NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

LABORATORY CORPORATION OF AMERICA HOLDINGS,
Appellant

v.

RAVGEN, INC.,
Appellee

2023-1517

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2021-01026.

Decided: January 29, 2025

GREGORY A. CASTANIAS, Jones Day, Washington, DC, argued for appellant. Also represented by AMELIA A. DEGORY, BRENDAN D. DUFFY, TRACY A. STITT, JENNIFER L. SWIZE; GASPER LAROSA, New York, NY; JOHN C. ALEMANNI, Kilpatrick Townsend & Stockton LLP, Raleigh, NC; CYNTHIA B. ROTHSCHILD, I, Winston-Salem, NC.

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Before LOURIE, BRYSON, and STARK, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Laboratory Corporation of America Holdings ("Labcorp") appeals from the final written decision of the U.S. Patent Trial and Appeal Board ("the Board") holding that claims 1–9 and 21–30 of U.S. Patent 7,727,720 ("the '720 patent") had not been shown to be unpatentable. *Lab'y Corp. of Am. Holdings v. Ravgen, Inc.*, No. IPR2021-01026, 2022 WL 17583185 (P.T.A.B. Dec. 12, 2022) ("*Decision*"). For the following reasons, we *affirm*.

BACKGROUND

The instant case is a companion to *Laboratory Corporation of America Holdings v. Ravgen, Inc.*, No. 2023-1342, 2025 WL 32904 (Fed. Cir. Jan. 6, 2025) ("*Labcorp*") addressing related U.S. Patent 7,332,277 and decided by this court on January 6, 2025. In that case, we affirmed the Board's upholding of similar claims against overlapping prior art. Ravgen, Inc. ("Ravgen") owns the '720 patent, which is directed to a "rapid, non-invasive method for determining the sequence of DNA from a fetus" that can be used "for detection of chromosomal abnormalities." '720 patent, col. 1, ll. 23–27. The '720 patent describes a method of adding an agent that impedes cell lysis to a maternal blood sample to increase the percentage of cell-free fetal DNA relative to the cell-free maternal DNA in the sample. *Id.* at col. 210, ll. 19–24; *id.* at col. 89, ll. 35–37. The specification lists various agents as membrane stabilizers, cross-linkers, and cell lysis inhibitors, including formaldehyde and glucose. *Id.* at col. 32, l. 65–col. 33, l. 28.

Claim 1 is representative for the issues on appeal and reads as follows:

> 1. A method for detecting a free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid from a non-cellular fraction of a sample, wherein said sample comprises an agent that *impedes cell lysis, if cells are present*, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; and (b) detecting the presence or absence of the free nucleic acid.

Id. at col. 535, ll. 15–21 (emphasis added).

In its petition for *inter partes* review, Labcorp asserted three grounds of unpatentability with Lee[1] as the primary reference, and a fourth ground with Sorenson[2] as the primary reference. For the Lee-based grounds, Labcorp asserted that all challenged claims would have been anticipated or rendered obvious by Lee alone or in combination with Sorenson. For the Sorenson-based ground, Labcorp asserted that all challenged claims would have been rendered obvious by Sorenson in combination with Rao.[3]

Lee reports a study on quantitating cell-free genomic DNA in serum and in plasma. J.A. 3017. Lee discusses a protocol that collected blood samples in tubes with either acid citrate dextrose ("ACD"), ethylenediaminetetraacetic

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[1] Tzong-Hae Lee et al., *Quantitation of Genomic DNA in Plasma and Serum Samples: Higher Concentrations of Genomic DNA Found in Serum than in Plasma*, 41 TRANSFUSION 276 (2001), J.A. 3017–23.

[2] George D. Sorenson et al., *Soluble Normal and Mutated DNA Sequences from Single-Copy Genes in Human Blood*, 3 CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION 67 (1994), J.A. 3024–29.

