United States Court of Appeals for the Federal Circuit

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,
Appellant

v.

PERSONAL GENOMICS TAIWAN, INC.,
Cross-Appellant

2022-1410, 2022-1554

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2020-01163, IPR2020-01200.

Decided: January 9, 2024

EDWARD R. REINES, Weil, Gotshal & Manges LLP, Redwood Shores, CA, argued for appellant. Also represented by DEREK C. WALTER.

KEITH ORSO, Irell & Manella LLP, Los Angeles, CA, argued for cross-appellant. Also represented by ALAN J. HEINRICH; MICHAEL RICHARD FLEMING, Washington, DC.

Before PROST, TARANTO, and HUGHES, *Circuit Judges*.

TARANTO, *Circuit Judge*.

Pacific Biosciences of California, Inc. (PacBio) filed two petitions with the Patent and Trademark Office under 35 U.S.C. §§ 311–19, each one seeking an inter partes review of a group of claims of U.S. Patent No. 7,767,441, which is owned by Personal Genomics Taiwan, Inc. (PGI). The Patent Trial and Appeal Board, acting for the PTO's Director, instituted both IPRs, which overlapped in the claims challenged but differed in the prior art invoked. The Board eventually issued final written decisions in the IPRs. In one of the IPRs, the Board rejected PacBio's challenge to claims 1–2, 6–7, 10–22, 24, and 27–36. *Pacific Biosciences of California, Inc. v. Personal Genomics Taiwan, Inc.*, No. IPR2020-01200, 2022 WL 214042 (P.T.A.B. Jan. 18, 2022) (*'1200 Decision*). In the other IPR, the Board agreed with PacBio's challenge to claims 1–6, 9, and 43–58. *Pacific Biosciences of California, Inc. v. Personal Genomics Taiwan, Inc.*, No. IPR2020-01163, 2022 WL 212276 (P.T.A.B. Jan. 18, 2022) (*'1163 Decision*). Under those two decisions, claims 7, 10–22, 24, and 27–36 survive; claims 1–6, 9, and 43–58 do not.

Both parties appeal. Appellant PacBio principally challenges the Board's construction of the claim phrase "identifying a single biomolecule," while also briefly challenging the Board's finding that the prior art PacBio invoked in the '1200 IPR to meet this limitation does not teach it under the Board's construction. Cross-appellant PGI, besides defending the Board's construction of the disputed claim phrase, challenges the Board's factual findings that the PacBio-invoked prior art in the '1163 IPR teaches the disputed claim phrase. We affirm both decisions.

I

U.S. Patent No. 7,767,441 describes and claims an "apparatus for identifying a single biomolecule" as well as methods of using or making that apparatus. '441 patent, col. 26, line 11; *see also id.*, col. 26, line 10 through col. 30, line 5. The patent describes an apparatus that uses many

"optical detection apparatuses" to "monitor a large number (e.g., in some embodiments, more than 10,000) of single biomolecules in parallel," and thereby determines the identity of many biomolecules in a sample "with high throughput." *Id.*, col. 3, lines 55–65; *see also id.*, col. 4, lines 11–16. The "optical detection apparatus" uses a "light detector" that is in close proximity to (*e.g.*, "less than or equal to 100 micrometers" from) a "linker site" that is "treated to affix the biomolecule" to be identified. *Id.*, col. 2, lines 30–44. The light detector can measure a signal from some light-emitting molecule—*e.g.*, "a fluorophore attached to the biomolecule," a "labeled probe," or "labeled nucleotides"—and thereby identify the affixed biomolecule. *Id.*, col. 2, lines 43–62; *see also id.*, col. 17, lines 58–62 (discussing "chromophores"); *id.*, col. 18, lines 18–21 (same).

Claim 1 is representative for present purposes:

> 1. An apparatus for identifying a single biomolecule, comprising:
>
> > a substrate having a light detector; and
> >
> > a linker site formed over the light detector, the linker site being treated to affix the biomolecule to the linker site;
> >
> > wherein the linker site is proximate to the light detector and is spaced apart from the light detector by a distance of less than or equal to 100 micrometers.

