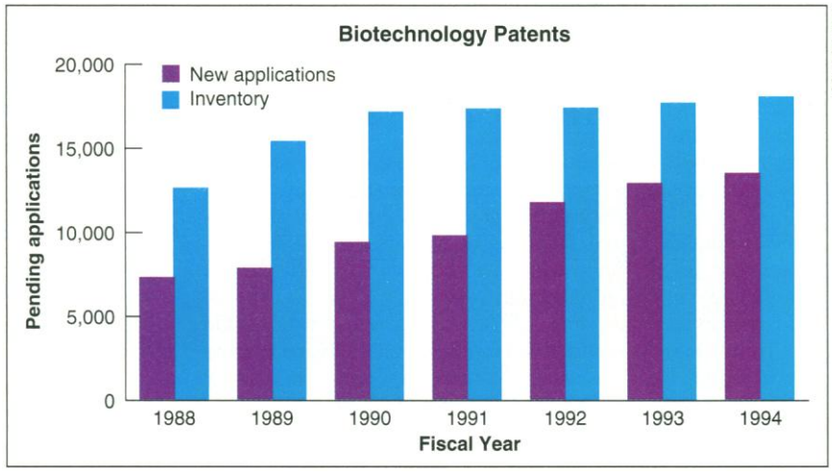
BIOTECHNOLOGY

Biotech Leaders Give Patent Office a Litany of Complaints

As biologists identify more and more human genes and proteins, they're peppering the U.S. Patent and Trademark Office (PTO) with a growing number of intellectual-property claims on all manner of medical applications—from synthetic tissue to AIDS vaccines to new types of gene therapy. The patent office has responded to this surge in applications by hiring extra biotechnology examiners and beefing up intramural training courses—a response that has reduced the average lag time for initial review of a biotech patent from 15 months in 1987 to around 7 months today, even as filings jumped from 7300 to more than 13,300 a year.

But biotech industry leaders are far from satisfied with the PTO's performance. The patent process, they complain, remains confused, unpredictable, and governed by intramural rules that aren't made public. And the resulting uncertainty, the industry claims, makes it difficult to attract investors. To face these criticisms head-on, PTO Commissioner Bruce Lehman last week invited leaders of the biotech community to come to a meeting in San Diego and speak their minds. He got an earful, and later promised to make changes.



Coping with the flood. The PTO has kept the backlog of biotech cases from growing as fast as the number of new applications.

Charles Ludlam, vice president of the Biotechnology Industry Organization (BIO) of Washington, D.C., brought along a 224-page tome of scientific and legal critiques drafted by 54 experts drawn from BIO's membership. It attempts to make the case, as Ludlam says, that barriers have been raised against biotech patents that are "inconsistent and discriminatory" and cry out for "fundamental reform."

BIO's book may be the heftiest expression of discontent, but it wasn't the first. An authoritative early protest came in the form of a hand-delivered letter to Lehman, dated 2 May and signed by S. Leslie Misrock and Albert Halluin, patent attorneys at Pennie & Edmonds of New York City. Patent lawyers are reluctant to criticize PTO in public for fear that it might hurt their prospects before the agency, which does most of its work in secret. But Misrock, a senior figure in the patent bar, wrote to express what he said was a widely held view that "distinct changes" have taken place at PTO in the past 4 years that "threaten the continued growth of the biotechnology industry."

Specifically, Misrock objected that examiners were more critical of biotech patent applications, demanding that researchers submit "conclusive proof of therapeutic utility in humans"—clinical data of the kind normally required at a later stage of drug development by the Food and Drug Administration (FDA). As an example of this problem, a university official who insisted on anonymity told *Science* of a case in which a PTO examiner is refusing to allow a patent on a diagnostic test for a chronic disease until one patient under treatment dies "so that we can confirm the diagnosis with an autopsy."

Misrock and others contend that in demanding such thorough proof of efficacy, the PTO staff is poaching on FDA's turf. To ask for clinical data is simply "wrong as a matter of law," Misrock argues, citing a 1985 decision by the Court of Appeals for the Federal Circuit (*Cross* vs. *Iizuka*), which concluded that data collected in vitro may be sufficient proof of efficacy in patenting a pharmaceutical for human use.

Biotech executives and attorneys who submitted statements and spoke with *Science* also urged PTO to consider such problems as:

- The existence of what attorney Jorge Goldstein of Sterns, Kessler, Goldstein & Fox calls a double bind that makes it difficult for academic researchers to obtain human gene patents. Many applications may get caught between a requirement that a gene sequence be entirely new (never published) and the requirement that its use in a medical application be tested and fully explained. The double bind occurs because it's often difficult to explore medical applications without support from private investors. Yet funding for expensive clinical research is hard to obtain if gene patents are not routinely available. This problem may be acute for those who want to patent DNA-based probes and markers, because the patent seeker may not know the biological function of the marker gene being patented.
- Inconsistent demands for evidence to support biotechnology claims and conflicting reasons cited for rejecting applications.
- Concern that inventors will need a longer period of patent protection if the United States adopts an international standard for patents, as proposed by the General Agreement on Tariffs and Trade. A PTO official says biotech companies are seeking an increase in the 5-year extension that's sometimes granted patents that get caught in a prolonged regulatory review at FDA.

The session, Lehman's legislative aide Jeffrey Kushan says, was "hectic," lasting more than 10 hours and including 57 witnesses. But Kushan notes that it was "very productive," for Lehman and the PTO staff learned how frustrating the system can appear to outsiders. Kushan adds: "Now it's just a matter of sorting through the rubble ... and looking to see more carefully just what our examiners are doing."

Lehman says "We're definitely reviewing our policies ... and people can expect changes to be made, period." The clinical data issue was "the most serious concern" that arose in San Diego, he thinks. Next was the need to compensate for regulatory delay. Lehman plans to move on changes at PTO "right away." He hopes to issue a draft biotech policy statement in a matter of weeks and get public comment "before the end of the year."

Lehman has already won praise from some of PTO's critics for acknowledging that there are problems. Ludlam, for example, says, "We were encouraged by the fact that [Lehman] held the meeting" and is taking the matter seriously. Lehman listened to the entire grueling review, Ludlam says, accompanied by a "very high-level delegation" of PTO officials. Ludlam was pleased that the PTO delegation had "clearly read our book."

–Eliot Marshall