[3] International Patent Application Publication WO 2003/018757.

acid ("EDTA"), or no anticoagulant. J.A. 3018. The samples were processed, and DNA was quantitated using a PCR assay daily for up to seven days. *Id.* It is undisputed that ACD includes dextrose and that dextrose is a form of glucose. *Decision*, at *8. Sorenson reports a study on extracellular DNA in cancer patients. J.A. 3024. The study identified increased quantities of extracellular DNA and mutated sequences in patients with pancreatic cancer. *Id.* Sorenson reports that "cellular DNA can be released during clotting of whole blood." *Id.* And Rao discloses a method of stabilizing rare cancer cells in a blood sample using paraformaldehyde. Rao at Abstract; *see id.* at p. 3, ll. 12–19.

The Board concluded that the challenged claims had not been shown to be unpatentable. First, in interpreting the claim, the Board explained that the plain language of claim 1 requires that, "if cells are present," the claimed agent "impedes cell lysis." *Decision*, at *9. Based on that understanding, the Board determined that, to establish anticipation by Lee, Labcorp needed to show that the dextrose present in Lee's blood samples, by way of the addition of ACD, *actually impeded* cell lysis. *Id.* The Board noted that Labcorp could satisfy its burden if it could show that the dextrose in Lee "even minimally impeded cell lysis" because the claims "do not require any particular degree of lysis impedance." *Id.* at *14. But after reviewing the disclosures of Lee and the testimony of the parties' competing experts, the Board found that "the preponderance of the evidence does not support that the dextrose in Lee impeded cell lysis." *Id.* at *15. Accordingly, the Board determined that the challenged claims had not been shown to be anticipated by Lee. *Id.* The Board determined that the Lee-based obviousness grounds failed for the same reason. *Id.*

With respect to the Sorenson-based ground, the Board concluded that Labcorp failed to show that a person of ordinary skill in the art "would have been motivated to add formaldehyde to Sorenson's method of detecting cell-free

DNA in plasma." *Id.* at *16. The "key question" the Board addressed in its analysis was whether a person of ordinary skill in the art "would have been concerned with formaldehyde's potential effects on DNA, and cell-free fetal DNA in particular." *Id.* at *17. The Board found that "formaldehyde was known to have detrimental effects on nucleic acids" and that a person of ordinary skill in the art would not have known how to "tailor the use of formaldehyde to ameliorate" those expected detrimental effects. *Id.* at *20. The Board therefore determined that Labcorp had not shown that a person of ordinary skill would have been motivated to combine Sorenson and Rao in the manner proposed. *Id.*

Labcorp timely appealed, and we have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

Labcorp's primary argument on appeal is that the Board engaged in improper implicit or *post hoc* claim construction of the term "agent that impedes cell lysis" and that, under the proper construction of the "agent" term, Lee anticipates the claims. According to Labcorp, all that the claims require is for dextrose to be present in the sample because it was known to impede cell lysis. Alternatively, Labcorp argues that even under the erroneous construction, the Board findings on the Lee-based grounds were not supported by substantial evidence. Labcorp also argues that the Board legally erred in considering the motivation to combine Sorenson and Rao and that, in any event, the Board's findings on that issue were not supported by substantial evidence. We address each argument in turn.

I

Claim construction is a question of law reviewed *de novo*. *Intel Corp. v. Qualcomm Inc.*, 21 F.4th 801, 808 (Fed. Cir. 2021). The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the relevant art at the time of the

invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

The Board expressly construed the claim term "agent that impedes cell lysis" to "exclude chelators used as anti-coagulants." *Decision*, at *6. Neither party challenges that express construction. The Board, in analyzing Lee, then explained that "[b]y its plain language, claim 1 requires that 'if cells are present,' as they are in Lee's samples, the claimed agent 'impedes cell lysis.'" *Id.* at *9. Labcorp argues that the Board's understanding of the plain language of the claims amounts to an improper implicit or *post hoc* construction because the claims do not require the agent to *actually impede* cell lysis. According to Labcorp, the "agent" term "could not be simpler" and requires nothing more than "an agent selected from one of the three enumerated categories (membrane stabilizers, cross-linkers, and cell-lysis inhibitor[s])." Labcorp Br. 30. We disagree with Labcorp.

