Keywords: **Enablement; Non-Patent Publication, Inequitable Conduct, Prophetic Examples, Past Tense, Materiality, Deceptive Intent**

General: **The presumption of enablement does not appear to hold for non-patent publications used as anticipatory references. A prophetic example drafted in the past tense may be used to find inequitable conduct in some circumstances.**

Novo Nordisk Pharmaceuticals Inc. v. Bio-Technology General Corp
76 U.S.P.Q. 2d 1811 (Fed. Cir. 2005)
Decided October 5, 2005

I. Facts

Novo Nordisk A/S ("Novo") is the assignee of U.S. Patent No. 5,633,352 (the '352 patent) directed to the production of human growth hormone (hGH). The hGH protein has a specific sequence of 191 amino acids and has many medically useful properties. Until the mid-1980's, hGH protein for therapeutic use was obtained from the pituitary glands of cadavers, which carried a risk of infection and contamination for the patient. Prior to the '352 patent, attempts to produce biosynthetic hGH that would function the same as pituitary-derived hGH were unsuccessful.

The '352 patent discloses the production of hGH using recombinant DNA techniques. In particular, the '352 patent teaches the production of hGH in bacteria, such as *E. coli*, using a "fusion protein" coded by a gene sequence for both a bacterial protein and for the hGH. The bacteria synthesize the fusion protein, which is cleaved using a proteolytic enzyme to separate the portion of the fusion protein corresponding to the bacterial protein from the hGH. The '352 patent discloses that the cleavage is preferably accomplished using dipeptidyl aminopeptidase I (DAP I).

The '352 patent traces priority back to a Danish patent application filed on December 10, 1982 via a PCT application filed on December 9, 1983. Unlike the '352 patent, the PCT application discloses the use of leucine aminopeptidase (LAP) as the preferred proteolytic enzyme. The use of DAP I was not disclosed until November 12, 1992 when it was disclosed in the first of the series of applications claiming priority to the Danish application via the 1983 PCT application. This series of applications culminated in the filing of the application on March 10, 1995 which issued as the '352 patent on May 27, 1997. Claim 1 of the '352 patent recites: [b]iosynthetic ripe human growth hormone free of contaminants from pituitary derived human growth hormone.

On July 7, 2000, the Board of Patent Appeals and Interferences (the "Board") declared an interference between the '352 patent and U.S. Application Serial No. 09/023,248 (the '248 application) to Bio-Technology General Corp. ("Bio-Technology"). The Board accorded the '352 patent priority based on the August 8, 1984 filing date of the U.S. counterpart to the 1983 PCT application. In due course, Novo sought the benefit of priority based on the 1983 PCT application itself. Bio-Technology moved to deny Novo the benefit of the filing date of the PCT application as well as of the U.S. counterpart based on the failure of those applications to disclose the use of DAP I and on the basis that the LAP enzyme disclosed in those applications was ineffective to produce "ripe" hGH protein. The Board was not convinced by the evidence provided by Bio-Technology that LAP was not effective to produce ripe hGH in accordance with the methods described in the PCT application and the U.S. counterpart. Therefore, on March 12, 2002, the Board awarded priority to Novo.

Bio-Technology appealed the decision of the Board to the District Court for the District of Delaware on April 1, 2002. The district court reversed the Board's decision awarding priority to

Novo and ruled that the 1983 PCT application was not enabled. The court based its determination, in part, on a finding that Novo itself was unable to synthesize ripe hGH using the technique disclosed in the 1983 PCT application. The court remanded the case to the Board for consideration of motions by Novo previously dismissed as moot.

On April 30, 2002, Novo filed a complaint in the District of Delaware against Bio-Technology and Teva Pharmaceuticals (collectively "Bio-Technology") for infringement of the '352 patent. On June 12, 2002, Bio-Technology asserted a counterclaim for a declaratory judgment that the '352 patent was invalid and unenforceable. Following a bench trial, the district court found claim 1 of the '352 patent was anticipated by a December 1981 article by Pavlakis. Based on this finding, the court invalidated claims 1 and 2 of the '352 patent. In addition, the court held that the '352 patent was unenforceable based on inequitable conduct during prosecution of the '352 patent and during the interference proceeding before the Board. Novo timely appealed this decision.

