United States Court of Appeals for the Federal Circuit

2008-1453
(Serial No. 10/346,493)

IN RE MARTIN GLEAVE and MAXIM SIGNAEVSKY

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Appealed from: United States Patent and Trademark Office
Board of Patent Appeals and Interferences

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Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences.

DECIDED: March 26, 2009

Before MICHEL, Chief Judge, PROST and MOORE, Circuit Judges.

PROST, Circuit Judge.

Martin Gleave and Maxim Signaevsky (collectively, "Gleave") filed U.S. Patent Application No. 10/346,493 ("'493 application") on January 17, 2003. The examiner rejected claims 1, 4, 15, and 18–21 as indefinite under 35 U.S.C. § 112, ¶ 2 and as anticipated or obvious under 35 U.S.C. § 102(b)/103(a). The United States Patent and Trademark Office Board of Patent Appeals and Interferences ("Board") reversed the examiner's § 112, ¶ 2 rejection and affirmed the § 102(b)/103(a) rejection. Ex parte Gleave, No. 2007-4154, 2008 WL 867799 (B.P.A.I. Mar. 31, 2008). Gleave appeals the § 102/103 rejections. For the reasons set forth below, we affirm.

BACKGROUND

Gleave's '493 application is entitled "Bispecific Antisense Olignucleotides [sic] that Inhibit IGFBP-2 and IGFBP-5 and Methods of Using Same."[1] The claims are based on the understanding that certain antisense oligodeoxynucleotides can simultaneously bind to and prevent the translation of mRNA into two types of human Insulin-Dependent Growth Factor Binding Protein ("IGFBP"). The application claims antisense oligodeoxynucleotides, methods of making pharmaceutical compounds containing the oligodeoxynucleotides, and methods of treating endocrine-regulated cancers by using the oligodeoxynucleotides to prevent the formation of IGFBP-2 and IGFBP-5. The examiner rejected claims 1, 4, 15, and 18–21, all of which were composition claims directed to antisense oligodeoxynucleotides.

The Board selected claims 1 and 4 as representative. Claim 1 recites

> [a] bispecific antisense oligodeoxynucleotide, wherein substantially all of the oligodeoxynucleotide is complementary to a portion of a gene encoding human IGFBP-2 and substantially all of the oligodeoxynucleotide is also complementary to a gene encoding human IGFBP-5, and wherein the oligodeoxynucleotide is of sufficient length to act as an antisense inhibitor of human IGFBP-2 and human IGFBP-5.

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[1] We described antisense technology in greater detail in Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362 (Fed. Cir. 1999), and thus only give a brief overview for purposes of this opinion. In double-stranded deoxyribonucleic acid ("DNA"), only particular segments (called genes) actually encode proteins. Typically, this double-stranded DNA is "transcribed" into messenger ribonucleic acid ("mRNA"), which is complementary to one strand of the DNA. This mRNA then moves into the ribosome, where the mRNA is "translated" into a series of amino acids. Together, these amino acids form a single protein. Antisense technology is used to interrupt this process, thereby preventing certain proteins from being synthesized by the cell. Short segments of single-stranded DNA (called oligodeoxynucleotides) that are complementary to the mRNA are introduced, and physically bind to the mRNA. This prevents the mRNA from being translated into a protein. Some of these oligodeoxynucleotides are "bispecific," meaning that they can bind to mRNAs transcribed from two distinct genes and prevent the formation of both proteins.

Claim 4 recites "[t]he antisense oligodeoxynucleotide according to claim 1, wherein the oligodeoxynucleotide consists essentially of a series of bases as set forth in any of Seq. ID. Nos. 3 through 7." Those sequences range from eighteen to twenty-two DNA bases in length. Before the examiner, Gleave elected Sequence No. 5, a twenty-base oligodeoxynucleotide. The specification notes that the invention does not exclude "minor modifications in sequence, such as the addition of one or two terminal bases, or single base substitutions which might depart from perfect complementarity."

The examiner initially rejected the claims over the published PCT application 00/78341 of Wraight et al. ("Wraight"). In Wraight, the applicants listed every fifteen-base-long sense oligodeoxynucleotide in the IGFBP-2 gene. The list includes more than 1400 sequences. Wraight also disclosed the general concepts that antisense oligonucleotides are preferably between fifteen and twenty-five bases in length, and that some antisense oligonucleotides may be bispecific (i.e., capable of inhibiting "an IGFBP such as IGFBP-2 and/or IGFBP-3"). Finally, Wraight states that "[a]ntisense oligonucleotides to IGFBP-2 may be selected from molecules capable of interacting with one or more" of the sense oligonucleotides described in the long list.