There is no ambiguity in the claim language; "if cells are present," the claimed agent is required to "impede[] cell lysis." '720 patent, col. 535, ll. 15–21. That understanding is confirmed by the structure of the claims. Claim 1, from which all challenged claims depend, contains two wherein clauses describing the agent; the first requires "an agent that impedes cell lysis, if cells are present," and the second requires the agent to be "selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor." *Id.* Labcorp's proposed construction would essentially read the first clause out of the claim, as its construction requires only that the agent be "selected from" one of the three enumerated categories. *See* Labcorp Br. 30–33; *see also id.* at 35 ("The claimed 'agent' need be nothing more than one that is known to impede cell lysis."). Claims, however, should be interpreted to give effect to all their terms. *Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 950 (Fed. Cir. 2006). As such, the plain language of the claims requires both that the agent "impedes cell lysis, if cells are present"

and that the agent is selected from the enumerated group. The specification further confirms that understanding of the claims, *i.e.*, that the agent must actually impede cell lysis. *See, e.g.*, '720 patent, col. 6, ll. 49–50 (explaining that a stabilizing agent "may be added to the maternal blood sample *to reduce maternal cell lysis*" (emphasis added)).

The Board properly determined that the plain language of the claims required Labcorp to show that "dextrose in Lee's samples 'impedes cell lysis' 'if cells are present.'" *Decision*, at *9. The Board even agreed with Labcorp that "the challenged claims do not require any particular degree of lysis impedance," *Decision*, at *14; *see also* Labcorp Br. 32–33, and that "even minimally imped[ing] cell lysis" is all the claims required, *Decision*, at *14. Labcorp's proposed construction, however, would allow any agent that is merely capable of impeding cell lysis to satisfy the claims. But, as discussed above, the plain language of the claims requires not just an agent *capable of* impeding cell lysis, but one "that *impedes* cell lysis." We therefore see no error in the Board's understanding of the claims through implicit claim construction, *post hoc* claim construction, or otherwise.

II

We next address Labcorp's arguments with respect to the Lee-based grounds. The only dispute between the parties is whether Lee discloses the "agent" limitation. According to Labcorp, the Board failed to evaluate Lee from the perspective of a person of skill in the art, and its finding that Lee did not disclose or suggest that the dextrose (in ACD) added to the blood sample impeded cell lysis was not supported by substantial evidence. Labcorp Br. 38–44. We disagree.

Anticipation is a question of fact reviewed for substantial evidence. *Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1337 (Fed. Cir. 2020). Obviousness is a question of law based on underlying findings of fact. *KSR Int'l Co. v.*

Teleflex Inc., 550 U.S. 398, 427 (2007). We review the Board's legal conclusion on obviousness *de novo* and its underlying findings of fact for substantial evidence. *HTC Corp. v. Cellular Commc'ns Equip., LLC*, 877 F.3d 1361, 1369 (Fed. Cir. 2017). What a reference teaches and the presence or absence of a motivation to combine references are questions of fact. *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1196–97 (Fed. Cir. 2014).

Contrary to Labcorp's assertions, the Board carefully considered Lee from the perspective of a person of skill in the art. Indeed, the Board considered each of the three mechanisms through which Labcorp alleged a person of ordinary skill in the art would have understood the dextrose in Lee to *actually* impede cell lysis. *Decision*, at *10–11. It did so by considering the disclosures of Lee, the testimony of both experts, and the specific circumstances present in Lee. *See, e.g.*, *id.* at *10 (noting that Dr. Edwards' testimony that carbohydrates, like dextrose, were known to have a role in membrane stabilization was "consistent with the teaching in the '720 patent"); *id.* (noting that "failure to maintain isotonicity does not necessarily cause cell lysis"); *id.* at *11 (finding that dextrose's ability to prevent cell lysis by providing a nutrient source was reduced by Lee's storage temperature). Based on that evidence, the Board reasonably concluded that "any effect that [dextrose] has . . . to improve the health and stability of cells is not realized in any of the Lee experiments." *Id.*

