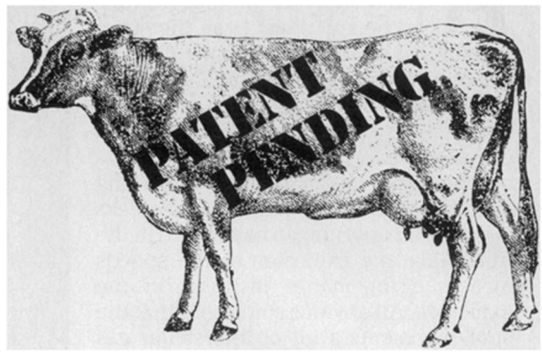
# Of Judges, Genes and Genetic Engineers

## Biotech attorneys approach the bench




By RICK WEISS

Is litigation becoming the premier product of the biotechnology revolution? Biotech patent disputes are multiplying like clones, and with more than 6,000 new biotech patents currently pending in the United States alone, the case load is destined to grow. Indeed, as biotech companies move from basic research into full-scale production and marketing of their first products, patent protection is becoming an increasingly important — and contentious — cornerstone of corporate well-being.

Although only five genetically engineered products have so far been approved for sale in the United States, biotechnology companies are already staking their claims to the dozens of diagnostic, pharmaceutical and agricultural products that are expected to emerge from the industry in the next few years. The roster of resulting patent disputes reads like a Who's Who of biotechnology:

- Hoffmann-LaRoche and Eli Lilly are suing Genentech over patent rights to genetically engineered human growth hormone.
- Amgen and Cetus are in court over their rights to market interleukin-2.
- Genetics Institute recently beat out rival Amgen for the first U.S. patent on erythropoietin, although Amgen claims it developed the product first.
- Hybritech successfully defended a patent infringement suit brought by Monoclonal Antibodies, and was recently granted a preliminary injunction to prevent Abbott Laboratories from selling certain diagnostic assays.
- Scripps Clinic is suing Genentech over rights to genetically engineered Factor VIII, the clotting factor that's missing in hemophiliacs.

The stakes in these and other ongoing cases are substantial; with biotech budgets depleted after years of preliminary research, and a number of companies racing to produce some very similar products, patent lawyers are anxious to win for their companies the lucrative market monopolies provided by U.S. patent law. But attorneys are facing some crucial questions about how to apply America's 197-year-old patent laws to the ultramodern biotechnology industry.

United States patent law was first written in 1790, and its principal author, Thomas Jefferson, didn't have much to say about monoclonal antibodies, erythropoietin or tissue plasminogen activator. As revised in 1861, the law grants to "inventors and authors" a 17-year monopoly over the production, use and sale of their products — with the condition that the applicant supply to the public a detailed description of the invention so that others may immediately learn from and build upon that knowledge. In this and other respects the law was designed to "promote the progress of science and the useful arts," with the 17-year limit being settled upon by Congress as the amount of time it might take to train two apprentices to make the new concoction.

But with the increasing rate of technological change, and with skyrocketing investments in research and development, patent protection has taken on added significance. According to Jack Doyle, an attorney with the Environmental Policy Institute in Washington, D.C., "In modern corporate terms, patents are often viewed as a way to maintain and expand a company's market share." And in the biotechnology industry, market share can easily translate into hundreds of millions of dollars per year.

Recently, for example, Genentech Corp. of South San Francisco lost a crucial round in its legal battle with London-based Wellcome PLC over British patent rights for its genetically engineered human tissue plasminogen activator. Analysts estimate that the clot-dissolving drug (SN: 1/17/87, p.42), which is expected to gain Food and Drug Administration approval later this year, may be worth more than $1 billion in sales worldwide — to the company or companies that win appropriate patents.

In the Wellcome-Genentech case, the dispute boils down to the question of how broad a patent claim can reasonably be: Can the original developer of a new product get patent protection for a broad family of related products, or only for a very specific form of that product? The question is particularly significant in the biotech age, as scientists find that substances can take on radically different properties with the simple addition of, say, a single methyl group.

"There seems to be some degree of uncertainty about the law with regard to making what would appear to be minor changes in the molecule, when those changes in fact have dramatic results," says Albert Halluin, vice-president and chief intellectual property counsel for Cetus Corp., an Emeryville, Calif.-based biotechnology company. Is it reasonable, he asks, for someone to claim, "'We want all derivatives, substitutions and deletions that anybody can think of,' thereby blocking someone else who comes along and actually does the work and finds that some things work and some things don't?"

Along with the question of patent breadth, a number of related issues complicate the application of current patent law to biotechnology:

- What constitutes "prior art"? Patent protection is granted only to products that are deemed novel in relation to preexisting inventions, which together are referred to as "prior art." Many genetically engineered products are actually *identical* to substances already found in nature, but with biotechnology can be produced in much larger quantities or in more purified forms. The patent office has so far held to a liberal interpretation of the novelty requirement, allowing patents on highly purified but otherwise naturally occurring substances. But at-

torneys say that there remains some uncertainty about the legal definition of the word "new."

• What constitutes "obviousness"? According to U.S. patent law, patents are not granted to inventions that, although entirely new, may be considered obvious "to a person of ordinary skill in the art." This issue arose most recently in the highly publicized April 1987 patent office decision to allow patents on higher life forms (SN: 4/25/87, p.263). While holding that higher organisms are *in theory* patentable, the patent appeals board in fact rejected – on grounds of obviousness – the particular patent applied for in that case. It may be, some attorneys have since concluded, that the patenting of higher organisms will not get very far. Patent officials may deem the entire animal kingdom to be prior art – and claim that any genetic manipulation of that medium is "obvious."