The Board found that to anticipate claim 1, the prior art had to describe an oligodeoxynucleotide of sufficient length to act as an antisense inhibitor to human IGFBP-2 and IGFBP-5, and substantially all of the oligodeoxynucleotide had to be complementary to a portion of the gene encoding human IGFBP-2 and complementary to the gene encoding human IGFBP-5. The Board found that Wraight satisfied these requirements and anticipated the claims. The Board also affirmed the § 103 rejection.

The issue presented on appeal, therefore, is whether a reference that lists every fifteen-base sense oligodeoxynucleotide in a known nucleic acid sequence anticipates or renders obvious claims to specific antisense sequences having particular properties. We have jurisdiction over the appeal under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

As an initial matter, the parties disagree over the proper standard of review. Under 35 U.S.C. § 102(b), a patent applicant cannot receive a patent if the invention was "described in a printed publication in this or a foreign country . . . more than one year prior to the date of the application for patent in the United States." Gleave claims that the issue at hand is "in essence" one of statutory construction (i.e., what a reference must disclose to "describe" an invention under § 102(b)); thus, Gleave argues we should review the Board's decision de novo.[2] Yet Gleave has not unearthed for us some previously hidden requirement for a reference to anticipate an invention under § 102(b).

A reference is anticipatory under § 102(b) when it satisfies particular requirements. First, the reference must disclose each and every element of the claimed invention, whether it does so explicitly or inherently. Eli Lilly & Co. v. Zenith Goldline Pharms., Inc., 471 F.3d 1369, 1375 (Fed. Cir. 2006). While those elements must be "arranged or combined in the same way as in the claim," Net MoneyIN, Inc. v. VeriSign, Inc., 545 F.3d 1359, 1370 (Fed. Cir. 2008), the reference need not satisfy an ipsissimis

[2] The PTO argued that Gleave "waived review of the legal issue he now asserts by failing to raise it before the Board." We disagree. The entire thrust of Gleave's brief on appeal to the Board was the "significance" of Wraight's disclosure in an anticipation analysis. Gleave argued this position as early as his first office action response on March 12, 2005.

verbis test, In re Bond, 910 F.2d 831, 832–33 (Fed. Cir. 1990). Second, the reference must "enable one of ordinary skill in the art to make the invention without undue experimentation." Impax Labs., Inc. v. Aventis Pharms. Inc., 545 F.3d 1312, 1314 (Fed. Cir. 2008); see In re LeGrice, 301 F.2d 929, 940–44 (CCPA 1962). As long as the reference discloses all of the claim limitations and enables the "subject matter that falls within the scope of the claims at issue," the reference anticipates—no "actual creation or reduction to practice" is required. Schering Corp. v. Geneva Pharms., Inc., 339 F.3d 1373, 1380–81 (Fed. Cir. 2003); see In re Donohue, 766 F.2d 531, 533 (Fed. Cir. 1985). This is so despite the fact that the description provided in the anticipating reference might not otherwise entitle its author to a patent. See Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1562 (Fed. Cir. 1991) (discussing the "distinction between a written description adequate to support a claim under § 112 and a written description sufficient to anticipate its subject matter under § 102(b)").

As this summary makes clear, the outcome in this case depends largely on the facts. After all, anticipation is a question of fact, including whether an element is inherent in the prior art. Eli Lilly, 471 F.3d at 1375. And as with 35 U.S.C. § 112, "[w]hether a prior art reference is enabling is a question of law based upon underlying factual findings." Minn. Mining & Mfg. Co. v. Chemque, Inc., 303 F.3d 1294, 1301 (Fed. Cir. 2002). We review the Board's factual determinations for substantial evidence. In re Gartside, 203 F.3d 1305, 1315 (Fed. Cir. 2000). The Board's legal conclusions, on the other hand, we review de novo. In re Elsner, 381 F.3d 1125, 1127 (Fed. Cir. 2004).

A

Gleave frames the issue presented for review as "the meaning of the term

'described' in 35 U.S.C. § 102(b) and the type of disclosure that is therefore required for a reference to be anticipatory." Specifically, Gleave claims that "Wraight does not describe any particular individual antisense species," because Wraight merely gives the public "ink, formed into strings of letters, without inventive thought and without placing the public in possession of anything new. There is no guidance to make particular selections, and no understanding of which of the targets would be useful, and what the properties of the related antisense would be."

