United States Court of Appeals for the Federal Circuit

01-1621
(Interference No. 102,728)

ARJUN SINGH,

Appellant,

v.

ANTHONY J. BRAKE,

Appellee.

DECIDED: October 16, 2002

Before LOURIE, Circuit Judge, FRIEDMAN, Senior Circuit Judge, and PROST, Circuit Judge.

LOURIE, Circuit Judge.

Arjun Singh appeals from the remand decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences awarding judgment in an interference to Anthony Brake. Brake v. Singh, Inter. No. 102,728, Paper No. 199 (Bd. Pat. App. & Inter. June 19, 2001). Because the Board's decision was supported by substantial evidence and was not contrary to law, we affirm.

BACKGROUND

This case arises out of an interference declared on November 12, 1991, involving a count

corresponding to all thirty-seven claims of Brake's U.S. Patent 4,870,008 (hereinafter "the Brake patent") and claims 8 and 19-21 of Singh's U.S. Application 07/552,719.

The Brake patent issued from U.S. Application 07/081,302, filed August 3, 1987, which was a continuation of, and was accorded the benefit of, U.S. Application 06/522,909 (hereinafter "Brake 2"), filed August 12, 1983, assigned to Chiron Corporation. Singh's Application 07/552,719 was filed July 16, 1990, and was accorded the benefit of U.S. Application 06/506,098 (hereinafter "the Singh application"), filed June 20, 1983, and U.S. Application 06/488,323, filed April 25, 1983, both assigned to Genentech, Inc.

Because the earlier Singh application predated Brake 2, Singh was initially designated the senior party in the interference. However, Brake 2 was a continuation-in-part of U.S. Application 06/457,325 (hereinafter "Brake 1"), filed January 12, 1983, and Brake successfully moved for the benefit of the filing date of Brake 1 with respect to the count in the interference. Brake also successfully moved to attack the benefit accorded Singh of the April 25, 1983 filing date of U.S. Application 06/488,323. Brake was then designated as the senior party.

The count, which is identical to claim 1 of Brake 2, reads as follows:

1. A DNA construct comprising a sequence of the following formula:

5'-L-S-Gene*-3',

where:

L encodes a Saccharomyces alpha-factor leader sequence recognized by a yeast host for secretion;

S encodes a spacer sequence providing processing signals resulting in the enzymatic processing by said yeast host of a precursor polypeptide encoded by L-S-Gene* into the polypeptide encoded by Gene*, S containing the sequence 5'-R_1-R_2-3' immediately adjacent to the sequence Gene*, R_1 being a codon for lysine or arginine, R_2 being codon for arginine, with the proviso that S not contain the sequence 5'-R_3-R_4-X-3', where R_3=R_1, R_4=R_2, and X encodes a processing signal for dipeptidylaminopeptidase A; and Gene* encodes a polypeptide foreign to Saccharomyces.

Brake, Paper No. 199 at 6.

The DNA construct of the count thus includes three basic components: (1) a segment, "L," which encodes an alpha-factor leader sequence;[1] (2) a segment, "S," which includes a first codon,[2] R_1, encoding either lysine or arginine, followed by a second codon, R_2, encoding arginine; and (3) a gene, "Gene*," which encodes a protein of interest, in particular, a polypeptide foreign to (i.e., not naturally produced by) Saccharomyces. See Brake patent, col. 2, ll. 11-16, 38-43.

After the DNA construct has been introduced into the yeast cell, e.g., via a plasmid vector, the cell "translates" the construct, producing a polypeptide having the sequence of amino acids encoded by the DNA. The sequence of the resulting polypeptide, like the DNA encoding it, is divided into three regions: the alpha-factor leader, the spacer sequence including either a lysine-arginine or an arginine-arginine two-amino acid block, and the amino acid sequence of the protein of interest ("gene product").

According to the record in this case, the leader sequence functions to target the polypeptide for secretion from the yeast cell. During secretion, the yeast enzyme KEX-2 recognizes the lysine-arginine or arginine-arginine spacer sequence in the polypeptide and cleaves the polypeptide at the junction between the spacer and the gene product. As a result, the desired gene product is released into the extracellular medium, free of the leader and spacer portions of the polypeptide. See Brake, Paper No. 164 at 2. Because the yeast cell exports rather than retains the desired protein, protein purification is considerably simplified. See id.

