

BUSINESS & REGULATORY NEWS

Appeal court grants Genentech's growth market to Novo Nordisk

Novo Nordisk (Bagsvaerd, Denmark), until now an onlooker in the human growth hormone (hGH) market, has jumped into the game courtesy of the US Court of Appeals for the Federal Circuit. As a result of an injunction filed by Genentech (S. San Francisco, CA), Novo had been blocked from selling its hGH product—Norditropin—on the grounds that Novo had violated Genentech's patent describing a method for producing the protein. But the court of appeals waived the injunction and, in an unprecedented step, then invalidated Genentech's patent.

It is the first time that the federal circuit court has—on its own initiative—invalidated a patent after stopping an injunction, according to Albert L. Jacobs, a partner with the law firm of Graham & James (Washington, DC), Novo's representatives in the case. By doing so, many believe that the court has sent a clear message that it will require greater disclosure in biotechnology patents. The decision was a particular surprise because it came so early in the appeals process, says patent attorney Kenneth Chahine of Madson & Metcalf (Salt Lake City, UT). Usually, the appeals court will consider any issues relevant to an assessment of an injunction. But if issues without a direct bearing on the case are raised, it will usually just "flag" those for the subsequent attention of the district court. Chahine says that "the court has taken (concerns about disclosure) into its own hands, without even hearing argument from both sides." Because the original appeal was made by Novo to challenge the injunction—and not the patent itself, "Genentech didn't even have a chance to [defend the patent]," he says.

At issue is the provision for enablement—the requirement that the inventor provides sufficient detail to enable the invention to be reproduced. The patent in question described a generic method that uses bacterial expression followed by cleavage with trypsin to produce the final protein of interest. But it only speculated that the expressed protein could be hGH with an amino acid extension to serve as a trypsin cleavage site; this prompted Novo to argue that the patent did not fulfill the requirement for enablement. "The specification didn't

show the basic parameters of how (to produce hGH)." says Jacobs, "I think the [US Patent and Trademark Office] examiner saw this patent application as just another in a long series of Genentech patents, and didn't look at it as closely as one might have."

The importance of the appeals court

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decision may be its implication that those who file patents in biotechnology may have to be more careful than those in more established technology areas in describing an invention. "The court [may be] saying that in technologies that are embryonic. . .you may have to exercise even more care," says Jacobs.

The decision is likely to change the face of the human growth hormone market. According to Jacobs, "Novo Nordisk was certainly at a disadvantage in the marketplace, having been [prevented from marketing Norditropin] the last two years."

And the legal battles aren't over. "We're studying the decision that was made by the court," says Paul Laland, associate director of corporate communications at Genentech. As Genentech mulls over an appeal, Novo has not forgotten Genentech's successful block of Norditropin sales. "Since the injunction was decided by the federal circuit court to have been wrongly issued, Novo Nordisk is examining whether it may be able to recover some of its losses [from Genentech]," says Jacobs.

The court's apparently headstrong opinion on enablement raises another specter: In seeking to protect themselves against cherry-picking competitors who might change a few amino acids in a protein to avoid infringement, biotechnology companies may be a little vague on the details of the structures their patents should cover. Given its response to Genentech's reference to hGH in its patent, the court could frown upon such tactics, Chahine says. Despite the fact that substitutions in amino acids or base pairs can often be safely made without affecting the biological activity of a protein or gene product, "[the courts] see biotech as this black box. . . everything is unpredictable to them."

It is important for biotechnology companies to submit patents with both broad and narrow claims, he says, "so that even if their broad claims are invalidated, they have narrow claims to fall back on." "You have to write (patents) with one eye on the patent office and one on the federal circuit court," he concludes.

Jim Kling

Novartis find sparks new GABA drug search

The development of therapeutics for memory and learning defects and absence-type epilepsy have been given a fresh impetus by a newly cloned neurotransmitter receptor, the γ -aminobutyric acid GABA_B receptor (*Nature*, March 20, 1997). The receptor has been sought since 1980, when Norman Bowery of the University of Birmingham (Birmingham, UK) and colleagues reported its existence. Indeed, GABA_B receptors are the last class of

receptors for the major known neurotransmitters to be isolated. Although companies such as Schering-Plough (Union, NJ) and SmithKline French (now part of SmithKline Beecham; London) abandoned their programs on the GABA_B receptor, researchers at Novartis (Basel, Switzerland) who made the recent advance believe the cloned receptor should provide a crucial tool for finding receptor subtypes and developing high-throughput screening for selective drugs that target them.

Although its physiological role is only partially understood, animal studies indicate

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