We have at times framed the issue of enablement under § 102 as a question of whether one of ordinary skill in the art would know how to "make and use" the invention based on the reference's disclosure. See, e.g., Impax Labs., Inc. v. Aventis Pharms., Inc., 468 F.3d 1366, 1381 (Fed. Cir. 2006) ("[A] prior art reference must be enabling so that the claimed subject matter may be made or used by one skilled in the art."); Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1374 (Fed. Cir. 2001) ("To anticipate, the reference must also enable one of skill in the art to make and use the claimed invention."). Taken out of context, these formulations of our § 102 enablement standard arguably support a use or utility requirement divorced from any "make" requirement. A thorough reading of our case law, however, makes clear that a reference need disclose no independent use or utility to anticipate a claim under § 102. E.g., Novo Nordisk Pharms., Inc. v. Bio-Tech. Gen. Corp., 424 F.3d 1347, 1355 (Fed. Cir. 2005) ("The standard for enablement of a prior art reference for purposes of anticipation under [§] 102 differs from the enablement standard under 35 U.S.C. § 112."); Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318, 1326 (Fed. Cir. 2005) ("[A] prior art reference need not demonstrate utility in order to serve as an

anticipating reference under [§] 102."); In re Hafner, 410 F.2d 1403, 1405 (CCPA 1969) ("[Section] 112 provides that the specification must enable one skilled in the art to 'use' the invention whereas § 102 makes no such requirement as to an anticipatory disclosure.").

The confusion stems from the fact that where a method claim is at issue, it is a largely meaningless formulation of the standard to require a reference to disclose how to "make" that method in order to anticipate. For method claims, the "make" requirement becomes, in effect, a "use" requirement. The only way one can show that a reference enables the method is to show that a person of ordinary skill would know how to use—in other words, to practice or to carry out—the method in light of the reference. This does not mean, however, that the prior art reference must demonstrate the invention's utility. For instance, in the context of a claimed method for treating a disease, a prior art reference need not disclose "proof of efficacy" to anticipate the claim. Impax Labs., 545 F.3d at 1315; Rasmusson, 413 F.3d at 1326. Gleave's claims are to compositions of matter—oligonucleotides—and therefore a reference satisfies the enablement requirement of § 102(b) by showing that one of skill in the art would know how to make the relevant sequences disclosed in Wraight. Thus, the fact that Wraight provides "no understanding of which of the targets would be useful" is of no import, because Gleave admits that it is well within the skill of an ordinary person in the art to make any oligodeoxynucleotide sequence. See Appellant's Br. 10. As such, Wraight is an enabling disclosure sufficient to anticipate Gleave's invention under § 102(b).

Gleave also points out that "[n]o example of an actual antisense oligonucleotide complementary to a sequence on [Wraight's] list is shown to have antisense activity."

Id. at 4. We need not address any inherency issues, however, because the simple fact is that Gleave's composition claims do not require antisense activity either. The claims at issue merely require the oligodeoxynucleotides to be "of sufficient length to act as an antisense inhibitor of human IGFBP-2 and human IGFBP-5." See Oral Arg. at 1:18, available at http://oralarguments.cafc.uscourts.gov/mp3/2008-1453.mp3 (Judge Prost: "I'm a little confused by this, and I guess turning to the language in claim 1, doesn't it just disclose an oligo 'of sufficient length to act as an antisense inhibitor?' And I'm not seeing where the language requires that the oligo actually acts as an antisense inhibitor." Gleave's counsel: "No, it doesn't."). As explained above, evidence as to whether particular compounds work for their intended purpose is irrelevant to our § 102(b) analysis. Certainly where the claims themselves do not require a particular activity, we have no call to require something more from the anticipating reference.

B

At its core, Gleave's primary argument is rooted in policy:

> Where the allegedly anticipatory disclosure is only a small part of a much larger and exhaustive listing and there is no basis in the art for selecting some individual members of the listing over others, what is actually described and what is actually disclosed to the public is no more than the generic concept underlying the list.

Appellant's Br. 6. In other words, Gleave argues that we should collapse the distinction between a list and a genus disclosure. See Oral Arg. at 4:42, available at http://oralarguments.cafc.uscourts.gov/mp3/2008-1453.mp3 (Judge Moore: "I understand what you're saying—from a policy perspective, you'd like us to say when a list gets long enough, you ought to treat them the same." Gleave's counsel: "No, I'm not even saying when a list gets long enough. I'm saying when a list provides no more

information to an inve—to the public than the generic statement would.") If we did, the argument goes, then we would recognize that Wraight simply provides a "long winded form of a statement that 'you could make antisense that targets IGFBP-2.'"

Gleave also cites In re Wiggins for the proposition that a list of compounds, "without any direction as to selection among the targets, is not a description of any one of these targets." Gleave urges us to find that Wiggins "clearly expressed the policy concerns which this case exemplifies, that giving prior art effect to individual members of lists of thousands of theoretically possible compounds would be contrary to the purpose sought to be effectuated by the patent law." Reply Br. 7–8 (citing In re Wiggins, 488 F.2d 538, 543 (CCPA 1973) (quotations omitted)).

In Wiggins, the Court of Customs and Patent Appeals stated:

> In our view, [the alleged anticipatory reference's] listing of the compounds by name constituted nothing more than speculation about their potential or theoretical existence. The mere naming of a compound in a reference, without more, cannot constitute a description of the compound, particularly when, as in this case, the evidence of record suggests that a method suitable for its preparation was not developed until a date later than that of the reference.
>
> If we were to hold otherwise, lists of thousands of theoretically possible compounds could be generated and published which, assuming it would be within the level of skill in the art to make them, would bar a patent to the actual discoverer of a named compound no matter how beneficial to mankind it might be.