II. Issues

A. Was the Pavlakis article enabled?

B. Did Novo commit inequitable conduct during prosecution of the '352 patent and during the interference proceeding?

III. Discussion

A. Yes. The Federal Circuit previously held that both the claimed and unclaimed disclosures of a prior art patent are presumptively enabled. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1355, 65 U.S.P.Q.2d 1385 (Fed. Cir. 2003). The Federal Circuit, however, did not decide at that time whether the presumption applied to non-patent publications. Novo argued that proving enablement of a non-patent prior art reference by clear and convincing evidence should remain on the alleged infringer. Bio-Technology argued that the district court correctly held the Pavlakis article was presumptively enabled or, alternatively, that, even if the article is not presumptively enabling, that the district court held on separate grounds that it enabled the subject matter of claim 1.

In reviewing the relevant law, the panel noted that the standard for enablement of a prior art reference under § 102 differs from the enablement standard under § 112. In particular, the panel noted that § 112 required that the specification "enable one skilled in the art to 'use' the invention" while § 102 makes no such requirement of an anticipatory disclosure. The panel emphasized instead that the Federal Circuit had stated that "anticipation does not require actual performance of suggestions in a disclosure. Rather, anticipation only requires that that those suggestions be enabled to one of skill in the art." *Bristol-Myers Squib Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1379, 58 U.S.P.Q.2d 1508 (Fed. Cir. 2001).

With this in mind, the panel read the district court's opinion as not relying solely on the *Amgen* presumption in finding the Pavlakis article enabled and that the district court determined that Bio-Technology affirmatively established enablement of the Pavlakis article. The panel noted that the critical inquiry was whether the Pavlakis article disclosed in an enabling manner the production of ripe hGH. The panel noted that the Pavlakis article discussed particular materials and methodology to produce hGH and, therefore, disclosed the production of ripe hGH in an enabling manner. The panel, therefore, affirmed the district court's finding that the Pavlakis article was sufficiently enabled to be an anticipatory reference.

B. Yes. Example 1 of the 1983 PCT application describes the use of the LAP enzyme in producing ripe hGH. Example 1 was phrased in the past tense. The district court found, however, that when the 1983 PCT application was filed, the inventors had not successfully prepared hGH with LAP. On March 7, 1984, Novo did successfully produce hGH with a

LAP preparation which , unknown to them, was contaminated with DAP I. On October 18, 1984, Novo scientists concluded that the active component in the solution which produced the ripe hGH was not LAP but was in fact the contaminant, i.e., the DAP I.

This discovery led to the filing of a PCT application in 1986 disclosing the production of hGH using DAP I. On April 11, 1990, during prosecution of the '230 application, which claimed priority to the 1986 PCT application, Novo argued against a prior art reference which disclosed the use of LAP. In particular, Novo stated that they had tested LAP with bacterially produced hGH and it was shown to *not* be effective. In addition, on September 12, 1990, Novo filed a declaration on behalf of the inventors of the '230 application, who were also inventors on the '352 application. In this declaration, the inventors stated that a pure LAP preparation would not convert amino extended hGH to mature hGH. Instead, only LAP preparations containing relevant impurities would have the desired effect. Thus, during prosecution of the '230 application, Novo sought to overcome a prior art rejection based on the ineffectiveness of LAP in producing hGH.

Novo was unable to overcome the rejection of the '230 application and abandoned the case. Subsequently, on November 12, 1992, Novo filed the '856 application which disclosed the use of DAP I in producing hGH. In a preliminary amendment filed on October 13, 1992, Novo amended the specification of the '856 application to claim a priority date of December 10, 1982, (i.e., the Danish patent application) via the 1983 PCT application. The Examiner did not initially accept this amended priority claim and rejected the application based on art having a priority date later than the amended priority claim.