The following is a statement of the facts as set forth in our earlier opinion in this case. Singh v. Brake, 222 F.3d 1362, 55 USPQ2d 1673 (Fed. Cir. 2000). As we noted in that opinion, the factual context of Singh's alleged conception of the claimed DNA construct is based on his statements to the PTO and other record evidence. Absent qualification, the facts set forth here are not disputed by the parties.

> In the course of Singh's attempts to design the claimed DNA construct in August 1982, he prepared plasmid p57, a circular DNA molecule containing the alpha-factor leader sequence and a spacer sequence directly adjacent to it. See Singh Decl. ¶ 21. During that same month, Singh incorporated the gene for human protein interferon D ("IFN-D") into p57, thereby yielding plasmid p58. See id. In p58, the gene was also positioned adjacent to the spacer sequence, such that the leader, spacer, and gene sequences were all oriented in a fashion identical to the claimed construct. From

> September 6 to 11, 1982, Singh's assistant, Dr. June Lugovoy, isolated the DNA segment from p58 containing the alpha-factor leader, spacer, and IFN-D sequence, and inserted that segment (hereinafter "the p60 DNA construct") into yeast plasmid YEp9PT ("p60"). See id. ¶ 26. Plasmid p60 was then introduced into yeast cells to determine whether the p60 DNA construct would generate IFN-D. See id. ¶ 27.
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> On October 1, 1982, protein sequencing chemist Bill Kohr informed Singh that the IFN-D expressed by yeast cells transformed with p60 contained eight additional amino acids not normally present in natural IFN-D. See id. ¶ 33. On approximately that same date, Singh alleges that he conceived the claimed DNA construct, i.e., he devised a plan to redesign the p60 DNA construct in order to obtain the desired gene product, IFN-D, free of those additional amino acids. See id. ¶ 34. Specifically, Singh claims that he realized that he would need to remove eight unwanted codons (twenty-four nucleotides) from the p60 DNA construct, and that he planned to accomplish this deletion by use of a technique known as "loop deletion mutagenesis."
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> On November 24, 1982, Singh wrote a laboratory notebook entry setting forth the undesired eight codons in the p60 DNA construct, as well as the twelve nucleotides on either side of that eight codon segment (the "flanking sequences"). See Singh Decl. ¶ 45. On that date, Singh also ordered a linear, 24-nucleotide sequence (a "24-mer") that comprised the nucleotides of the flanking sequences.[3] This order was canceled on the same day, and a notation in Singh's laboratory notebook stated that Singh would perform the deletion experiment in a different way "without changing codons." Id. On December 1, 1982, Singh ordered another 24-mer for the deletion experiment. This 24-mer was precisely complementary to the flanking sequences set forth in the November 24 entry. See Singh Decl. ¶ 47. DNA chemist Peter Ng testified that he synthesized the 24-mer for Singh on December 20, 1982. See Ng Decl. ¶ 11; Ng Dep. at 36. Singh affixed the order into his notebook on December 21, 1982, with a notation "oligonucleotide for making in-frame deletion of alpha pro-IFN-D junction."[4] Singh alleges that these facts corroborate his testimony that he conceived the claimed DNA construct before January 12, 1983, the filing date of Brake 1.

Id. at 1364-65, 55 USPQ2d at 1674-75 (footnote omitted).

At final hearing on May 11, 1998, Singh sought: (1) to contest the interlocutory order granting Brake the benefit of Brake 1; (2) to prove Singh's conception of the invention of the count prior to Brake 1's January 12, 1983 filing date; and (3) to

show diligence throughout the "critical period" from just prior to January 12, 1983, until actual reduction to practice. Singh was unsuccessful with respect to all three issues, and final judgment was issued in favor of Brake on August 31, 1998. Brake, Paper No. 164.

Singh appealed to this court, contesting Brake's entitlement to the benefit of Brake 1 and contesting the Board's finding that Singh had failed to prove conception prior to the Brake 1 filing date. We held that certain of the Board's key findings underlying its conclusion that Singh had failed to prove

conception of the subject matter of the interference prior to the effective filing date of Brake were unsupported by substantial evidence, and we vacated and remanded. Singh, 222 F.3d at 1370, 55 USPQ2d at 1679. We also found that the Board did not address whether Brake 1 adequately described and enabled the disputed subject matter of the count under 35 U.S.C. § 112, ¶ 1, and we remanded for determination of those issues as well. Id. at 1371, 55 USPQ2d at 1679.

