Ruling on Heart Drug May Boost Research

But the patent decision, by a British court, is a blow to Genentech

WHEN a British court recently declared a patent on a major new heart drug invalid, the decision was a blow to Genentech, Inc., the drug's manufacturer. But the decision encourages research and competition in the biotechnology industry, according to some patent attorneys and Wall Street analysts who specialize in genetic engineering issues.

On 7 July, the High Court in London ruled that Genentech's patent claims covering a clot-dissolving agent, tissue plasminogen activator or TPA, were too sweeping. According to a transcript of the proceedings, which was released 13 July, Justice John Whitford held that only 1 of 20 of Genentech's claims is valid.

The decision is another setback for Genentech. On 29 May, an advisory panel to the Food and Drug Administration voted not to approve Genentech's version of TPA, known as Activase, for use. But the verdict was a first-round victory for the British pharmaceutical company, Wellcome Foundation Limited, which contested Genentech's patent on TPA. The two companies are among several competing in an intense race to market TPA, which is expected to be the first billion dollar drug of the biotech industry (*Science,* 10 July, p. 120). So far, Activase is approved for use only in the Phillipines, France, and New Zealand.

Thomas Kiley, Genentech's vice president for corporate development, said the company will likely appeal the decision. "We're at war with Wellcome," he said. Wellcome noted Whitford's decision "with satisfaction."

The patent ruling has no legal bearing in the United States, where a TPA patent has not yet been issued. But the British verdict "from a psychological standpoint, has a lot of precedence [in the United States]," says James Haley, a New York patent attorney who handles biotechnology cases. "A judge will think more carefully" when considering a patent on TPA, he said.

The only claim upheld by the British court covers a particular plasmid, which carries genetic material into a cell and is of minor importance. The other claims included coverage of the TPA molecule itself and the process by which it is made. Genentech's patent, for example, broadly covered the TPA molecule produced by any known or future method of recombinant DNA. This patent protection "is too wide and is bad," Whitford stated in his 87-page decision. "There is no basis for it."

He said, "Had Genentech first discovered TPA, or had they at least been the first to discover its desirable properties as an activator, they . . . might well have been entitled to a broad claim. . . . " But, as the judge noted, the drug's effectiveness was already known before the company set out in the early 1980s to clone and express the TPA gene.

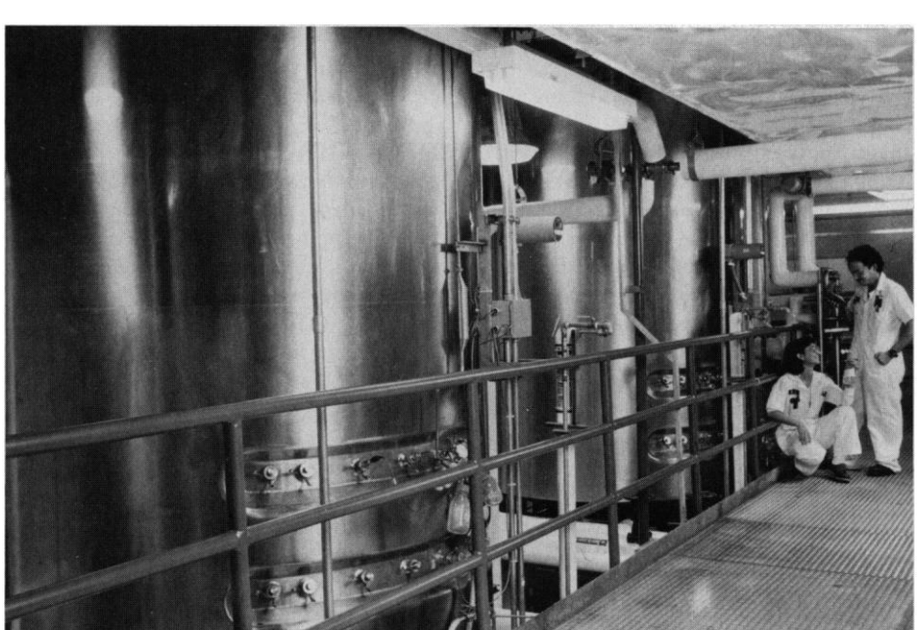
Whitford did say that Genentech was the first to discover the full TPA sequence and that, based on this work, Genentech might have a "limited process claim. . . . " He acknowledged that Genentech spent a lot of time, money, and effort to clone and express TPA and that the company discovered "a particular route to a known end" to make TPA.

But this alone, he commented, is not enough to grant Genentech a monopoly on TPA. Whitford said granting Genentech broad protection would stop others from trying to invent new and improved forms of TPA and could "stifle research, which, in the public interest, it ought to be open to other investigators to pursue" and ought to be patentable.

Wellcome's main argument during the 3–week patent trial in June was that Genentech's work on TPA was not novel, especially in its use of genetic probes, and therefore not patentable. But the judge did not address the issue of novelty directly in his decision. "He sidestepped the issue," said Bruce Eisen, patent counsel for Genetics Institute, which licensed and assigned worldwide marketing rights for its TPA technology to Wellcome.

According to some observers, the patent decision sends a positive signal to competing companies. Haley said that the decision "encourages other companies to do research and should reassure them that they won't lose in a high–stakes race. The pioneering company, however, may not get the broad protection it wants." David Manyak, an analyst at Merrill Lynch, said, "The key issue is that some of the patent claims were allowed." But, he said, the court sent a signal that it "doesn't want to cover a product to the extent that improvements on a molecule can't be made."

In Kiley's opinion, the judge's decision "throws a wet blanket on research." Wellcome spokesman Martin Sherwood said that the ruling is "neutral as far as its impact on research." The verdict, he said, "is a sign post of what you may or may not expect" from the courts. ■ MARJORIE SUN



TPA tanks. *Fermentation tanks at Genentech where TPA-producing cells are grown.*