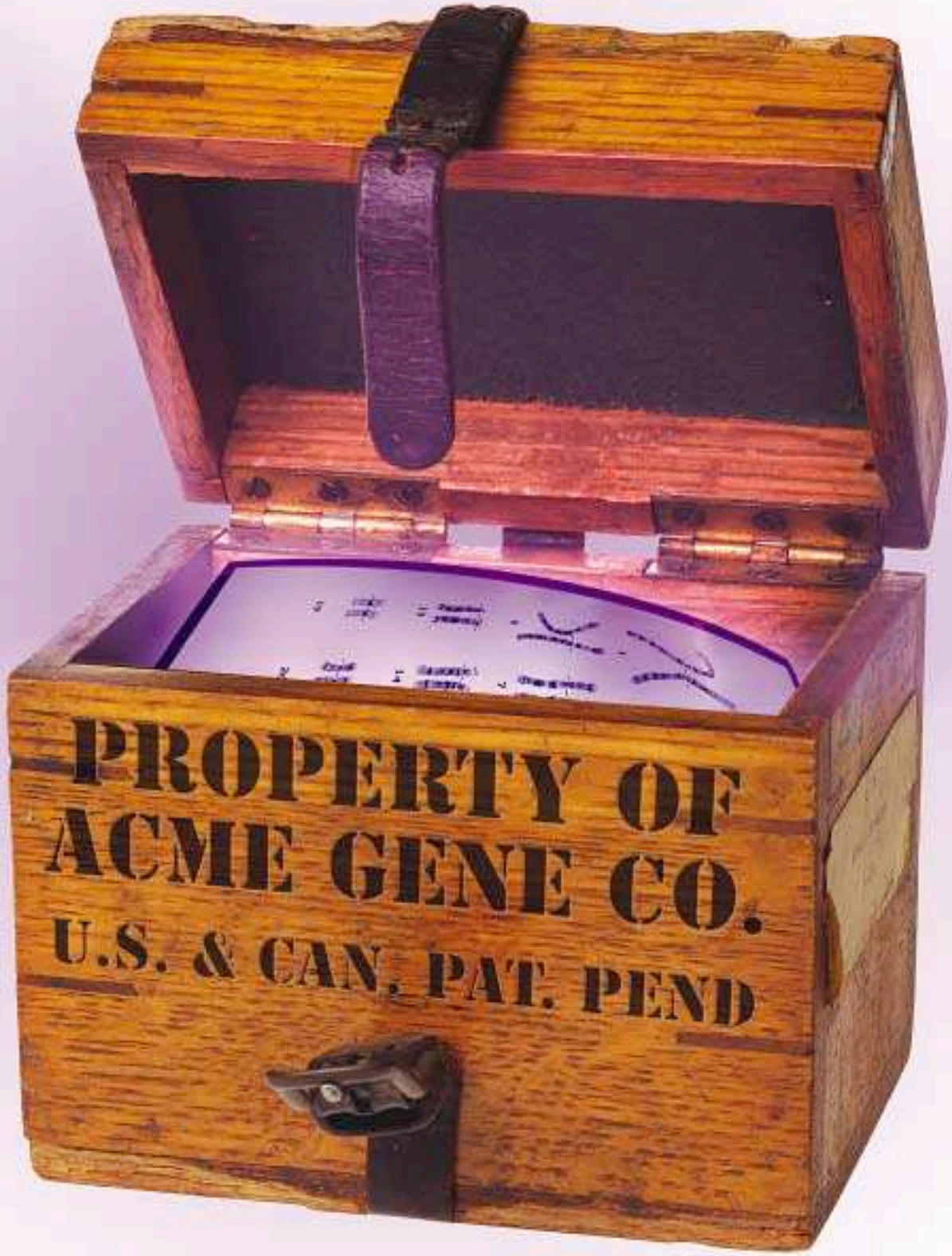

PhotoDisc, Reuther/EHP

Pending Resolution:

The Question of Who Owns DNA

Gene sequencing, says Sailen Barik, is no longer "rocket science." Barik, an associate professor of molecular biology at the University of South Alabama in Mobile, says that most of his lab students are capable of finding genes—in fact, hundreds per student over a few months' time—and sequencing them. "It is not difficult to do," he says. "It does not require you to go to a rain forest in Brazil. It's not a natural product that's hard to isolate or purify. Everyone has DNA and genes. . . . You don't have to invent anything new." So why, he asks, should discovering genetic sequences lead to patent protection for their finders? "The sole argument that 'I did it first' or 'no one has done it before' does not make either the procedure or the result patentable," he says.

The biotechnology industry, however, is adamant about making the distinction between genes that appear in nature and those that have been isolated, cloned, and had their utility determined. Patent law is clear, they point out, that while living matter is patentable, it must be living matter that has been altered by humans for a utilitarian—and thus, patentable—purpose. A gene itself, in other words, is not patentable. And therefore, industry says, people who are sounding the alarm about "patenting human life" are simply wrong. But critics contend that the U.S. Patent and Trademark Office (PTO) has often been overly liberal in its intepretation of when these criteria are sufficient to reward a patent.

