NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

INTEGRATED DNA TECHNOLOGIES, INC.,
Appellant

v.

PILLAR BIOSCIENCES, INC.,
Appellee

2022-2172

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2021-00401.

Decided: December 20, 2024

RONALD E. CAHILL, Barnes & Thornburg LLP, Boston, MA, argued for appellant. Also represented by MATTHEW S. GIBSON, MARK CHRISTOPHER NELSON, Dallas, TX; STEVEN SHIPE, Washington, DC.

BRIAN ROBERT MATSUI, Morrison & Foerster LLP, Washington, DC, argued for appellee. Also represented by MATTHEW IAN KREEGER, San Francisco, CA; JIAN XIAO, Palo Alto, CA.

Before REYNA, MAYER, and CUNNINGHAM, *Circuit Judges*.

CUNNINGHAM, *Circuit Judge*.

Integrated DNA Technologies, Inc. ("IDT") appeals from a final written decision of the Patent Trial and Appeal Board in an *inter partes* review, finding claims 1–6 of U.S. Patent No. 10,316,359 unpatentable. *Pillar Biosciences, Inc. v. Swift Biosciences, Inc.*, No. IPR2021-00401, 2022 WL 2308112, at *1 (P.T.A.B. June 27, 2022) ("*Decision*").[1] On appeal, IDT challenges the Board's claim construction, argues that the Board's factual findings were not supported by substantial evidence, and asserts that the Board erred in ruling that IDT had forfeited[2] certain arguments. For the reasons below, we *affirm* the Board's decision.

I. BACKGROUND

The '359 patent is titled "Methods for Multiplex PCR." It is generally directed to methods for the preparation of polymerase chain reaction ("PCR") mixtures and for performing multiplex PCR amplification that limit the production of non-target amplicons. '359 Patent, Abstract. Claim 1 is illustrative of the issues on appeal and recites:

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[1] Swift Biosciences, Inc. was the named patent owner when the IPR was filed. J.A. 608. While the IPR was pending Swift Biosciences merged with IDT, making IDT the real party-in-interest. J.A. 609.

[2] The parties and the Board use the term "waiver," but for consistency we use "forfeiture" throughout this opinion. *See In re Google Tech. Holdings LLC*, 980 F.3d 858, 862 (Fed. Cir. 2020) ("By and large, in reviewing this court's precedent, it is evident that the court mainly uses the term 'waiver' when applying the doctrine of 'forfeiture.'").

1. A method of multiplex PCR amplification of a target nucleic acid substrate comprising the steps of:

(i) combining a plurality of target-specific primers with the target nucleic acid substrate to yield a single polymerase chain reaction (PCR) reaction mixture, wherein the plurality of target-specific primers comprise a first forward primer, a second forward primer, a first reverse primer and a second reverse primer, wherein each of the first and second forward and reverse primers comprise a 3′ complementary sequence that is complementary to the target nucleic acid substrate and a 5′ noncomplementary sequence that is not complementary to the target nucleic acid substrate, wherein the 3′ complementary sequence for each of the first and second forward and reverse primers is different;

(ii) subjecting the PCR reaction mixture to a multiplex polymerase chain reaction thereby generating at least three amplicons, wherein the at least three amplicons comprise a first amplicon produced by the first forward primer and the first reverse primer, a second amplicon produced by the second forward primer and the second reverse primer, and a third amplicon produced by the second forward primer and the first reverse primer, wherein at least a portion of the 5′ noncomplementary sequence of the second forward primer and the first reverse primer is the same such that each strand of the third amplicon comprises a 3′ end and a 5′

> end that are complementary to each other, wherein the third amplicon possesses overlapping sequence with the first and second amplicons, wherein the first amplicon possesses overlapping sequence with the second amplicon, wherein when the third amplicon is denatured, each strand of the third amplicon forms a secondary structure as a result of the 3′ end being complementary to the 5′ end, and wherein the secondary structure is stable during a primer annealing step of the multiplex polymerase chain reaction.

Id. col. 133 ll. 56–67, col. 134 l. 55 to col. 135 l. 12.