488 F.2d at 543 (emphases added).

Gleave reads Wiggins to suggest that a description of a compound cannot be anticipatory where it appears in a long list of other compounds. That conclusion, however, ignores the facts at issue in that case. Contrary to Gleave's representations, no evidence existed that a person of ordinary skill in the art could make the compounds

disclosed in the alleged anticipatory reference at the time of disclosure. The reference, published in 1957, mentioned by name two compounds that fell within the scope of Wiggins's claims. But the reference also noted that the synthesis of these compounds had been unsuccessful; further, the only publication of record that disclosed a method of making the compounds was not published until two years later. In short, the reference was not an enabling reference—no person of ordinary skill in the art could make the claimed invention in 1957.[3]

The Wiggins court stated that "[t]he mere naming of a compound in a reference, without more, cannot constitute a description of the compound." 488 F.2d at 543. We agree. The mere naming of a theoretical compound, without more, cannot constitute a description under § 102(b). "Without more" is the key phrase, and read as a whole Wiggins makes clear just what this something "more" is—a person of ordinary skill in the art's ability to make the claimed compound. See also Donohue, 766 F.2d at 533–34; In re Samour, 571 F.2d 559, 562–64 (CCPA 1978); In re Brown, 329 F.2d 1006, 1009–10 (CCPA 1964) (discussing In re Von Bramer, 127 F.2d 149 (CCPA 1942)). This point is underscored by the excerpt: not once, not twice, but three times the court pointed out that its discussion was in the context of "potential or theoretical" compounds. That was the issue presented to the court, and that was the issue it decided.

[3] It is true that "[e]nablement of an anticipatory reference may be demonstrated by a later reference." Bristol-Myers Squibb, 246 F.3d at 1379. But in Wiggins, our predecessor court did not elect to decide the case on this ground. 488 F.2d at 543 n.4 ("We do not mean to suggest that we have actually evaluated the process taught by [the later reference] and concluded that it could be used to prepare the claimed compounds. As this is irrelevant to our decision, we express no opinion on this point.").

For the purposes of whether they are anticipatory, lists and genera are often treated differently under our case law. Compare Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1376 (Fed. Cir. 2005) (rejecting "the notion that [a compound] cannot anticipate because it appears without special emphasis in a longer list") with Atofina v. Great Lakes Chem. Corp., 441 F.3d 991, 999 (Fed. Cir. 2006) ("It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus."). This distinction collapses when the class of compounds that falls within the genus is so limited that a person of ordinary skill in the art can "at once envisage each member of this limited class." Eli Lilly, 471 F.3d at 1376. In that limited circumstance, a reference describing the genus anticipates every species within the genus. See Perricone, 432 F.3d at 1377. In this case, Gleave's arguments fail for two reasons. First, Wraight expressly lists every possible fifteen-base-long oligodeoxynucleotide sequence in IGFBP-2, and under our precedent, this list anticipates Gleave's claims. Second, even if we were to accept Gleave's invitation to treat Wraight as equivalent to the statement that one "could make antisense that targets IGFBP-2,"[4] which we decline to do, a person of ordinary skill in the art equipped with an IGFBP sequence is admittedly capable of envisioning how to make any antisense sequence. Thus, even if we were to adopt Gleave's policy position, Gleave's claims would not be entitled to a patent over Wraight.

The rest of Gleave's arguments fare no better. For instance, Gleave protests that Wraight "does not show that sequences antisense to any of the sequences in this

[4] We note that this is not the full extent of Wraight's disclosure. See supra at 3.

list were actually made and tested." As we have already made clear, it is not "necessary that an invention disclosed in a publication shall have actually been made in order to satisfy the enablement requirement." Donohue, 766 F.2d at 533. In light of the foregoing, we agree with the Board's conclusion that Gleave's claims are invalid as anticipated by Wraight.

CONCLUSION

In sum, "[t]he discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition." In re Spada, 911 F.2d 705, 708 (Fed. Cir. 1990). The compositions described in the '493 application are simply not new—they were described in Wraight's enabling disclosure. As we explained in In re Schoenwald, Gleave's contribution, at best, is "finding a use for the compound, not discovering the compound itself." 964 F.2d 1122, 1124 (Fed. Cir. 1992). If the use Gleave discovered is new, he will be able to patent that method of use—"any more would be a gratuity." Id. Therefore, we affirm the Board's rejection of claims 1, 4, 15, and 18–21 of the '493 application under § 102(b). We need not reach the § 103 obviousness rejection.

AFFIRMED