Id., col. 26, lines 11–18.

In the '1200 IPR, PacBio challenged claims 1–2, 6–7, 10–22, 24, and 27–36—all claiming the apparatus of claim 1 or its use and many, though not all, focusing specifically on nucleic acids and determining their nucleotide sequences—as unpatentable for anticipation or obviousness based principally on the Hassibi reference, a published United States patent application, U.S. Patent Application

Publication No. 2004/0197793 A1 (filed Jul. 24, 2003) (published Oct. 7, 2004) (Hassibi); J.A. 1638–1706. The Board issued a final written decision determining that PacBio had not shown any of the challenged claims to be unpatentable. *'1200 Decision*, at *21.

In the '1163 IPR, PacBio challenged claims 1–6, 9, and 43–58—which refer to biomolecules generally, not to nucleic acids specifically—as unpatentable for anticipation or obviousness based principally on the Choumane reference, an international patent application, PCT Application Publication No. WO 2007/045755 A1 (filed Oct. 17, 2006) (published Apr. 26, 2007) (Choumane); J.A. 5533–62. The Board issued a final written decision determining that PacBio had proved all the challenged claims to be unpatentable. *'1163 Decision*, at *26.

In reaching its decisions, the Board adopted a claim construction of the preamble phrase "identifying a single biomolecule," setting forth reasoning that is materially identical in the two opinions. *Compare '1200 Decision*, at *6–11, *with '1163 Decision*, at *6–11. In a conclusion not challenged on appeal, the Board determined that the preamble phrase is a limitation on the claimed subject matter because it provides antecedent basis for references to "the biomolecule" in the body of the relevant claims. *See '1200 Decision*, at *7, *9 (claim 1); *'1163 Decision*, at *7, *9 (same).[1] In another conclusion not challenged on appeal, the Board determined that the full phrase "for identifying a single biomolecule" refers to a capability of the apparatus. *See '1200 Decision*, at *9–10; *'1163 Decision*, at *9–

[1] All independent claims either require the apparatus of claim 1 (claims 11, 12, 16, 30, 43), whether expressly or indirectly, or have the same relevant preamble language tied to "the biomolecule" language in the body (claims 48, 53–55). *See* '441 patent, col. 26, line 10 through col. 30, line 5.

10 (same); *see ParkerVision, Inc. v. Qualcomm Inc.*, 903 F.3d 1354, 1361–62 (Fed. Cir. 2018) (explaining that capability is one meaning of "for" language).

The claim-construction dispute central to the appeals before us involves the Board's understanding that the "identifying a single biomolecule" phrase, in the context of the "[s]pecification of the '441 patent," "contemplates running myriad optical detection apparatuses in parallel to detect a *single* or individual biomolecule in each such apparatus." *'1200 Decision*, at *8; *'1163 Decision*, at *8. That construction requires that the apparatus have the capability to characterize (determine the identity of) a biomolecule by examining that biomolecule alone, with no copies created to form an ensemble for examination. In adopting that construction, the Board rejected PacBio's argument that an apparatus would come within this claim phrase if the apparatus, though not capable of characterizing a biomolecule by examining it alone, had the capability to characterize a biomolecule by making copies, examining the resulting ensemble, and inferring the identity of the starter biomolecule. *'1200 Decision*, at *8 (rejecting PacBio's construction as "inapposite when the challenged claims are read in light of the [s]pecification of the '441 patent"); *'1163 Decision*, at *8 (same).

In the *'1200 Decision*, the Board found that PacBio failed to establish that this limitation was taught by the Hassibi reference—on which PacBio relied for this essential point in the only ground raised in PacBio's appeal to us. *'1200 Decision*, at *12–17. That determination sufficed to reject PacBio's challenge to the claims at issue in that IPR. *Id.* at *21.