On January 7, 2021, Pillar Biosciences, Inc. ("Pillar") filed the IPR underlying this appeal, challenging claims 1–6 of the '359 patent. *Decision* at *1; *see also* J.A. 162. Among other things, Pillar asserted that the claims of the '359 patent were obvious over the combination of prior art references Lao[3] and Gardner.[4] *Decision* at *1. The Board instituted review on July 19, 2021. *Id.* The Board subsequently held that Pillar proved by a preponderance of the evidence that all challenged claims were unpatentable under 35 U.S.C. § 103(a) over Lao and Gardner. *Decision* at *13.

IDT timely appeals. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

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[3] U.S. Patent Application 2009/0291475 (filed Apr. 22, 2009), J.A. 940–87 ("Lao").

[4] Shea N. Gardner et al., *Multiplex Degenerate Primer Design for Targeted Whole Genome Amplification of Many Viral Genomes*, Advances in Bioinformatics, Aug. 3, 2014, J.A. 1000–07 ("Gardner").

II. STANDARD OF REVIEW

"We review the Board's legal conclusions de novo and its fact findings for substantial evidence." *Game & Tech. Co. v. Wargaming Grp. Ltd.*, 942 F.3d 1343, 1348 (Fed. Cir. 2019). "Substantial evidence means such relevant evidence as a reasonable mind might accept as adequate to support a conclusion." *Fanduel, Inc. v. Interactive Games LLC*, 966 F.3d 1334, 1343 (Fed. Cir. 2020) (internal quotation marks and citation omitted).

"Whether a claimed invention is unpatentable as obvious is a question of law that is reviewed de novo, based on underlying findings of fact reviewed for substantial evidence." *Redline Detection, LLC v. Star Envirotech, Inc.*, 811 F.3d 435, 449 (Fed. Cir. 2015). "The Court can review de novo, however, whether the Board failed to consider the appropriate scope of the patent's claimed invention in evaluating the reasonable expectation of success." *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1366–67 (Fed. Cir. 2016) (cleaned up).

"Decisions related to compliance with the Board's procedures are reviewed for an abuse of discretion." *Id.* at 1367. "An abuse of discretion is found if the decision: (1) is clearly unreasonable, arbitrary, or fanciful; (2) is based on an erroneous conclusion of law; (3) rests on clearly erroneous fact finding; or (4) involves a record that contains no evidence on which the Board could rationally base its decision." *Ericsson Inc. v. Intell. Ventures I LLC*, 901 F.3d 1374, 1379 (Fed. Cir. 2018) (quoting *Bilstad v. Wakalopulos*, 386 F.3d 1116, 1121 (Fed. Cir. 2004)).

III. DISCUSSION

IDT presents several arguments on appeal. IDT argues that the Board erred in construing "each strand of the third amplicon forms a secondary structure . . . and wherein the secondary structure is stable during a primer annealing step." Appellant's Br. 31–35; Appellant's Reply

Br. 17–18. IDT also argues that the Board's finding of a motivation to combine the prior art contained factual and legal errors. *See* Appellant's Br. 46–55. IDT further contends that the Board's finding of a reasonable expectation of success was based on hindsight. *See id.* at 35–46. Lastly, IDT argues that the Board erred in ruling that IDT had forfeited arguments based on an additional reference, Schenk.[5] *Id.* at 55–57. We address each argument in turn.

A.

IDT argues that the Board erred in its claim construction of "each strand of the third amplicon forms a secondary structure . . . and wherein the secondary structure is stable during a primer annealing step" by concluding that "the claims did not require complete elimination of short amplicons." Appellant's Br. 31 (internal quotation marks omitted). At oral argument, IDT presented a different construction, arguing that the quantity of short amplicons "needs to be reduced to a level [at which] it doesn't dominate." Oral Arg. 12:50–13:02, https://oralarguments.cafc.uscourts.gov/default.aspx?fl=22-2172_02092024.mp3.

Regardless of which claim construction position IDT presents, we need not reach the merits of IDT's claim construction arguments because it has forfeited them. *See In re Google Tech. Holdings LLC*, 980 F.3d 858, 862 (Fed. Cir. 2020) (explaining that Google forfeited the claim construction arguments that it failed to present to the Board). IDT concedes in its briefing that neither party

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[5] Desiree Schenk et al., *Amplification of Overlapping DNA Amplicons in a Single-Tube Multiplex PCR for Targeted Next-Generation Sequencing of BRCA1 and BRCA2*, PLoS ONE, July 12, 2017, J.A. 1700–15 ("Schenk").

proposed a construction for the term at issue, and neither party briefed a construction for this term before the Board. Appellant's Br. 33; Oral Arg. 12:34–13:23. Generally, absent exceptional circumstances, we will not consider on appeal claim construction arguments that were not first presented to the Board.