Most patent attorneys, however, disagree with that view. "If you can show me that it would be obvious to monkey with your nuclear cells and jazz up your chromosomes, then that's fine," says Eric P. Schellin, director of the National Patent Council, an Arlington, Va.-based business lobby that supports patent protection. But in many cases, he says, "you're not going to be able to do that. I'm going to show you that it's brand new and that it's not obvious. And the fact that it comes out squeaking like an animal is beside the point."

• How can patent protection be properly enforced when the patented organism is self-replicating? The product may be a microbe, a mouse or a dairy cow, but the question remains as to whether patents are passed on to progeny. If so, royalties may be due to the original holder of the patent for all subsequent generations of the gene-altered life form – and enforcement would necessitate methods of family-line testing that are still not very reliable.

• How will the patent law "enablement requirement" be fulfilled? The law requires that a patent application include a detailed description of how the invention was made and how to use it. "If something is alive – and you can't create life – how do you on a piece of paper describe how to make it?" asks Howard Stanley, patent attorney for Monsanto Co. in St. Louis. "You can store samples of microbial material in suspended animation" in special storehouses such as the American Type Culture Collection in Rockville, Md., he notes, and by making such frozen samples available to interested parties the enablement requirement is aptly fulfilled. "But suppose that the thing you were modifying was an elephant," Stanley says. "I don't think Rockville is going to be too thrilled if you show up with an elephant and say that you'd like to store it in case somebody comes along wanting to know, 'How did you make that elephant?'"

These questions and others will begin to be answered with some soon-to-be-published clarifications from the Patent and Trade Office. But the courts must ultimately interpret such rules, so it will be some time before the issues are resolved.

"Many applications are pending right now at the patent office—either in front of examiners or at the board of appeals level – and as these applications are decided we'll be getting some guidance," says Steve Odre, a patent attorney with Amgen Inc. in Thousand Oaks, Calif. "For now I think that everyone would like to see some case law, but that's not going to happen tomorrow. Meanwhile, everyone will have to proceed until there is a definitive text on biotechnology patent law"

The decision-making process may be further slowed by the growing political and ethical controversy surrounding the commercialization of living organisms (SN: 8/1/87, p.69). Already, church groups, farm organizations, chemical companies and Congress are jockeying for some influence over what has traditionally been the purview of an essentially apolitical Patent and Trademark Office.

"We have generally remained separate from the regulatory scheme," says Charles Van Horn, director of the organic chemistry and biotechnology examiners group at the patent office. "But biotechnology is a highly visible technology at this time, and when you work in a fishbowl it can sometimes distract you from getting your work done."

Legal and political delays aside, the sheer volume of pending paperwork makes a speedy resolution to the problem unlikely. "The volume of literature and art relating to pharmaceutical patents alone has been growing geometrically," says Halluin, of Cetus. "Examiners have an awful lot more to consider than they did 20 years ago."

As the patent office makes increasing use of computer searches and augments its staff with biotech-savvy examiners, the bottleneck should gradually resolve itself, Halluin says. However, says Van Horn of the patent office, "even though we're increasing our ability to turn the work over faster, it's coming in at a rate that we have yet to keep up with. I don't anticipate things calming down in this area for a number of years to come." □

## The new breed of patent attorney

Of the many intriguing hybrids born of the biotechnology revolution, perhaps the most useful is a multicellular organism called the biotech intellectual property attorney—a variety of patent lawyer with specialized expertise in biochemistry, genetics or pharmaceutical medicine. Like so many products of the gene-splicing age, these specialists have not been around for very long, but they are already having a profound influence on the course of the biotechnological revolution. Indeed, a biotech company can have the best scientists in the land, but without a good shot at patent protection all of that research may be for naught.

Who are these legal guardians of recombinant remuneration? Alphabetically speaking, they are for the most part MSs or PhDs who have subsequently earned a JD or LLM. Despite their substantial training in the sciences, however, the "new breed" is not necessarily more specialized than previous varieties of patent attorneys, says Irving Kayton, a professor of patent law at George Washington University Law School in Washington, D.C. After all, he notes, "By definition, whatever a patent lawyer deals with is 'new.'" But many more people are coming into patent law with specialties in chemistry and biotechnology, he says, as it becomes clear that living cells are to become a major source of patentable products in the 21st century.

In addition to having advanced degrees in such areas as biochemistry or chemical engineering, says Albert Halluin, chief patent attorney for Cetus Corp., biotech patent lawyers tend to be extremely well versed in one or several scientific subspecialties. This helps to ensure that their highly technical patent applications will stand up against competing claims.

"I once met an attorney who was already a chemical engineer but who didn't know much about polymers," Halluin recalls. "He had a new client who was doing some kind of work with a new kind of polymer. He had two books under his arms, and he said he was going to spend the next few days reading through these books until he learned it. Then he was going to spend some time with some professors, and finally he would start writing these patent applications." Even then, Halluin says, it would take some time before the chemist-*cum*-attorney would be proficient in patent law as it applies specifically to polymers.

How big is the future in biotech patent law? At least one New York law firm, Pennie & Edmonds, has gone so far as to recruit scientists directly from research labs and then pay their way through law school, according to the firm's legal recruiter, Patricia Stacey. "From what I'm hearing," she says, "biotech is going to be *the* big thing in patent law."

*– R. Weiss*