On remand, the Board permitted the parties to submit briefs on the remanded issues, but returned Singh's enablement and written description briefs (as well as Brake's corresponding reply briefs) with its opinion, stating that Singh had failed to comply with the requirements of 37 C.F.R. § 1.655(a) and (b) by presenting new arguments not raised in the original opposition.

In an 89-page opinion with an additional 17-page concurrence, Brake, Paper No. 199, the Board addressed each of the issues on remand and concluded: (1) that Brake 1 adequately described and enabled the invention of the count, and Brake was therefore entitled to the benefit of Brake 1's filing date; (2) that Singh had not met his burden of proving conception prior to the filing date of Brake 1; and (3) that even if it were assumed, arguendo, that Singh had conceived the invention prior to Brake's filing date, Singh had not met his burden of demonstrating diligence between conception and reduction to practice.

Singh now appeals again. We have jurisdiction pursuant to 35 U.S.C. § 141 and 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

A. Return of Briefs

Pursuant to our earlier decision's remand "for determination of those issues that were properly raised during the earlier proceedings," Singh, 222 F.3d at 1371, 55 USPQ2d at 1679, the Board invited the parties to submit briefs on the issues of Singh's case for priority and Brake's sustenance of his burden of proof with respect to written description and enablement. Brake, Paper No. 199 at 12. After the parties submitted the invited briefs, the Board determined that Singh had presented new arguments

in derogation of the Board's reminder that only issues that were properly raised in the original opposition were entitled to review at final hearing. Id. at 13. In response, the Board returned all of the newly submitted briefs to the parties without further consideration, holding that the briefs contained, "almost exclusively, new arguments, and lack the showing that Preliminary Motion 2 [concerning the Brake patent's entitlement to the Brake 1 filing date] should be modified." Id. at 15.

Singh argues that the Board erred in refusing to consider briefs submitted by Singh on remand. We review the Board's application of its rules for an abuse of discretion. Brown v. Barbacid, 276 F.3d 1327, 1332, 61 USPQ2d 1236, 1238 (Fed. Cir. 2002). Although returning the briefs to the parties is a rather extraordinary measure, we do not find any abuse of discretion in the Board's doing so. 37 C.F.R. § 1.655(b) states:

> A party shall not be entitled to raise for consideration at final hearing any matter which properly could have been raised by a motion under § 1.633 or 1.634 unless the matter was properly raised in a motion that was timely filed by the party under § 1.633 or 1.634 and the motion was denied or deferred to final hearing, the matter was properly raised by the party in a timely filed opposition to a motion under § 1.633 or 1.634 and the motion was granted over the opposition or deferred to final hearing, or the party shows good cause why the issue was not properly raised by a timely filed motion or oppositions.

37 C.F.R. § 1.655(b) (2002).

Because the Board found that Singh was attempting to raise in his briefs matters that could have been but were not raised at the outset of the interference, see Brake, Paper No. 199 at 12, the Board was acting properly within its discretion when it refused to consider the briefs. Singh could have raised his written description and enablement arguments at the outset of the interference; to the extent that he did not do so, those arguments have been waived. As we held in Credle v. Bond, 25 F.3d 1566, 30 USPQ2d 1911 (Fed. Cir. 1994), the Board does not abuse its discretion when it declines to consider untimely arguments. Id. at 1572 n.14, 30 USPQ2d at 1916 n.14. Furthermore, because the Board explicitly stated in its November 2, 2000 order that additional briefing was optional, Brake, Paper No. 179 at 5, it is difficult to see how the subsequent refusal to consider the briefs could have been an abuse of discretion.

Singh also asserts that the Board refused to consider certain arguments made in his "original" Main Brief. We find no abuse of discretion. Again, Singh did not show good cause for failing to raise these arguments at the preliminary motion stage, and the Board was entitled to decline to consider them.

B. Conception and Reduction to Practice

"Conception is the formation 'in the mind of the inventor of a definite and permanent idea of the complete and operative invention, as it is therefore to be applied in practice.'" Kridl v. McCormick, 105

F.3d 1446, 1449, 41 USPQ2d 1686, 1689 (Fed. Cir. 1997) (citations omitted). A conception must encompass all limitations of the claimed invention, see id., and "is complete only when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation," Burroughs Wellcome Co. v. Barr Labs. Inc., 40 F.3d 1223, 1228, 32 USPQ2d 1915, 1919 (Fed. Cir. 1994).