IDT argues that it has not forfeited its claim construction arguments because the Board construed the "each strand" limitation in its final written decision inconsistently with the plain and ordinary meaning of the term after both parties had relied on the plain and ordinary meaning throughout the proceedings below. Appellant's Reply Br. 16–18. However, the Board was only applying the plain and ordinary meaning of the challenged claims, which nowhere reference "complete elimination of short amplicons." *See, e.g.*, *Decision* at *9. To the extent that IDT thinks that complete elimination of short amplicons is required, or that the short amplicons had to be reduced to a level that does not dominate the PCR amplification process, IDT was required to raise those arguments to the Board to preserve them on appeal.

B.

IDT further argues that the Board's finding of a motivation to combine Gardner and Lao was not supported by substantial evidence because there was allegedly no dispute that the combination "does not work for its intended purpose[;] Gardner teaches away from the combination[;] and the combination would result in the loss of key functionality in Gardner." Appellant's Br. 46. IDT additionally faults the Board for purportedly short-circuiting the proper analysis without considering whether the proposed combination would provide the advantages that Gardner specifically sought. *Id.*; *see also id.* at 48–49. IDT's arguments are unpersuasive.

IDT's main argument for why the Board lacked substantial evidence for its determination that a skilled

artisan would have had a motivation to combine Gardner and Lao concerns the size of the overlapping amplicons in each of the references. *See* Appellant's Br. 46–55. According to IDT, there is no motivation to combine the prior art references because 30 of the 36 overlapping amplicons in Gardner exceeded 100 base pairs and Lao does not suppress amplicons of that size. *Id.* at 38, 49. The Board addressed this argument in the final written decision, finding that "even under the most restrictive reading of Lao," "six of the amplicons listed in Gardner's example are shorter than 100 nucleotides and therefore would have been removed." *Id.* at *10. There is no dispute about the relevant teachings of Gardner and Lao. Oral Arg. 4:24–4:30 (IDT agreeing "that Gardner discloses at least some amplicons that are within Lao's size limitations"). For example, Gardner expressly teaches "a step to remove short amplicons before sequencing," J.A. 1003, and Lao discloses the ability of "shorter insert sections to self-hybridize, and thus take themselves out of a reaction."[6] J.A. 972 ¶ 116. In summary, we conclude that there is substantial evidence support for the Board's conclusion that a skilled artisan would have had a motivation to combine Gardner with Lao, *see Decision* at *7–9, and thus we conclude that the Board did not err in its motivation-to-combine determination.

C.

Substantial evidence also supports the Board's factual finding that a skilled artisan would have a reasonable

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[6] Lao defines insert sections as the portion of the amplicon between the complementary ends of the linear primers used to form the amplicon. J.A. 965 ¶ 0064. The size comparisons in this case were done on an apples-to-apples basis, and "amplicons," "insert sections," and "insert regions" are terms all used by the parties. J.A. 1800–01; *see* Appellant's Br. 42 n. 5.

expectation of success in combining Lao and Gardner to achieve the claimed invention. IDT argues that the Board's conclusion was unsupported by substantial evidence because there is "undisputed evidence that the combination of Gardner with Lao will fail abjectly . . . for the purpose of claim 1 of the '359 patent, . . . for the purpose of Gardner, and . . . for the stated motivation for making the combination." Appellant's Br. 30. "The reasonable-expectation-of-success analysis must be tied to the scope of the claimed invention." *Teva Pharms. USA, Inc. v. Corcept Therapeutics, Inc.*, 18 F.4th 1377, 1381 (Fed. Cir. 2021). IDT does not demonstrate any flaw with the evidence the Board did rely on in reaching its conclusion regarding reasonable expectation of success. *Decision* at *10 (citing evidence from Lao, Gardner and the testimony of Pillar's expert in support of a reasonable expectation of success); Appellant's Br. 35–43. The Board did not err in finding that a skilled artisan would have a reasonable expectation of success in combining Gardner with Lao to achieve the claimed invention.