In the *'1163 Decision*, the Board found, in contrast, that PacBio did establish that the "identifying a single biomolecule" limitation was taught by the Choumane reference, *i.e.*, that Choumane taught an apparatus with the capability required by the Board's claim construction. *'1163*

Decision, at *12–16. The Board added, *id.* at *22, that this limitation was also taught by a second reference that PacBio invoked for obviousness in combination with Choumane, namely, a published patent application, U.S. Patent Application Publication No. 2002/0182716 A1 (filed Feb. 12, 2002) (published Dec. 5, 2002) (Weisbuch); J.A. 5563–80. The Board found the requisite proof as to the other limitations of the challenged claims, by Choumane alone or in the specified combinations for obviousness, but those findings are not at issue on appeal. The Board therefore found that PacBio had shown unpatentability of the claims challenged in the '1163 IPR. *'1163 Decision*, at *26.

The Board issued both of its final written decisions on January 18, 2022. PacBio filed a timely notice of appeal from the *'1200 Decision* on January 24, 2022, and PGI filed a timely notice of appeal from the *'1163 Decision* on March 18, 2022. The appeals are authorized by 35 U.S.C. §§ 141(c) and 319, and we have statutory jurisdiction under 28 U.S.C. § 1295(a)(4)(A). PGI's pending infringement suit against PacBio under the '441 patent supports constitutional standing. *See* PacBio's Opening Brief at 1.

II

A

PacBio's appeal principally challenges the Board's construction of the "identifying a single biomolecule" claim limitation. We review this construction, which rests on intrinsic evidence, without deference. *Polaris Innovations Ltd. v. Brent*, 48 F.4th 1365, 1372 (Fed. Cir. 2022). We affirm the Board's construction of "identifying a single biomolecule" as requiring an apparatus capable of ascertaining the identity of one single, individual biomolecule by examining only that biomolecule.

It is undisputed before us that the claim language at issue—"for identifying a single biomolecule"—refers to a capability of an apparatus. What is disputed is the

meaning of "identifying a single biomolecule." That phrase has an ordinary meaning on its face and in context. The language refers to (a) ascertaining the identity of a biomolecule, *i.e.*, what that biomolecule is, and (b) doing so by examining just that one biomolecule, not others (even copies). It is that capability the apparatus must have, no matter what other capabilities it has or how the apparatus may be used in a particular instance.

The proper construction in this case is determined by the ordinary meaning of the claim language understood in the context of the patent document. *See World Class Technology Corp. v. Ormco Corp.*, 769 F.3d 1120, 1123 (Fed. Cir. 2014); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–17 (Fed. Cir. 2005) (en banc). The ascertainment of the identity of a molecule is the ordinary meaning in this context of 'identify,' as the aim of the invention is to ascertain the identity, *e.g.*, the nucleotide sequence, of the single biomolecule. *See* BRYAN A. GARNER, GARNER'S MODERN AMERICAN USAGE 435 (3d ed. 2009) (defining "identify" as "(2) to ascertain or demonstrate what something . . . is"); RANDOM HOUSE WEBSTER'S UNABRIDGED DICTIONARY 950 (2d ed. 2001) (defining "identify" as "1. to recognize or establish as being a particular . . . thing; verify the identity of"). That aspect of the claim meaning is not in genuine dispute. Only the above-stated second part of the meaning is disputed.

We agree with the Board that this identifying-by-examining-one-alone meaning is the ordinary meaning of the phrase in context. The striking feature of the phrase is its inclusion of the word "single." There is no apparent reason for the inclusion of the word "single" in the phrase except to indicate that the capability required is to identify a molecule with just that one molecule in view.

The '441 patent's specification confirms this understanding by repeatedly stressing that this "single biomolecule" capability is critical to the invention. It states that it is describing "a bioassay system for identifying a single

biomolecule at a detecting unit." '441 patent, col. 2, lines 30–31. In such a bioassay system, the specification indicates, "[e]ach optical detection apparatus may sense the existence of a fluorophore on the single molecule by detecting photons emitted from the fluorophore." *Id.*, col. 3, lines 59–61. When the patent illustrates optical detection apparatuses "identifying a single biomolecule," it depicts examination of one individual biomolecule, not an ensemble or cluster consisting of multiple biomolecules. *See id.*, figs. 2 & 6–8.