Priority of invention and its constituent issues of conception and reduction to practice are questions of law predicated on subsidiary factual findings. Brown, 276 F.3d at 1332, 61 USPQ2d at 1238; Hitzeman v. Rutter, 243 F.3d 1345, 1353, 58 USPQ2d 1161, 1166 (Fed. Cir. 2001). Accordingly, we review de novo the Board's legal conclusions with respect to priority, conception, and reduction to practice, 5 U.S.C. § 706; Brown, 276 F.3d at 1332, 61 USPQ2d at 1238; Hitzeman, 243 F.3d at 1353-54, 58 USPQ2d at 1166-67, and we review factual findings by the Board for substantial evidence, Dickinson v. Zurko, 527 U.S. 150 (1999); In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000).

A junior party seeking a determination of priority must demonstrate by a preponderance of the evidence either reduction to practice before the senior party's priority date, or prior conception coupled with reasonable diligence in reducing the invention to practice from a time just prior to the senior party's entry into the field to the junior party's own reduction to practice. 35 U.S.C. § 102(g); Griffin v. Bertina, 285 F.3d 1029, 1032, 62 USPQ2d 1431, 1433 (Fed. Cir. 2002); Mahurkar v. C.R. Bard, Inc., 79 F.3d 1572, 1577, 38 USPQ2d 1288, 1290 (Fed. Cir. 1996).

It is well established that when a party seeks to prove conception via the oral testimony of a putative inventor, the party must proffer evidence corroborating that testimony. See Mahurkar, 79 F.3d at 1577, 38 USPQ2d at 1290; Price v. Symsek, 988 F.2d 1187, 1194, 26 USPQ2d 1031, 1036 (Fed. Cir. 1993). That rule addresses the concern that a party claiming inventorship might be tempted to describe his actions in an unjustifiably self-serving manner in order to obtain a patent or to maintain an existing patent. See Kridl, 105 F.3d at 1450, 41 USPQ2d at 1689 ("The tribunal must also bear in mind the purpose of corroboration, which is to prevent fraud, by providing independent confirmation of the

inventor's testimony."); Price, 988 F.2d at 1194-95, 26 USPQ2d at 1036-37; Eibel Process Co. v. Minn. & Ont. Paper Co., 261 U.S. 45, 60 (1923). There is no particular formula that an inventor must follow in providing corroboration of his testimony of conception. See Kridl, 105 F.3d at 1450, 41 USPQ2d at 1689. Rather, whether a putative inventor's testimony has been sufficiently corroborated is determined by a "rule of reason" analysis, in which "an evaluation of all pertinent evidence must be made so that a sound determination of the credibility of the inventor's story may be reached." Price, 988 F.2d at 1195, 26 USPQ2d 1031 at 1037. However, that "rule of reason" analysis does not alter the requirement of corroboration of an inventor's testimony. Brown, 276 F.3d at 1335. Evidence of the inventive facts must not rest alone on the testimony of the inventor himself. Cooper v. Goldfarb, 154 F.3d 1321, 1330, 47 USPQ2d 1896, 1903 (Fed. Cir. 1998).

Singh argues that the Board did not consider the totality of the corroborative evidence establishing Singh's conception, but only considered individual pieces of evidence in "total isolation from one another." Specifically, Singh argues that his November 24, 1982 notebook entry and his ordering of the specific 24-mer oligonucleotide ultimately used to carry out the loop deletion mutagenesis method (in February 1983) establish that he had a definite and permanent idea of the structure of a DNA construct within the count and of an operative way of making it prior to Brake 1's filing date.

We disagree. First, as we stated in our earlier opinion, Singh, 222 F.3d at 1368, 55 USPQ2d at 1677, the Board correctly held as a matter of law that Singh failed to prove that he conceived the claimed construct prior to December 1, 1982. In his November 24, 1982 notebook entry, Singh identified the twenty-four nucleotides encoding the eight extraneous amino acids present in the IFN-D generated by the p60 DNA construct, labeling them with the notation, "sequence to be removed." He also identified in that entry the twelve nucleotides immediately upstream and the twelve nucleotides immediately downstream from those twenty-four, i.e., the flanking segments. Accordingly, he may have articulated in that entry the problem to be solved, namely, the need to eliminate the twenty-four nucleotides encoding the extraneous amino acids. Nonetheless, substantial evidence supports the Board's finding that that entry alone was insufficient to corroborate Singh's testimony. Even if the entry

expressed the problem, it did not provide the solution. See Brake, Paper No. 164 at 22-24. The Board's key findings in this regard, both of which are supported by substantial evidence in the notebook entry itself, are: (1) that a linear 24-mer other than the one necessary to accomplish the deletion was first ordered, and (2) that the order was canceled the same day, with a notation "will do in a different way and w/o changing codons." Id. at 23-24.

