

COHEN-BOYER: A BRIEF HISTORY

The Cohen-Boyer patent has become a landmark in the genetic engineering industry, albeit a landmark of uncertain fate. The volatile history of the patent has created confusion about both the scope and nature of its claims, and it probably will take several years and millions of dollars to resolve all the challenges and counterclaims. Here is a brief summary of the history and present status of the patent.

1974: Coinventors Stanley Cohen (Stanford University) and Herbert Boyer (University of California, San Francisco) file a patent application with the U.S. Patent and Trademark Office (PTO), assigning rights to the two universities. The broad claims of

the patent application include the process of inserting foreign genes into microbial plasmids, the genetically engineered plasmids themselves, and microorganisms containing the plasmids.

1978: At the suggestion of the PTO, which had judged the claims of the original application to be too broad, the patent application is split into two independent applications. One application covers the process of genetically engineering the plasmids and another the products of this process, i.e., the plasmids and microbes that contain them.

1980: The PTO approves the process patent application but renders no decision on the second patent covering the products.

1982: The PTO informs Stanford that the patent will be approved in July and assigns it a number, but then reverses its decision, notifying Stanford on June 30 that it is withdrawing approval. In August PTO announces an office action rejecting the patent, giving Stanford 90 days to file an appeal. Later in the year, Stanford requests the PTO to close its file on the application, eliminating public ac-

cess. Negotiations between Stanford and the PTO continue on a point-by-point basis—PTO raises a question or objection, Stanford supplies an answer.

1983: Rumors that approval of the product patent is imminent surface every few months, but neither the PTO nor Stanford make any definitive announcements.

1984: Stanford announces in a letter to its licensees that the patent will be granted, but the claims of the final patent are considerably narrower than those of the previous version. Most notably, the patent covers only bacterial plasmids in bacterial hosts, although Stanford asserts it will continue to prosecute the broader claim that covers non-bacterial microbes such as yeast.

The difficulties encountered in obtaining the patent may be minor compared to the Sisyphean labor of defending it. Although the \$2.7 million in revenues Stanford has collected from its 79 licensees is small by pharmaceutical industry standards, it provides a tidy war chest for what promises to be a long legal battle.

—Tazewell Wilson

and trademark counsel at Cetus, thinks many biotechnology process patent applications suffer from inadequate preparation and lack of knowledge about the patenting system. "Biotechnology has produced some very important process patents—manufacture of high fructose corn syrup and citric acid are two notable ones—because the process claims were well defined and the patents were properly prepared," he says. "However, in the rush to protect many genetic engineering techniques, a lot of applications have been prepared by individuals not aware of the details of patenting. These cases may have a very difficult time."

Since most industrial markets involve pre-existing products that cannot be patented, many industrial innovations must rely on process patent protection. Genex concentrates on industrial products; Glick complains, "We cannot afford to avoid patenting, but we do it primarily as a defensive measure. Everybody has to do this to protect themselves, but it really is an unproductive use of resources."

Companies concentrating on health care markets tend to have aggressive patenting policies, since their patents usually protect products rather than processes. Patenting is also part of business strategy for many fledgling biotech firms. In the absence of products or even revenues,

many companies hold their intellectual property a primary asset. "A patent position is an automatic entry in the game," says Fildes.

As the industry matures and the pace of innovation slows, other forms of protection—product patents and trade secrets—will become more important, he predicts. This is particularly true for back-end processes like purification. "We don't automatically patent every process we develop," notes Fildes. "We consider many techniques 'knowhow' and don't necessarily want to make them public." Trade secrets, however, are a calculated risk because someone else may obtain a patent on the process and preclude its use.

Genetic engineering firms hope to avoid many of the problems associated with process patents by developing second-generation products that can be protected with product patents. Second-generation products are usually modified versions of biological substances with somewhat altered biological activity. Scientists at Cetus claim they have engineered molecules such as beta interferon, incorporating specific features that make them more clinically effective, and that the redesigned molecules are truly novel, but patent agencies have yet to rule on these claims.

The challenges to Cohen-Boyer probably will result in the first major

recombinant DNA patent court decisions, and the scope of these challenges may well indicate just how aggressive the biotech industry will be in patent litigation. There are other patent battles shaping up as well. Genentech Inc. (South San Francisco, CA) has challenged a decision by the European Patent Office to award Biogen (Geneva, Switzerland) rights to produce recombinant alpha interferon. Although this type of challenge is not uncommon, both the specialty companies and Hoffman-LaRoche and Schering-Plough, the multinational pharmaceutical firms sponsoring their interferon work, are taking pug-nacious positions. However, industry sources say this fight probably has more to do with public relations than the substantive patent issues—each company wants desperately to be able to claim being first on the market with interferon.

Although everyone knows the cost of litigation will be exorbitant, both attorneys and executives think it is inevitable. The optimists hope reason will prevail and most intellectual property disputes will be settled by negotiation rather than litigation. "I would much rather sit down as businessmen than fight in the courts," claims Fildes. "I think it will be most unfortunate if biotechnology ends up making the patent attorneys wealthy."

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