BIOTECHNOLOGY PATENTS

Chiron Challenged on Hepatitis-C Patent

A protracted dispute between a prominent hepatitis researcher and Chiron Corp. of Emeryville, California, landed in court last month. At stake: royalties—potentially amounting to millions of dollars—from a test for the virus that causes hepatitis-C (sometimes called non-A non-B hepatitis). The test, used to screen blood donations in the United States and many other countries, is one of Chiron's major revenue sources.

On 20 December, Daniel W. Bradley, a virologist who spent 23 years at the Centers for Disease Control and Prevention (CDC) in Atlanta, filed a federal suit against Chiron, claiming the company had used his research to isolate and clone the hepatitis-C virus and then shut him out of a patent resulting from the discovery. (Bradley also sued the federal government over an agreement it reached with Chiron, which he signed.)

Chiron, in a public statement issued on 28 December, said Bradley did not contribute to the key part of the research; the company characterized the suit as part of a "desperate strategy" by companies that have tried unsuccessfully to challenge Chiron's hepatitis-C patents. Chiron noted that Bradley is being represented by Leslie Misrock, a prominent biotechnology patent lawyer whose firm represents a Dutch company that has fought Chiron's claims on hepatitis-C.

This legal battle stems from what was once a fruitful collaboration between Bradley and Chiron. Bradley, who retired from CDC in May 1994 and is now chair of the World Health Organization's Steering Committee on Polio and Hepatitis Vaccines, says in his complaint that he became interested in hepatitis in 1977, when he was approached by a company that provided Factor VIII to hemophiliacs. The company was concerned that non-A non-B hepatitis might be transmitted through its product.

Bradley managed to infect chimpanzees with the suspect Factor VIII and concluded that the animals were an appropriate model to study non-A non-B hepatitis. In particular, he discovered that levels of certain liver enzymes provided a key marker for high titers of hepatitis virus in the blood during the chronic phase of the disease.

That discovery caught Chiron's attention, and in 1982 Chiron entered into a collaboration with Bradley. Over the years, Bradley says he supplied Chiron with "over 2500 milliliters of a very rare commodity, a unique commodity,"—the high-titer plasma. In May 1988, Chiron announced that it had isolated the hepatitis-C virus from these samples and cloned its genome. The achievement brought scientific recognition to Bradley and Chiron researchers Michael Houghton, Qui Lim Choo, and George Kuo, in the form of several joint awards.

But harmony did not last long. One of the first breaks in the apparent amity came when Chiron filed a patent application that did not include Bradley as a co-inventor. Bradley says federal lawyers challenged the claim in 1989 and proposed an agreement that would assign CDC a half interest in patents relating to hepatitis-C. Chiron would be given a 10-year exclusive license and would pay a royalty of 3% of net sales. Chiron declined to go along and hired former Department of Health and Human Services Secretary Joseph Califano to represent it. Califano sent a letter disputing Bradley's claims and arguing that the company did the key work in isolating and cloning the virus. Califano noted in particular that the hepatitis-C clone was "obtained by using a specific protocol designed by a Chiron scientist."

In 1990, the government reached an agreement with Chiron under which the company would pay Bradley $67,500 a year for 5 years "in recognition of his contributions to the field of [non-A non-B] research," and enter into a $2.5 million, 5-year cooperative research and development agreement with the federal government on hepatitis-C research and tissue culture. Bradley says he did not take part in the negotiations. He signed the agreement (in March 1990), he says in his complaint, because he had been diagnosed with prostate cancer and was concerned about his ability to provide financially for his family. Chiron was awarded a U.S. patent for a hepatitis-C test on 27 September 1994; the company has 26 similar patents in 20 other countries.

If Bradley's suit goes to trial, the outcome is likely to hinge on whether Bradley's level of collaboration was sufficient to be named co-inventor—a legal standard more stringent than the requirements for co-authorship. Bradley claims his development of the capacity to produce high-titer material "was a critical step that enabled the [non-A non-B] viral genome to be cloned." But Chiron Vice President Robert P. Blackburn says the work, while important, was not sufficient to give Bradley co-inventor status. "It's not enough to make the clone, but you have to select the proper clone out of millions of wrong ones," he says.

–Victoria Slind-Flor

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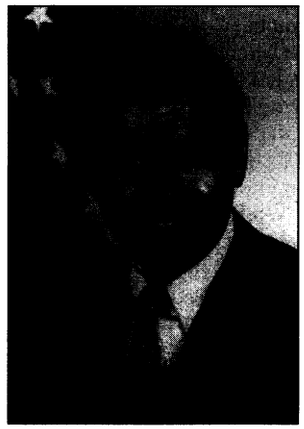
Rules Would Drop Need for Clinical Data

The biotechnology industry has wrung a significant concession from the U.S. Patent and Trademark Office (PTO). Last month, PTO Commissioner Bruce Lehman announced that patent examiners will no longer require companies to back up their patent applications with clinical data showing a product works in people. From now on, less expensive animal tests or in vitro data will be sufficient evidence that a product is likely to be effective, at least as far as PTO is concerned.



Responsive. Patent chief Bruce Lehman has listened to concerns of biotech companies.

The industry has long argued that the PTO has usurped the role of the Food and Drug Administration (FDA) in forcing companies to spend millions of dollars to conduct clinical trials to prove that their products will be effective. This requirement, they say, presents them with a Catch-22: It's hard to raise venture capital to test a product that isn't patented, but they can't get a patent until they have conducted the tests (*Science*, 28 October 1994, p. 537). Biotech officials have also complained that patent applications are frequently stalled for months because PTO examiners challenge the clinical data. David Beier, vice president of public policy for Genentech Inc., says, for example, that "well over half" of his company's 212 patent applications snagged on the requirement for clinical data before a patent was issued. "This is an unrealistic standard," says Daniel Chambers, counsel for Viagene Inc.

Lehman concedes that this has been a problem. "Many people say that some examiners routinely challenge the sound scientific conclusions of recognized experts in the field. This practice will not be condoned under the new guidelines," Lehman said at a press conference last month. The PTO's new policy, which is expected to be published this week in the *Federal Register*, requires patent examiners to have compelling evidence that an invention will not be useful in order to reject it on those grounds. "No longer will examiners act like