THE LAST WORD

PATENTING: A TWO-ARMED STRATEGY

by George M. Gould

Patenting. C'mon, who deserves proprietary rights to a natural biological compound? A variant, yes. A manufacturing process, sure. But the substance itself?...If you can patent natural IL-2, why *not* patent breathing?" (Editorial, *Bio/Technology* **6**:5, Jan. '88.)

Rhetorical questions, to be sure, but vitally important to the pharmaceutical industry, particularly those companies developing products via biotechnological means. Patenting breathing aside, it is axiomatic within the ethical pharmaceutical industry that patent protection on the ultimate product is critically important to a company's ability to recoup the enormous development costs—as high as $125,000,000, according to a recent estimate. To justify the risk of supporting an R&D program of this magnitude, the party responsible for making the go/no go decision will generally demand that the product have some reasonable period of market exclusivity, so the company has a chance to recover its original capital investment and even earn a competitive profit on that investment. And the best way for a company to achieve such exclusivity is to hold a patent with broad, dominating claims directed to the compound *per se*.

Alternate patent protection—such as claims directed to intermediates or to manufacturing processes—can be valuable in helping a company develop a competitive advantage over others forced to use less efficient means to produce the desired end product. Such types of protection rarely afford complete exclusion, however; they usually can be invented around, and often provide limited temporal or territorial protection.

The initial products targeted by biotechnology companies consisted primarily of recombinant DNA-produced versions of pre-existing proteins. An ever-expanding group of start-up companies, plus the pharmaceutical giants with in-house molecular genetics capabilities, have found themselves vying for patent positions on a limited list of products—insulin, growth hormone, interferon, thrombolytic factors, lymphokines, and hemopoietic factors. Patent conflicts were predictable and inevitable.

I believe the most effective patent strategy for companies involved in this highly competitive R&D field is to attempt to protect the targeted end product by a two-armed approach. One arm should be directed towards achieving a patent position on the product by being the first to purify and characterize the natural protein (if that has not been previously accomplished by prior art). Although U.S. patent law does not allow an inventor to patent a natural substance in its natural state, it *does* provide protection if the compound's purity has been modified—and improved—by human intervention. The second arm of this patent strategy is directed to protecting the recombinant DNA-produced aspects of the product. It is already possible to obtain protection of recombinant proteins as compounds complementary to their natural counterparts where structural novelty can be established—such as the presence of an N-terminal methionine, the absence of glycosylation, or modifications in the primary amino acid sequence.

The practical impact of these various patent strategies is becoming clear—especially in Genentech's (So. San Francisco, CA) various litigations. For instance, Genentech (and its licensee Cutter Labs, Emeryville, CA) did not have patent protection on purified natural Factor VIII: Scripps Clinic & Research Foundation (La Jolla, CA), however, had obtained a patent on this invention. The preliminary rulings of San Francisco's Federal District Court have supported Scripps' position that its claims to the purified, natural protein are infringed by Genentech's development of the recombinant molecule—even though there are structural differences between the two. Moreover, Genetics Institute (Cambridge, MA) has recently received a U.S. patent covering claims on producing Factor VIII using recombinant DNA technology. Such a tactically poor patent position may force Genentech and its licensee to reconsider their continued investment in Factor VIII.

Genentech's position is somewhat different with respect to its initial commercial product, recombinant human growth hormone (hGH). On one hand the company is involved in an infringement suit on a patent for synthetic hGH brought by the Hormone Research Foundation and its exclusive licensee Hoffmann-La Roche. A recent District Court decision granted Genentech summary judgment on issues of non-infringement and validity. An appeal to the Court of Appeals is likely. On the other hand, Genentech is litigating with Eli Lilly & Co. (Indianapolis, IN) on a series of Genentech U.S. patents directed to the recombinant production of hGH. In this instance Genentech has the patent cards needed to stay in the game.

And for tissue plasminogen activator (t-PA), Genentech is clearly hoping to get a patent stranglehold on the U.S. market by employing a dual strategy. The first shoe dropped when a patent claiming purified, natural t-PA was issued to Genentech's licensor Innovi N.V. The company immediately sued Burroughs-Wellcome (Research Triangle Park, NC) and Genetics Institute, seeking to protect product development costs of nearly nine figures. The recombinant-based patent on t-PA has also just issued in the U.S. and was quickly added to the litigation. Wellcome successfully challenged the corresponding U.K. patent on recombinant human t-PA. It is not clear whether this adverse decision will influence the U.S. proceedings. Thus, the purified natural protein patent represents a potentially important asset in this action.

Can a patent directed to the purified, natural protein secure the desired prize of market exclusivity for the patent owner? Time will tell, as the litigations now ongoing reach final decisions. The stakes for the players are clearly high. Individual companies, however, are not alone in having to live with the outcomes—and their ramifications. They can—and will—influence issues as diverse as which countries will dominate in biotechnology R&D, which companies will continue to do business, and whether capital investments will be forthcoming in the future for this growing industry. While admittedly we are not dealing with patents on breathing, patents can be, in fact, the life-blood of this industry.

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