Secondly, as noted above, the 24-mer sequence that Singh initially ordered on November 24, 1982, was not identical to the nucleotides of the flanking sequences. Instead, he included several "preferred codons," casting doubt on the accuracy of Singh's statement that he ordered that 24-mer "[i]n order to remove this sequence by oligonucleotide deletion mutagenesis." While it remains unclear exactly what Singh "planned" to do on November 24, 1982, his identification of preferred codons suggests to us that his plans may not have included the use of loop deletion mutagenesis.

The Board duly considered the fact that the 24-mer ordered by Singh on December 1, 1982, was indeed complementary to the four codons on each side of the sequence Singh allegedly desired to delete. See, e.g., Brake, Paper No. 199 at 13-14, 19, 58-59, 77-78. The Board also reviewed Singh's notebook pages purporting to demonstrate conception. The Board concluded, and we agree, that "Singh's entire case for conception rests on the order of a 24-mer and an uncorroborated notation in a corner of Dr. Singh's notebook." Id. at 84.

There is nothing in Singh's notebook that corroborates his testimony that the November 24, December 1, and December 21 entries were meant to be read together. Even viewing all of these entries together, however, we find that the sum falls short of proving by a preponderance of the evidence that Singh had a definite and permanent idea of an operative method of making the DNA construct of the count prior to Brake 1's filing date. As the Board observed, the notebook entries do not provide any protocol or outline of the loop deletion mutagenesis procedure: "At best, the notation states a goal which Dr. Singh hopes to achieve; i.e., an in-frame deletion of the a pro-IFN-D junction." Id. at 61. Adelman et al., *In Vitro* Deletional Mutagenesis for Bacterial Production of the 20,000-Dalton Form of Human Pituitary Growth Hormone, 2 DNA 183 (1983), which described the loop deletion mutagenesis

procedure, also described using oligonucleotides complementary to nucleotide sequences flanking codons to be deleted as probes for identifying plasmids from which the codons had been deleted. Id. at 188. We find it no less plausible that Singh was ordering the 24-mer for use as a probe than it was that he was ordering it for use in the loop deletion mutagenesis procedure. Indeed, Singh has pointed to no evidence in the record in support of his assertion that loop deletion mutagenesis was developed at Genentech in late 1982 (the Adelman et al. paper was published in 1983), let alone that Dr. Singh knew of any such developments prior to Brake 1's filing date. The burden was on Singh to prove that he as the inventor had a definite and permanent idea of how to make the construct. See Coleman v. Dines, 754 F.2d 353, 360, 224 USPQ 857, 863 (Fed. Cir. 1985). That he did not do.

Finally, we address Singh's argument set forth in his brief that, "[w]ith respect to the issue of conception, this Court previously made specific findings . . . that Singh articulated a specific plan to design the claimed construct by the loop deletion method on November 24, 1982." That statement is a mischaracterization of our earlier opinion, in which we simply said that the Board needed to consider the totality of the evidence. We are satisfied that the Board has done so.

Thus, after review of the record evidence in light of the proper legal standards, we conclude that substantial evidence supports the Board's key finding that no evidence links the nucleotide Singh ordered on December 1, 1982, with a plan to design the claimed construct prior to January 12, 1983.

Because we find that Singh did not meet his burden of demonstrating conception prior to Brake 1's filing date by a preponderance of the evidence, we need not address Singh's arguments regarding reduction to practice. However, we note the Board's finding that, apart from attorney argument, "Singh's evidence of diligence primarily consists of various pages from Dr. Singh's laboratory notebook which are (i) unexplained as to content and relevance to the invention of the Count, and (ii) uncorroborated." Brake, Paper No. 199 at 88. We agree that Singh's activities completed on December 20, 1982, were the only relevant, corroborated activities performed by Singh prior to Brake 1's January 12, 1983, filing date, and, as a result, Singh failed to prove reasonable diligence toward reduction to practice by a preponderance of the evidence.