On January 7, 1994 the Examiner held a personal interview with a Novo in-house attorney, a Novo in-house patent advisor, and two of the inventors of the '856 application. The Examiner's interview summary states that the priority date should be 1982 and that the Novo attorney would point out where in the priority documents enablement was present. In a subsequent amendment, Novo pointed to the 1983 PCT application as providing "the general concept of adding an amino-terminal extension with an aminopeptidase, and isolation of mature hGH." Novo also pointed to Example 1 of the 1983 PCT application as being directed to hGH. The Examiner agreed to Novo's priority claim, allowing Novo to overcome the cited prior art. In allowing the case, the Examiner specifically stated that the amended priority claim was what allowed the removal of the cited prior art.

The district court found inequitable conduct with respect to prosecution of the '856 application based on Novo's failure to disclose that Example 1 of the 1983 PCT application had never been performed. The district court found the element of materiality satisfied because the Examiner relied upon the example in determining that the 1983 PCT application enabled the invention of the '856 application, and thus entitled the '856 application to a priority date earlier than the cited art. The district court found the element of intent satisfied because Novo knew or should have known that the Examiner would have considered the fact that Example 1 was prophetic important in evaluating whether the U.S. counterpart to the 1983 PCT application enabled the invention of a subsequent application, particularly since Novo never successfully produced ripe hGH using the methodology of Example1.

Similarly, the district court found inequitable conduct with respect to the interference proceeding based upon Novo's failure to inform the Board that is was ultimately unable to produce ripe hGH using the methodology of Example 1 as set forth in the 1983 PCT application. The district court found the requisite materiality because the Board looked to Example 1 and reviewed expert testimony as to whether the described steps would enable one of ordinary skill in the art to produce ripe hGH. With respect to intent, the district court noted that Novo presented expert testimony to the Board about Example 1 knowing that Example 1 had never been successfully performed. The court found that "Novo knew or should have known that the Board would consider both Example 1 and [the expert testimony] material to

the question of enablement, particularly since this question was the sole focus of the interference." Further, after the interference Novo did not offer an explanation for its silence and merely asserted that "it was not required to provide the PTO with a running update of its efforts to make hGH."

On appeal Novo argued that it was able to make hGH using the methodology of Example 1 and pointed to its experiments using the LAP preparation which was inadvertently contaminated with DAP I. Novo, therefore, argued that because the methodology did work, there was no culpable failure to say that it did not work. The panel was unpersuaded by Novo's reasoning. In particular, the panel noted that it was undisputed that in the experiment in question Novo unintentionally used LAP which was contaminated by DAP I. The panel was unprepared to accept the proposition "that simply because fate interceded and Novo scientists unintentionally used LAP 'contaminated' with DAP I, Novo produced ripe hGH according to the methodology of Example 1."

Novo also argued that the district court erred in finding deceptive intent in the failure to disclose the prophetic nature of Example 1 to the PTO or the Board. According to Novo, there was no finding by the court that anyone had actual knowledge that Example 1 was prophetic and that Novo never successfully produced ripe hGH using the methodology of Example 1. In particular, Novo contends that there is no evidence that the inventor who wrote Example 1 knew or found out that drafting a prophetic example in the past tense was not a good procedure at the PTO or that he told any of Novo's attorneys that Example 1 was prophetic. Thus, Novo argued that it was impossible to disclose the unknown.

Bio-Technology countered that the drafting inventor was aware that Example 1 was prophetic and that knowledge of the law is chargeable to the inventor and that inventors represented by counsel are presumed to know the law. The panel agreed with Bio-Technology, noting the drafting inventor's participation in the interview with the Examiner, along with Novo's in-house patent attorney and advisor, discussing enablement of the 1983 PCT application. In particular, the panel characterized Novo's argument as "circular logic" in which "Novo asks us to hold, on the one hand, that the failure of Dr. Christensen and his co-inventors to disclose the truth about Example 1 to Novo's attorneys absolves them of their duty to disclose this information to the PTO or the Board, because without their attorney's consultation, they could not have known that this information was material. At the same time, Novo asks us to hold that its counsel's failure to disclose the truth about Example 1 to the PTO or Board is excused because the inventors failed to fully inform them of the details surrounding Example 1. The panel rejected this reasoning and found the district court's inference of deceptive intent was not erroneous.

IV. Conclusion

It appears that currently, there is no explicit presumption of enablement for non-patent prior art. There is such a presumption for patent prior art, however.

Do not draft prophetic examples in the past tense.