Significantly, in explaining the claimed bioassay system's single-molecule sensitivity, the specification differentiates, on one hand, "identifying a single biomolecule" by examining that individual biomolecule from, on the other, detecting a population-level signal from an ensemble or cluster of amplified or copied biomolecules. It indicates that the latter process involves problems that the former avoids. In particular, the patent requires that the claimed apparatus be capable of the former functionality, explaining that the claimed "devices should be capable of sequencing single molecules to avoid the known difficulty of asynchrony in both the amplification (e.g., drift between the sequences of ideally clonal templates) and sequencing (e.g., dephasing of the stepwise sequencing reactions amongst the sequencing templates) steps of clustered sequencing methods." *Id.*, col. 1, line 67 through col. 2, line 6. Avoiding those problems was accomplished by an apparatus with single-molecule detection sensitivity, enabling single-molecule examination for identification, confirming the proper understanding of the claim language here in dispute.

Other claims of the patent—method claims that call for particular uses of the claim 1 apparatus—provide support for this claim construction. Method claim 26 depends on claim 16, which claims a method (using a claim 1 apparatus) of "performing nucleic acid sequencing" of "one nucleic acid molecule," but adds the limitation "wherein the

nucleic acid is amplified." '441 patent, col. 27, lines 20–21 (claim 26); *id.*, col. 26, lines 59–64 (claim 16). Claim 30 claims a method (using a claim 1 apparatus) of "detecting" "one or more biomolecule." *Id.*, col. 27, lines 30–34. Those claims thus call for using the claim 1 apparatus for expressly described multiple-molecule examinations, including where amplification of a starter molecule produces the group examined, implicitly requiring a capability to do so. Dependent claims often add capabilities to those stated in the independent claim (where there is no inconsistency), and here the language used underscores what is not required by the claim 1 phrase itself.

We reject PacBio's contention that the Board's (and our) reading "conflates ***identifying*** a single molecule with ***detecting*** a single molecule." PacBio's Reply and Response Brief at 2. We need not deny that, in some contexts, one might say that a molecule can be identified by following processes for making copies, examining the resulting ensemble, and inferring the identity of the starting molecule. But the '441 patent recognizes the problems with such processes and seeks to avoid those problems by claiming an apparatus capable of identification by single-molecule examination. Such a claim does not "conflat[e]" identification with detection but instead uses a detection requirement to specify a particular identification capability.

For those reasons, we affirm the Board's construction of the claim language in dispute, understood as we have explained it.

B

Both PacBio and PGI challenge the Board's factual findings regarding the prior art. PacBio challenges the Board's finding in the '1200 IPR that Hassibi does not disclose "identifying a single biomolecule" under the claim construction we are affirming. PGI challenges the Board's finding in the '1163 IPR that Choumane does disclose "identifying a single biomolecule" under that construction.

We conclude that both findings are supported by substantial evidence, and we therefore affirm them. *See Shoes by Firebug LLC v. Stride Rite Children's Group, LLC*, 962 F.3d 1362, 1369 (Fed. Cir. 2020) (explaining that we review Board findings regarding the content of prior art for substantial-evidence support).[2]

1

In the '1200 IPR, the critical disclosure in Hassibi is that the principal embodiment of the described and claimed invention uses an assay—a bioluminescence regenerative cycle (BRC) assay—that Hassibi describes as having "a sensitivity of detection as low as 0.1 attomoles." J.A. 1670–71 ¶¶ 16–17; *see also* J.A. 1704, Claim 24 ("wherein sensitivity of detection is at least 0.1 attomol"). This is a minimum-detection limit of greater than 60,000 molecules. J.A. 3800, lines 1–4 (testimony of PacBio expert). This assay is referred to repeatedly in Hassibi for detection purposes, and in other places, Hassibi discloses an even higher minimum sensitivity. J.A. 1696 ¶ 325 (reporting a sensitivity of "1 amol to 100 amol"). The Board credited the testimony of Dr. Harris (PGI's expert) and Hassibi itself in finding that nothing in Hassibi or elsewhere in the record rebuts this evidence by demonstrating that Hassibi, instead, discloses the capacity to ascertain the identity of one individual biomolecule using either a more sensitive BRC assay or a different assay. *'1200 Decision*, at *15–17. This evidence provides substantial-evidence support for the Board's finding that Hassibi does not disclose "identifying a single biomolecule."