C. Written Description and Enablement

Whether a specification supports a claim corresponding to a count, and thus satisfies the written description requirement of 35 U.S.C. § 112, ¶1, is a question of fact, Vas-Cath v. Mahurkar, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991), and is, in appeals from the United States Patent and Trademark Office, reviewed under the substantial evidence standard. In re Gartside, 203 F.3d at 1315, 53 USPQ2d at 1775. Singh argues that the Board erred in concluding that Brake is entitled to the benefit of the Brake 1 application. First, Singh contends that Brake did not provide an adequate written description of the invention of the count in the Brake 1 application, and should not be entitled to its benefit. According to Singh, Brake 1 disclosed a large genus, allegedly encompassing over 9000 species[5] (n is 0 or 1 to 4), of which the count is directed to only two (i.e., those where n = 0). Secondly, Singh asserts that Brake 1 does not provide an enabling disclosure with respect to the invention of the count, arguing that Brake 1 does not disclose how to make and use the "n = 0" embodiment, and that "the techniques which were available to Brake at the time of filing the Brake 1 Application were not sufficient to obtain the DNA constructs of the Count." Singh also argues that Brake 1 "is replete with passages which guide one of ordinary skill in the art to constructs wherein n > 0, which constructs are not encompassed by the Count." Finally, Singh argues that "during prosecution of the Brake 2 Application, Brake argued that the results obtained with the n = 0 construct were unexpected, because those of ordinary skill in the art believed that the Glu-Ala sequences were required."

Singh's arguments are not persuasive. First, we disagree with Singh's argument that the invention of the count represents just two of 9000+ species disclosed in Brake 1. Singh's calculation of 341 permutations for $(GAXYCX)_n$ is apparently based on an unwarranted assumption that each iteration of the parenthetical sequence is independently chosen. However, as Brake pointed out, because the variable 'n' is outside the parentheses, $(GAXYCX)_n$ can code for either no amino acids (i.e., when n = 0), or 1 to 4 copies of one of four different amino acid sequences (i.e., Asp-Pro, Asp-Ala, Glu-Pro, or Glu-Ala). Brake, Paper No. 199 at 20-21 n.13. Thus, there are at most only $4^0 + 4^1 + 4^1 + 4^1 + 4^1 = 17$ permutations of that sequence. Even among those 17, however, we agree with Brake that there are only two meaningful embodiments: one in which a dipeptidylaminopeptidase A (DPAP) signal is present (i.e., n = 1 to 4), and one in which it is not (i.e., n = 0).

Moreover, Singh's calculation of 28 possibilities for the Lys/Arg sequences is artificially inflated because it ignores the disclosure of claim 5 of Brake 1:

5. A DNA construct comprising a sequence of the following formula:

$L\text{-}(R\text{-}S\text{-}(GAXYCX)_n\text{-}Gene^*)_y$

wherein:

L is a leader sequence recognized by yeast for secretion;

R and S are codons coding for arginine and lysine;

X is any nucleotide;

Y is guanosine or cytosine;

y is an integer of from about 1 to 10;

Gene* is a gene foreign to yeast; and

n is 0 or 1 to 4.

U.S. Application 06/457,325 at 16, ll. 20-32.

In claim 5, spacer R-S encodes four possible sequences (i.e., Lys-Arg, Arg-Arg, Arg-Lys, or Lys-Lys), not 28. Of these four, two permutations, Lys-Arg and Arg-Arg, are within the scope of the count.

Singh cites Fujikawa v. Wattanasin, 93 F.3d 1559, 39 USPQ2d 1895 (Fed. Cir. 1996), for the proposition that an application disclosing a generic chemical formula must provide adequate direction to those of ordinary skill in the art to lead them to a subgenus of the proposed count. We find Singh's reliance on Fujikawa to be unsound. In Fujikawa, we held that disclosure of a generic quinoline structure with four variable groups, each of which could be independently chosen from a list of functional groups, provided insufficient written description support for a count directed to a subgeneric structure having a single combination of the four groups. Id. at 1569-71, 39 USPQ2d at 1904-05. However, Brake 1's formula does not present the same issue as did the quinoline in Fujikawa. First, replacing a functional group on a chemical compound can often have highly unpredictable results. We

noted in Fujikawa that even a change as seemingly trivial as replacing an isopropyl group with the isosteric cyclopropyl group at issue in that case could result in either a significant improvement or reduction in the activity of the compound against a particular biological target. Id. In the present case, on the other hand, as mentioned above, there are only two subgenera that are biologically relevant: one in which a DPAP signal is present (i.e., n = 1 to 4), and one in which it is not (i.e., n = 0), a simpler case than in Fujikawa. Here, moreover, claim 5 of Brake 1 discloses that "n is 0 or 1 to 4," which is a clear "blaze mark" providing in ipsis verbis support for "n = 0" in the count. See In re Ruschig, 379 F.2d 990, 994-95, 154 USPQ 118, 122 (CCPA 1967).

