," says Patrick Dunkley, a senior counsel for the university. Despite Sayada's characterization, Dunkley emphasizes that the agreement with ABL is simply a covenant not to sue—not a patent license. "It's clear the university is not taking a license, or acknowledging the validity of the patents." By ending the patent dispute the way it did, Dunkley argues, Stanford got a favorable deal. If ABL had wound up suing Stanford and winning, he says, "then the HIVdb Web site may not have been available to anyone." Despite the ongoing conflict, he adds, the university continues to support Shafer, his research, and the database. (To fight ABL's suit, Stanford hired Pillsbury Winthrop Shaw Pittman partner Sarah Flanagan. Shafer has his own lawyer, Julie Turner of Turner Boyd LLP.)

Shafer's colleagues say that recognizing the validity of ABL's patents could harm all types of research. David Katzenstein, a Stanford scientist who studies HIV in the developing world, sees gene therapy as one area of study that could suffer. "If you read [ABL's patents] literally, anyone who is providing therapeutic options based on the sequence of a pathogen violates their patent, and that goes on in hundreds of contexts. It's truly a dangerous precedent."

On the other hand, if ABL's aim is to build a patent-licensing business, Katzenstein believes the company picked the wrong person to go after: "I think they've made a big strategic error, in the sense that Bob is not going to behave rationally about this," he says. "He's absolutely convinced that free access to published data is an intrinsic part of science and medicine, and should not be restricted." To Shafer, Stanford's reluctance to fight harder for that principle is hard to stomach.

Problematic patents are hardly a new phenomenon to most patent lawyers, who are also well-acquainted with the importance of moving aggressively to fight them off. That's not true for someone like Bob Shafer, who over the past two years has gotten a crash course in how the patent system works. To Shafer and others at Stanford who know what he's going through, it's amazing that the ABL patents were ever even issued—and that they could be used to dictate how Shafer chooses to share the fruits of his research.

As it happens, the question of just what can be patented is getting lots of attention from courts right now. In particular, method patents, the type being asserted by ABL, are matters of high-stakes controversies. In December's landmark *Bilski* ruling, the U.S. Court of Appeals for the Federal Circuit issued a decision that will clearly rein in software and business method patents—which began to be issued in large numbers in the 1990s—though it isn't clear how much. Under the test established in *Bilski*, patented methods must be transformational or tied to a particular machine; just how was left undefined. In recent months, patent litigators have been drafting and filing motions that will ultimately draw the lines of patentable subject matter in various industries. The *Bilski* patent holders have petitioned the U.S. Supreme Court to hear their case.

In the medical field, another controversial patent dispute—one that pits the organized patent bar against the medical profession—is bound for the Federal Circuit. In that case, pharmaceutical company Prometheus Labs sued

the Mayo Clinic, alleging that the clinic had violated a Prometheus-owned patent covering a method of diagnosing Crohn's disease by measuring metabolites. A federal district court judge invalidated Prometheus's patent.

The American Medical Association agreed with the judge that the patent asserted by Prometheus claimed unpatentable subject matter. The American Intellectual Property Law Association, representing the organized patent bar, filed an amicus brief slamming the judge's rejection of the Prometheus patent.

"Diagnostic methods such as those claimed by the patents-in-suit should remain patentable subject matter, among other things, to protect and encourage the development of personalized medicine," wrote Edward Reines, the Weil, Gotshal & Manges partner who authored AIPLA's brief.

The Prometheus case is likely to affect what kinds of diagnostic medical patents can be asserted in the post-*Bilski* era. Whatever case law emerges from that case, and others like it, is likely to draw a border around patent-licensing campaigns like ABL's. For now, beyond its dispute with Stanford and Shafer, ABL has just one active patent lawsuit, against Switzerland-based SmartGene GmbH. That suit has been stayed pending the results of the reexams requested by Shafer and two additional reexams brought by SmartGene.

It's worth noting that the medical profession is alone in having won a policy battle against the patent bar on its own turf, by setting a limit on

patentable subject matter. In 1996, Congress passed a law—endorsed by the AMA but opposed by the AIPLA and other legal groups—that prohibited enforcing patents on surgical methods against hospitals or doctors. The law followed on the heels of a doctor-on-doctor patent lawsuit over a method of performing surgery that riled the medical community. In the end, the medical profession won an exemption from surgical method patents—a feat that hasn't been repeated by any other profession.

Shafer's own battle has motivated him to educate others about what he sees as a flawed patent system. He has submitted a paper to the Public Library of Science, a publisher of well-known medical journals. In the paper, Shafer suggests that the system is a victim of "regulatory capture" by the patent bar. He has also created a Web site called Harmful Patents (harmfulpatents.org) to detail his dispute with ABL. It's a fight he doesn't plan to give up anytime soon.

"They want to make knowledge a commodity," Shafer says. "That's why I can't back down." ■

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