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[2] Because we affirm the Board's finding about the teaching of Choumane, we need not address PGI's challenge to the Board's finding about the teaching of Weisbuch.

The critical disclosure in Choumane is that the claimed invention can include "very small openings . . . of a dimension less than the wavelength of light emitted by chromophores," where "[t]hese openings delimit very small observation volumes . . . for the detection and observation of *individual chromophores*." J.A. 5551, lines 20–24 (emphasis added). The Board reasonably understood this to disclose the capacity to identify one individual biomolecule, given that a single chromophore is often used to tag a single biomolecule. *'1163 Decision*, at *15–16; J.A. 5360 ¶ 61; '441 patent, col. 3, lines 59–61. Added support is found in Choumane's description of "a biosensor with ultrasensitive detection" for detecting "biological probes," not merely chromophores in isolation. J.A. 5538, lines 3–6.

PGI's principal challenge to the Board's finding relies on a calculation, starting from (and perhaps extending a bit beyond) analysis supplied by its expert witness, that Choumane's disclosures do not disclose a detection sensitivity of less than 78 biomolecules. PGI's Principal and Response Brief at 68–73 (citing J.A. 7605–06 ¶ 86). Although PacBio seems to suggest otherwise, this type of calculation can be proper where based on the express disclosures of a piece of prior art. *See Perfect Web Technologies, Inc. v. InfoUSA, Inc.*, 587 F.3d 1324, 1329 (Fed. Cir. 2009) ("We therefore hold that while an analysis of obviousness always depends on evidence that supports the required *Graham* factual findings, it also may include recourse to logic, judgment, and common sense available to the person of ordinary skill that do not necessarily require explication in any reference or expert opinion."). In this case, however, the Board, considering the calculation, had sufficient reason, in light of the Choumane statement quoted above, to reject the inference about Choumane that PGI offered the calculation to support.

PacBio's expert provided rebuttal testimony stating that Choumane teaches "improv[ing] collection efficiency by a factor of 400," which, PacBio's expert ultimately concluded, allows a sensitivity increase over the prior art sufficient to disclose single-biomolecule detection capability. J.A. 7427–28 ¶ 6; *see also* J.A. 7428 ¶ 7 (calculating that Choumane discloses "a minimum detection of 0.975 chromophores (i.e. single molecule detection)"); *cf.* J.A. 7428–29 ¶ 8 (calculating that combining Choumane's disclosures with Weisbuch's results in "a minimum detection of 0.25 chromophores"). In contrast, PGI's expert stated that when Choumane expressly discloses improving sensitivity over the prior art only by "several tens of times," J.A. 5537, line 3, it means only about "30 or 40 or 50" times better, J.A. 7334, line 2, which, PGI has argued, is not sufficient for single-biomolecule detection sensitivity. *See* PGI's Reply Brief at 25 n.4 ("Substituting a **40**-fold improvement for [PacBio's expert's] 400-fold improvement would increase sensitivity . . . [to] about 9.5 chromophores."). Where the overall evidence reasonably allows the Board's factual finding on a point, we do not "reweigh the evidence" to reject that finding. *Regents of the University of California v. Broad Institute, Inc.*, 903 F.3d 1286, 1294 (Fed. Cir. 2018). Here, on the evidence before it, the Board could reasonably credit PacBio's expert, *'1163 Decision*, at *16, and rely on the "detection and observation of individual chromophores" language of Choumane, J.A. 5551, line 24, for its finding about Choumane's teaching.

III

We find none of PacBio's and PGI's remaining arguments persuasive. The Board's final written decisions in the '1200 IPR and the '1163 IPR are affirmed.

The parties shall bear their own costs.

AFFIRMED