In December 1999, the PTO published revised guidelines in the *Federal Register* that would tighten the requirements necessary for gene patents and issued a call for comments. The office received scores of responses, some perhaps predictable. Industry responders cautioned against tightening the requirements for patents too much, while many scientists and medical organizations supported a shift to looser definitions of what may be patentable. One of the scientists who responded was Barik, who applauded the PTO's strengthened requirements for demonstrating utility. "If you let greedy companies and their lawyers patent naïve sequences, just imagine the consequences," he wrote. "Tomorrow, Japan will sequence the whole rice genome, China will sequence zebrafish, Bill Gates will own *Plasmodium*, Donald Trump will invest in the Sanger Centre and own 80% of all coral reef anemones." Although the biotechnology industry contends that such rhetoric is misinformed, the issue is still hotly debated and, with the explosion of activity in gene sequencing, will likely continue to be so.

Patenting the Human Genome

The biotechnology industry responds to accusations like Barik's with vigorous denial. Nobody, they say, is trying to own life forms. Still, the mapping of the human genome opens huge potential markets for pharmaceutical and biotechnologic product developments, which take time and money. The question is, how much patent protection should those efforts enjoy?

The issue of gene patenting and its relationship to restriction on research surfaced loudly in March when U.S. president Bill Clinton and British prime minister Tony Blair issued a joint statement urging that genome information be made freely available to the public. The news sent many biotechnology stocks tumbling and prompted J. Craig Venter, president and chief scientific officer of Celera Genomics in Rockville, Maryland (which has predicted that it will have completed its mapping of the human genome by the end of 2000), to state that the company has never intended to keep other scientists from using the information it gathers. He said that Celera would release the entire human genome sequence when it was completed, and would seek patents on gene sequences for medically important uses.

The Clinton–Blair statement also acknowledged the role that patents play in providing an incentive for research, stating that "intellectual property protection for gene-based inventions will also play an important role in stimulating development of important new health care products." Clinton also spoke up for gene patents at a press conference following the market downturn, saying, "If someone discovers something that has a specific commercial application, they ought to be able to get a patent on it. And the question is always going to be, are you drawing the line in the right place?"

Celera's effort mirrors that of the publicly financed Human Genome Project (HGP), coordinated by the U.S. Department of Energy and the National Institutes of Health, which was created in 1990 for purposes of identifying all the genes in human DNA by first determining the sequence of some 3 billion nucleotides that make up human DNA. To accomplish this, the two agencies, along with the British Wellcome Trust, have funded genome research projects in nearly 200 laboratories around the world.

While private efforts are similar to those of the HGP, they see genetic information not as an end in itself, but as a starting point for development of compounds that may prove medically useful—and profitable. In exchange for these research investments, companies have turned to the agency where private industry always goes in hopes of securing financial protection for its efforts: the PTO.

Whom Do Patents Protect?

Ever since a landmark 1980 U.S. Supreme Court ruling in *Diamond v. Chakrabarty*, the patentability of some life forms has existed. In that case, the court found that a genetically engineered bacterium designed to "eat" oil (making it at least theoretically useful in cleaning up spills), invented by General Electric scientist Ananda M. Chakrabarty, was patentable because it was not found in nature. The key to its decision, the court stated, was that the organism was "made by the hand of man." In 1988, the "hand of man" concept took its most dramatic leap forward when the PTO granted a patent to Harvard University researchers for a genetically altered mouse used in cancer research.

> If someone discovers something that has a specific commercial application, they ought to be able to get a patent on it. And the question is always going to be, are you drawing the line in the right place?
>
> **President Bill Clinton**

With the emergence of the HGP and its private counterparts, the PTO began receiving applications for gene-related patents. While the limits of Chakrabarty would seem to remove discovered genes from patent protection, applicants have been successful in getting patents for certain genetic information. The key measure for applicants is in demonstrating ultimate utility, according to Lila Feisee, intellectual property counsel at the Biotechnology Industry Organization, a trade group of more than 900 members.

"When a gene is patented, it's not the gene that's in your body," she says. "[Scientists] take DNA, they characterize it, they identify what it does, how to use it, so it's not just something that's in your body. It's been industrialized. It does have the hand of man in it, and it is eligible for patenting." In addition, she says, a patent is not ownership. A patent gives the patentee the right to exclude others from making, selling, or offering to sell the invention for a limited period of time in exchange for full public disclosure.

One of the controversies that has arisen in the new realm of gene patenting, however, is that patents have been granted for mere gene fragments or partial sequences known as expressed sequence tags (ESTs), which are devoid of much demonstrable utility. "People make these ESTs, they know a little about the gene, but not much," says Louis Myers, an intellectual property lawyer and biologist based in Boston, Massachusetts, whose practice regularly brings him to the PTO. "They may know it's expressed in a certain kind of tissue, but they don't have the whole gene sequence. They really don't know much about it. The question, which has been hotly debated, is this: If I have an EST, should I be able to get a patent claim that will later dominate the person who [sequences] the whole gene, who finds out what it does, what it's useful for, and contributes a lot of useful information? Or should my patent claim be pretty strictly limited to just the EST, which is not tremendously useful?"