The Supreme Court has explained that "the possibility of drawing two inconsistent conclusions from the evidence does not prevent an administrative agency's finding from being supported by substantial evidence." In re Gartside, 203 F.3d at 1312, 53 USPQ2d at 1773 (citing Consolo v. Federal Maritime Comm'n, 383 U.S. 607, 620 (1966)). In Fujikawa, we said that "[w]hile Fujikawa's arguments are not without merit, we cannot say, on this record, that the Board's decision was clearly erroneous." 93 F.3d at 1571. Likewise, on the record in the present case, substantial evidence supports the Board's decision, and we decline to find legal error in the Board's conclusion.

Singh's reliance on Bigham v. Godtfredsen, 857 F.2d 1415, 8 USPQ2d 1266 (Fed. Cir. 1988), is also unavailing. In Bigham, Godtfredsen's first application disclosed a compound having a substituent "X", where X was defined as "a halogen atom." The application provided as its only example a compound in which X was chloro. Id. at 1416, 8 USPQ2d at 1267. This court ruled that that application's disclosure of "halogen" did not meet the requirements of § 112 as a written description of bromo or iodo species, particularly where Godtfredsen had earlier argued in the same case that bromo and iodo were patentably distinct from chloro in order to urge bifurcation of the count. Id. at 1417, 8 USPQ2d at 1268. In the present case, in contrast, "n = 0" was disclosed in Brake 1. If Godtfredsen had provided examples of fluoro, bromo, and iodo compounds in addition to the chloro compound, that case might have been decided differently, even in spite of Godtfredsen's "patentably distinct" argument.

Singh's arguments with respect to enablement are likewise unconvincing. Enablement is a

question of law based on underlying factual determinations. In re Swartz, 232 F.3d 862, 863, 56 USPQ2d 1703, 1704 (Fed. Cir. 2000). We review the Board's underlying findings of fact for substantial evidence, and review de novo its ultimate conclusion whether a disclosure is enabling. Id. Singh argues in his brief:

> The Board takes internally inconsistent positions with respect to whether methods for obtaining a construct of the Count using Brake's starting material were available to those of ordinary skill in the art at the time the Brake 1 Application was filed. To support its finding that Brake is entitled to benefit, the Board finds that such methods existed. However, to support its finding that Singh had not conceived of the invention prior to the Brake 1 Application filing date, the Board makes the contrary finding.

We find no error or inconsistency in the Board's analysis. As we wrote in Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1050, 34 USPQ2d 1565, 1569 (Fed. Cir. 1995), "the enablement requirement . . . looks to the objective knowledge of one of ordinary skill in the art." Id. (citing Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1532, 3 USPQ2d 1737, 1742 (Fed. Cir. 1987)). Thus, whereas the test for determining whether or not Singh conceived the construct of the count depended on Singh's own personal knowledge of methods for making the construct and his formulation of a definite and permanent idea therefor, whether Brake 1 enables an invention within the count does not depend on what Brake knew, but rather on whether the application enables one skilled in the art to make and use the invention, Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), "at the time the patent application was filed." Ajinomoto Co. v. Archer-Daniels-Midland Co., 228 F.3d 1338, 1345, 56 USPQ2d 1332, 1337 (Fed. Cir. 2000). The Board found that the testimony of Brake's witness, Dr. Patricia Tekamp-Olson, demonstrated that those of ordinary skill in the art had in their possession in 1982 various molecular biological methods sufficient to make and use the "n = 0" construct, including site-directed mutagenesis. Brake, Paper No. 199 at 24-27. The Board also found that Singh's expert, Dr. Joseph Falkinham, mischaracterized the teachings of the Fritz article on which he relied in his attempts to discredit Tekamp-Olson's testimony. Id. at 40.