Labcorp's disagreement with the Board's conclusions after weighing the evidence does not demonstrate a failure to consider Lee from the perspective a person of skill in the art. *Eli Lilly & Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331, 1347 (Fed. Cir. 2021) ("[D]isagreement with the Board's interpretations of [a reference] does not amount to a demonstration that the Board somehow failed to use the proper analysis."). We do not reweigh evidence on appeal. *In re NTP, Inc.*, 654 F.3d 1279, 1292 (Fed. Cir. 2011); *Regents of Univ. of Cal. v. Broad Inst., Inc.*, 903 F.3d 1286,

1294 (Fed. Cir. 2018) ("It is not our role to ask whether substantial evidence supports fact-findings not made by the Board, but instead whether such evidence supports the findings that were in fact made."). Here, we conclude that the Board's finding that Lee does not disclose the claimed agent that "impedes cell lysis" was supported by substantial evidence.

As the Board noted, "[n]owhere does Lee hint at the significance of dextrose in the samples or attribute any difference in the observed differences in DNA levels to any specific cause beyond clotting." *Decision*, at *14. Thus, Labcorp's evidence that the "dextrose in Lee impedes cell lysis rest[ed] primarily on the testimony of Dr. Edwards." *Id.* The Board considered that evidence but concluded that it was "circumstance specific" and that Labcorp had failed to persuasively address "the ability of dextrose to impede cell lysis under the conditions present in Lee." *Id.* Similarly, the Board's finding that the difference in cell-free DNA levels seen in serum compared to plasma was not shown to be attributable to dextrose was supported by substantial evidence. *See id.* at *12–14 (evaluating Lee Figure 4 and the associated expert testimony). The Board's conclusion that the Lee-based grounds did not render the challenged claims unpatentable was therefore supported by substantial evidence.

III

Finally, we turn to Labcorp's argument that the Board's analysis of the motivation to combine Sorenson and Rao was both legally flawed and not supported by substantial evidence. Labcorp largely repeats the arguments made against a motivation to combine in the companion case. *Compare* Labcorp Br. 48 ("[T]he Board here erroneously read various atextual limitations into the claims— . . . that the free-floating DNA not be damaged[.]"), *and id.* at 52 ("[T]he Board committed legal error in requiring a heightened and untenable standard for proving a motivation to

combine[.]"), *and id.* at 58 ("The Board likewise failed to consider Rao for everything it teaches."), *with Labcorp*, 2025 WL 32904, at *4 ("According to Labcorp, the Board read into the claims additional limitations prohibiting DNA damage[.]"), *and id.* at *2 ("Labcorp's first argument—that the Board imposed an improperly heightened standard for obviousness . . . ."), *and id*. at *4 ("Labcorp argues that the Board ignored Rao's teaching . . . ."). In fact, the same reference—Rao—was relied upon for its formaldehyde teachings in both cases. And as the Board noted, the "key question" in both cases was "whether a [person of ordinary skill in the art] would have been concerned with formaldehyde's potential effects on DNA, and cell-free fetal DNA in particular." *Decision*, at *17, *see Labcorp*, 2025 WL 32904, at *4. In both cases, the Board relied on similar reasoning to answer that question in the affirmative and find no motivation to combine the primary reference with Rao. *See Decision*, at *17; *Labcorp*, 2025 WL 32904, at *2. For reasons similar to those discussed in the companion case, we find that the Board's decision with respect to motivation to combine was not legally erroneous and was supported by substantial evidence. See *Labcorp*, 2025 WL 32904, at *2–5.

CONCLUSION

We have considered Labcorp's remaining arguments but find them unpersuasive. For the foregoing reasons, we *affirm* the Board's decision in IPR2021-01026, holding claims 1–9 and 21–30 of the '720 patent not shown to be unpatentable.

AFFIRMED