Myers says that, although there's an incentive for companies to seek patent protection on relatively meager genetic information, such patents can tie up subsequent research because it becomes costly for researchers to pay multiple patent royalty fees. "So you have to ask the question, was that early contribution significant enough that you're willing to allow that first person to dominate this downstream activity?" he says.

By all accounts, the PTO is now making it more difficult for applicants to

patent genetic products. PTO spokeswoman Brigid Quinn says that the move to revise the guidelines was prompted by two recent court decisions related to patent utility. But some observers believe that the PTO was under pressure from scientists and groups concerned about the ethics of patenting life forms.

"It had gotten so outrageous that they were getting flak even from within the industry," says Jonathan King, a professor of molecular biology at the Massachusetts Institute of Technology in Cambridge. "They'd started granting patents just on fragments. That's like saying, 'I haven't figured out how to put the whole windshield wiper together so it works, but I've got the tip.' There was enough opposition to that within the scientific community that they were forced to make some gesture."

King is also a board member of an advocacy group called the Council for Responsible Genetics, which arose with the advent of genetic engineering 25 years ago. He's been an outspoken opponent of any kind of life-form patenting since the days when the council tried unsuccessfully to stimulate a Congressional debate on the topic in the wake of the narrow 5–4 Chakrabarty decision.

King contends that the biotechnology industry is dodging behind semantics when it argues that genetic patents are not the same thing as patents on life forms. "Human gene sequences are not inventions," he says. "Sequences are discovered, but they're products of nature. When you discover a new mineral you can't patent it. Just like the bottom of the ocean, just like the atmosphere, just like the moon are the common heritage of the whole species, the genome is absolutely the common inheritance of the entire species. The notion that the human genome should be private property is an egregious form of theft of this common biological heritage."

The Effects of Gene Patenting on Research

Critics of gene patenting contend that one of its greatest dangers is that it retards research. "Scientists generally are eager—they can't wait—to tell their colleagues about their findings," King says. "But in patent law, if you publish a finding, it becomes 'prior art.' So you cannot patent a gene sequence once you've published it. As a result, those people who are trying to patent don't talk. You go to a scientific meeting, and you ask them a question, and they'll say, 'I can't answer that. There are intellectual property rights issues.' This whole rich culture of biomedical research, this culture of cooperation and communication, is now being strangled."

By the time Clinton and Blair issued their statement in March, troubling reports regarding gene patents had made their way into the news. A survey of U.S. laboratory directors by the Stanford University Center for Biomedical Ethics found that a quarter of them had received letters from lawyers representing biotechnology companies ordering them to stop clinical tests for a variety of disorders, including Alzheimer disease and breast cancer. Because the clinical tests that were stopped by legal threat were those that patients pay for, the patent holders were within their legal rights to order stops to the tests. In December 1999, the British newspaper *The Guardian* reported that one such letter, from Worcester, Massachusetts–based Athena Diagnostics, informed recipients that the company owned exclusive rights to certain tests for the diagnosis of late-onset Alzheimer disease under U.S. patent number 5,508,167—but that Athena would perform the tests for $195 per specimen, more than twice the standard rate being charged by most university medical labs. For many labs, the cost proved prohibitive.

There is no research exemption under patent law, but in practice patents are not enforced against researchers who use the information for noncommercial purposes. "There's never been an instance where a company has enforced a patent on somebody who's doing pure academic research," says Feisee. "In fact, it benefits companies if other people are doing research using their product. Now, the minute that an academic researcher tries to make money off it . . . then it becomes a problem."

Not surprisingly, the notion of gene patenting has also spurred a backlash on ethical grounds. In 1995, a coalition of more than 80 religious groups held a press conference denouncing all forms of gene patenting. In August 1999, the American College of Medical Genetics issued a position paper stating that genes are naturally occurring substances that should not be patented, and that licensing agreements should not be made prohibitive through excessive royalties and other unreasonable terms. In March 2000, the Council for Responsible Genetics responded to the Clinton–Blair announcement by issuing a statement calling for the exclusion of human genes from the patent system.

"This is a question of national policy, not administrative procedure," says King. "As a citizen, I don't care what patent lawyers might think about it. This is my DNA. These are my genes. I'm not willing to leave it to the Patent and Trademark Office to decide the fate of the human genome. I don't think that's appropriate in a democracy."

Regardless of the venue, the controversy over gene patenting will continue to be played out. Whether gene patenting will ultimately prevail in the public's consciousness, Myers says, "depends on whether or not you believe the patent system contributes to good for people. It depends on whether or not you think the patent system and its claims to be able to attract money and investment and capital and people into some areas to solve problems speeds up or slows down medical process. If you think it speeds it up, then I think you should be in favor of patenting genomic information. If you think it slows it down, then you should be against it."

Richard Dahl

> Just like the bottom of the ocean,
> just like the atmosphere,
> just like the moon
> are the common heritage
> of the whole species,
> the genome is absolutely
> the common inheritance
> of the entire species.
>
> **Jonathan King**
> **MIT**