Wellcome versus Genentech result

- TPA patent case ends with 90-page judgement
- Wellcome's 'victory' may not be decisive

London

THE confusion and controversy surrounding biotechnology patents seems no closer to resolution, following the British High Court decision declaring invalid the wide-ranging patent held by the US firm Genentech on the clot-dissolving agent, tissue plasminogen activator (TPA). Lawyers are still studying the highly complex 90-page decision which upholds the patent challenge by the UK drugs firm Wellcome, and the two sides disagree on exactly what the judge, Mr Justice Whitford, is saying about what he calls "the potential goldmine" of TPA production.

Wellcome has greeted the decision "with satisfaction", saying it vindicates their arguments that Genentech's patent failed to meet the criteria of novelty and inventiveness. Genentech lawyer Simon Cooke disagrees with that interpretation, and says the decision shows the judge believes the product is in fact novel and inventive. And Genentech's chief executive officer, Robert Swanson, says the company will appeal the decision rather than narrow its patent claims.

The decision includes a discussion of each of the 20 claims covered by Genentech's patent, ranging from processes for making TPA to pharmaceutical compositions containing it. One claim covers "human TPA as produced by recombinant DNA technology", and another covers "all processes for producing TPA by recombinant DNA technology."

The decision accepts that Genentech was the first to discover the full sequence for producing TPA, and as such "there might have been scope for a limited process claim"; but that discovery "does not justify the broad claims made." The claim covering any DNA technology for TPA "is too wide and is bad. There is no basis for it," the decision states.

The judge says, "What Genentech did was achieved by what, in my judgement, was rather more than the exercise of proficiency — it involved laborious and costly effort, and to deny any monopoly protection to those who are prepared to put as much time, skill and money into research as Genentech did is only too likely to discourage workers in this field from making advances which may be of the greatest public benefit." But in what might be viewed as a contradictory statement, he continues, "To grant them a monopoly which would stop others attempting to discover alternative, possibly wholly unknown and possibly better routes to that end, would be to stifle research which, in

the public interest, it ought to be open to other investigators to pursue and over which other investigators, in their turn, if they make a valuable contribution, might be able to secure proper protection."

Genentech's lawyer says the judge has "misunderstood the technology", and has made a decision that is "fundamentally wrong". Mr Cooke adds, "Genentech has given to the public the structure of the gene for TPA, and he's in effect said we should get no protection whatsoever".

But Genentech's patent claim is "too greedy", according to London patent attorney Iain Baillie. He predicts that the

company will find itself "in the same mess" if it has filed a similarly wide-ranging claim for a patent in the United States, and he also forecasts a loss for Genentech in the Court of Appeals. Wellcome says if a similar patent is granted in the United States, Genentech could expect to fight another court battle.

It is likely to be at least a year before the British Court of Appeals can hear what has now become a case of legal technicalities, and another year if the legal battle goes on to the House of Lords. Meanwhile, Wellcome is continuing to produce TPA for use in its clinical trials; under US law, this is not considered a patent infringement. The legal battle has done nothing to stop the race for the lucrative TPA marketplace.

Kathy Johnston

... US patents in the balance

Washington

As the first major biotechnology patent to be disputed in the United Kingdom, the TPA case is expected to serve as an indicator of how readily future broad biotech patents will be granted and upheld. But the British opposition to broad claims may not carry over the Atlantic, because the current US biotech patent climate is relatively liberal.

The bad news falls on Genentech just weeks after the United States Food and Drug Administration (FDA) withheld marketing approval for Activase, its version of TPA (see *Nature* 327, 450; 1987). But, of the 19 or so companies that are working on TPA, Genentech still leads the pack in the race for FDA approval. Stuart Weisbrod, a biotechnology stock analyst for Prudential-Bache, says Genentech has a two-year lead on the competition in the race for FDA approval despite the setback, and expects them to gain marketing approval by the end of the year. Wellcome does not expect to be able to sell its version of TPA until 1989. Genentech now has approval to market Activase in France, the Philippines and New Zealand.

Investors were not greatly dissuaded by the outcome of the case. On the day the news broke, Genentech's stock dipped \$1.375, to close at \$38.625 a share. This is in contrast to the day the FDA denied approval of Genentech's TPA, when its stock plummeted \$11.50 per share.

Most observers feel that Genentech will succeed in obtaining a patent that allows them access to at least a piece of the estimated \$1,000 million pie for worldwide TPA sales. But Wellcome, and collaborations between Smith-Kline and Biogen, and Hoechst and Chiron are reported to

be producing TPA by essentially the same process as Genentech, so patent coverage is vitally important. The company that gets the patent for the process can lock the others out, forcing them to develop another means to produce the drug. Using a new process would force those companies to start the FDA approval process all over again.

Genetics Institute is the furthest along in developing a "second generation" form of TPA that may make the current patent dispute over TPA moot. According to vice-president Robert Kamen, Genetics Institute has deleted the fibronectin and epidermal growth factor domains of the sprawling TPA molecule, and have removed three glycosylation sites. The resulting stream-lined version may have a half-life in the bloodstream of up to one hour, compared to 5 to 10 minutes for the natural molecule. This means it can be administered in one bolus injection to break down a clot, instead of requiring several injections, as does the natural version.

Genetics Institute plans to manufacture its second-generation TPA at WelGen, a joint mammalian cell production facility it is building with Wellcome, but Wellcome does not own any rights to Genetics Institute's TPA. Others working on second-generation TPA include Smith-Kline, Integrated Genetics, Eli Lilly, Searle, and Genentech.

Genetics Institute and Integrated Genetics have applied for patents for their modified forms of TPA. Theirs may eventually prove out to be the strongest patent positions, as it is easier to defend a modified molecule as novel than a slight variation on tried-and-true genetic engineering techniques.

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