As further "proof" that Brake 1 does not provide an enabling disclosure of the invention of the Count, Singh also alleges, for example, that "the Brake 1 Application actually steers the artisan to species clearly outside the Count," that "during prosecution of the Brake 2 Application, Brake argued

that the results obtained with the n = 0 construct were unexpected," and that "Dr. Brake did not realize the disadvantages of the n > 0 constructs until well after the Brake 1 Application was filed." We are not persuaded by any of these arguments, and conclude that Singh has apparently confused the criteria for proving obviousness with those for demonstrating that a disclosure is nonenabling. Although the questions (1) whether or not a reference "teaches away" from a claimed invention and (2) whether or not a claimed invention provides "unexpected results" are relevant in determining whether or not a claimed invention would have been obvious, W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983), they are not the primary questions bearing on enablement. The fact that the Brake patent states that n in the construct is "preferably 2 or 3" is also irrelevant to the question of enablement of the n = 0 construct. [6] Similarly, the fact that the n = 0 construct might have had after-discovered advantages over the n > 0 constructs has no bearing at all on whether or not Brake 1 contained an enabling disclosure.

We thus conclude that substantial evidence supports the Board's finding that Brake was entitled to the benefit of the Brake 1 application. We have considered Singh's other arguments and do not find them persuasive.

CONCLUSION

Because the Board's decision was supported by substantial evidence and contained no errors of law, the Board did not err in concluding that Singh failed to show (1) that Brake was not entitled to the Brake 1 filing date and (2) that Singh reduced the invention to practice before Brake's priority date. The Board's decision to award judgment to Brake is therefore affirmed.

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[1] Alpha-factor, also known as alpha-mating factor, is a peptide released by the budding yeast Saccharomyces cerevisiae when a haploid cell is prepared to mate. See Bruce Alberts et al., Molecular Biology of the Cell 722 (3d ed. 1994). The yeast cell exports alpha-factor by way of a "leader sequence," which is attached to alpha-factor and signals that the peptide is to be exported from the cell. See U.S. Application 06/506,098 at 3, II. 3-5. That sequence is typically removed from alpha-factor upon secretion. See id. at 3, II. 1-3. It is the alpha-factor leader sequence alone that is incorporated into the claimed construct.

[2] A "codon" is a set of three nucleotides that codes for a particular amino acid.

[3] Actually, this statement is incorrect. The 24-mer sequence that Singh ordered on November 24, 1982, was not identical to the nucleotides of the flanking sequences, but instead included several "preferred codons."

[4] This point is disputed. Singh has provided no corroboration of his assertion that this notation was actually made on December 21, 1982. Like the other pages of Singh's notebook, this page was not witnessed until 1986, and, even then, there is no proof that the notation existed at the time of the witnessing.

[5] Singh bases that number on the formula "$((R)_r$-$(GAXYCX)_n$-Gene*$)_y$" disclosed at page 3, line 33, of Brake 1, in which R = CGX or AZZ; r = "an integer of from 2 to 4, . . ., preferably 2"; X = T, G, C, or A; Y = G or C; y = "an integer of least one and usually not more than 10, more usually not more than four . . ."; Z = A or G; and n = "0 or an integer which will generally vary from 1 to 4, usually 2 to 3."

According to Singh, Each "R" can encode either Lys or Arg, so $(R)_r$ can encode $2^2 + 2^3 + 2^4 = 28$ different amino acid sequences. In addition, each "GAXYCX" sequence can encode any of four amino acid sequences: Asp-Pro, Asp-Ala, Glu-Pro, or Glu-Ala, so $(GAXYCX)_n$ can encode $4^0 + 4^1 + 4^2 + 4^3 + 4^4 = 341$ different amino acid sequences. Thus, Singh argues that the Brake 1 formula covers $28 \times 341 = 9548$ different species.

[6] The Board properly discredited Falkinham's testimony on that point. Paragraph 9 of Falkinham's Declaration states: "Although there was a theoretical presentation of the n=0 construct in the Brake 1 application, there was a clear statement that 'n' in the construct was 'preferably 2 or 3' (column 3, line 25) or 'usually 2 or 3' (column 2, line 68) . . . One skilled in the art would have determined from the Brake specification that the n=0 construct was not desirable." As the Board noted, Brake, Paper No. 199 at 36, Falkinham's citations to "columns" 2 and 3 obviously refer to the Brake patent (of which claim 1 is identical to the Count in this interference), and not to Brake 1.