A Bloody Battle Over an Anemia Treatment

A complex patent fight is being waged over a hormone that could have broad use in treating anemia

Two American biotechnology companies are locked in a high-stakes patent dispute that could have a major impact on their commercial prospects. At issue is who will control the U.S. market for erythropoietin (EPO), a hormone that promotes formation of red blood cells and is effective in treating anemia. Analysts estimate that the market could eventually be worth hundreds of millions of dollars a year.

The two companies, Amgen of Thousand Oaks, California, and Genetics Institute of Cambridge, Massachusetts, hold patents related to the production and use of EPO. Amgen's patent covers methods of producing EPO using recombinant DNA, while Genetics Institute has a patent that covers purification and use of the hormone.

Last fall, Amgen challenged the validity of the Genetics Institute patent in federal court and charged the company with infringing Amgen's own patent on the production of EPO. Genetics Institute has countered with a lawsuit of its own accusing Amgen of violating its patent.

While the companies are locked in legal battle, they are racing to bring the product to market. Amgen is viewed as the leader in this contest because it is likely to get Food and Drug Administration approval three or more months ahead of Genetics Institute's licensee, Chugai Pharmaceutical Co. Ltd. of Japan. This could position Amgen to dominate the American market.

Amgen received a setback last month, however, when a U.S. District Court judge in Boston issued a preliminary ruling that the company was infringing Genetics Institute's patent. If the ruling is upheld, Amgen could end up having to obtain a license from its competitor.

Linda Miller, a vice president at PaineWebber, Inc., observes that the legal wrangling between the two companies could take years to resolve. Ultimately, she says, the companies may have to settle their spat by granting each other licenses to use their respective EPO patents. That might be preferable to litigation, says Miller, who "would rather see these companies spending their money on research."

But that kind of advice is the last thing that Amgen President George B. Rathmann wants to hear. "We are not going to play the game," says Rathmann, who contends he would be letting his staff down if he were to negotiate a settlement.

EPO has long been identified as the product that would put the 8-year-old company's operations soundly in the black. The core market is the treatment of anemia induced by dialysis and Amgen hopes to serve most of the 30,000 dialysis patients in the United States that could benefit from EPO. Eventually, it is expected to be used to treat other anemia-related ailments. By 1992, says Stuart Weisbrod, senior biotechnology analyst for Prudential-Bache Securities, Inc., EPO could earn Amgen $175 million annually.

"At this point they are playing 'You bet your company.' "

The main obstacle, however, is the Genetics Institute patent. Filed by the company's director of protein chemistry, Rodney M. Hewick, on 11 January 1985, the patent covers the use of "highly purified EPO" as a treatment for anemia. And supporting language in the patent decision indicates that it applies both to EPO derived from natural sources and from engineered organisms employed in cell culture and fermentation.

The patent was awarded to Hewick on the basis of his discovery that EPO extracted from urine or blood using recognized procedures was, in fact, not pure. He found, however, that with the application of reversed-phase, high-performance liquid chromatography, a homogeneous EPO protein could be obtained.

On 28 October, Amgen filed a lawsuit against Genetics Institute and Chugai, contending that the patent office ruling is too broad and should not encompass EPO made with recombinant DNA techniques. Robert D. Weist, general counsel for Amgen, says Hewick's purification step is required in producing EPO, but claims it is obvious and does not warrant the broad use patent awarded to Genetics Institute.

The patent issued to Amgen on 27 October is not as comprehensive, covering only isolated DNA sequences for EPO, vectors for implanting DNA sequences into host cells, and transfected host cells carrying such DNA sequences. These inventions represent greater added value for EPO production than does Hewick's purification process, contends Weist. He adds that Amgen filed its patent application first and is asking the U.S. District Court in Boston to invalidate Genetics Institute's patent.

As part of the same legal action, Amgen also is charging that Genetics Institute and Chugai are using its patented host-cell technology for producing EPO. And in a related move, Rathmann has gotten the International Trade Commission to investigate whether Chugai is engaging in unfair competition by importing EPO into the United States.

Chugai admits it is importing small amounts of EPO now for use in clinical trials. Eugene Moroz, counsel to Chugai, says the firm is not infringing on Amgen's patent, but is using production technology obtained from Genetics Institute. Bruce Eisen, general counsel for Genetics Institute, says its mammalian cell culture process differs substantially from Amgen's and is not covered by its competitor's patent.

"At this point they are playing 'You bet your company,' " says Eisen, commenting on Amgen's legal strategy. If Amgen markets EPO and subsequently loses the patent dispute, it could face large penalties.

Bertram Rowland, a partner with the law firm of Leydig, Voit & Mayer of Palo Alto, notes that the outcome could hinge on how the U.S. Court of Appeals in San Francisco decides the case of *Scripps Clinic & Research Foundation* v. *Genentech*. This case should be decided soon and could serve as a precedent for deciding Amgen's challenge of the Genetics Institute patent. A lower court in 1987 upheld Scripps' patent covering a process for purifying the blood-clotting protein, Factor VIII:C, regardless of whether it was derived from natural sources or by recombinant means.

Sarah Gordon, an analyst with Hambrecht & Quist of New York, estimates that Amgen will capture 80% of U.S. sales when it begins marketing later this year. Upjohn, the U.S. distributor enlisted by Chugai, could grab a 20% market share, she says.

Given the legal and market uncertainties, litigation analysts such as Calvert Crary, a managing director of Martin Simpson & Co., Inc. of New York, wonder why Amgen does not negotiate a settlement. But Rathmann is turning away overtures from Genetics Institute and Chugai. "Both sides do not have equal positions," he says. ■

MARK CRAWFORD