IDT argues that the evidence the Board relied on was merely conclusory and that its finding was based on hindsight. *See* Appellant's Br. 42–43. We disagree. IDT's argument is premised on its claim construction arguments, which IDT forfeited. *See id.* at 42 ("This finding can only be justified by applying the Board's faulty claim construction where it found that removal of *some* amplicons met the claim."). Regardless, the Board found that Lao discloses "self-hybridizing," a process where amplicons take themselves out of the reaction. *Decision* at *4, 9. Contrary to IDT's assertions, that finding was not hindsight; it was based on the express disclosure of Lao. J.A. 972 ¶ 116. ("[T]he double extended linear primers having shorter insert sections to self-hybridize, and thus take themselves out of a reaction . . . ."). Indeed, several parts of Lao support the Board's determination. *See, e.g.*, J.A. 950 (Fig. 8), 961 ¶ 0034, 964 ¶ 0053. The expert

testimony the Board relied on provides additional support for this finding. *Decision* at *10.

IDT attempts to incorporate one reference's embodiments into the other reference. *See, e.g.*, Appellant's Br. 38, 40 (focusing its analysis on the interaction between a limitation present "in some embodiments" of Lao, J.A. 966 ¶ 73, and a subset of overlapping amplicons in an example in Gardner). Here too, we disagree with IDT's approach. "[A] determination of obviousness based on teachings from multiple references does not require an actual, physical substitution of elements." *In re Mouttet*, 686 F.3d 1322, 1332 (Fed. Cir. 2012). The correct inquiry is instead whether a skilled artisan would reasonably expect success in combining the prior art's teachings to achieve the claimed invention. *Intelligent Bio-Sys.*, 821 F.3d at 1367–68; *see also In re Applied Materials, Inc.*, 692 F.3d 1289, 1298 (Fed. Cir. 2012) ("A reference must be considered for everything that it teaches, not simply the described invention or a preferred embodiment."). We agree with Pillar that because "Gardner . . . teaches a multiplex PCR reaction with primers that produce overlapping amplicons" and "never suggests that its overlapping amplicons in multiplex PCR reactions must exceed Lao's supposed size limitation," the Board did not err in holding that a skilled artisan would reasonably expect to succeed in combining the prior art references to achieve the subject matter claimed by the '359 patent. Appellee's Br. 37–38; *Decision* at *12.

IDT argues that the Board erred by failing to consider all of IDT's arguments against finding a reasonable expectation of success. Appellant's Br. 43 (quoting *Decision* at *9). But the Board is "not required to address every argument raised by a party or explain every possible reason supporting its conclusion." *Yeda Rsch. v. Mylan Pharms. Inc.*, 906 F.3d 1031, 1046 (Fed. Cir. 2018) (cleaned up). The Board committed no reversible error here, and it

supported its factual determination with substantial evidence.

D.

IDT's contention that the Board erred by finding IDT's arguments based on Schenk forfeited under 37 C.F.R. § 42.23(b) is similarly unavailing. *See* Appellant's Br. 56–57. IDT argues that it maintained its reliance on the Schenk reference throughout the proceedings, *id.*, but IDT's characterization of the procedural history does not align with the record, and its argument therefore fails.

During the IPR, the Board cautioned IDT "that any arguments not raised in the response may be deemed [forfeited]." J.A. 315. Although IDT had extensively discussed Schenk in its preliminary response, J.A. 272–76, IDT's citations to Schenk in the Patent Owner's Response were minimal and without much elaboration. *See, e.g.*, J.A. 350, 353–55, 392. The Board did not abuse its discretion in finding that IDT had therefore forfeited the argument. *See Decision* at *11; *In re NuVasive, Inc.*, 842 F.3d 1376, 1380 (Fed. Cir. 2016) (finding the patent owner "[forfeited] its public accessibility arguments" where it challenged public accessibility "during the preliminary proceedings of the inter partes review but failed to challenge public accessibility during the trial phase" (citations omitted)); *Broadcom Corp. v. ITC*, 28 F.4th 240, 252 (Fed. Cir. 2022) (declining to address argument not raised with the Board and explaining that "[t]he Board's scheduling order specifically informed [patent owner] that 'any arguments not raised in the response may be deemed [forfeited]'"). The Board acted within its discretion when it found that IDT had forfeited the argument and that it would not consider the parties' arguments with respect to Schenk.

IV. CONCLUSION

We have considered IDT's remaining arguments and find them unpersuasive. For the above reasons, we *affirm*.

AFFIRMED