United States Court of Appeals for the Federal Circuit

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,
Plaintiff-Appellant

v.

OXFORD NANOPORE TECHNOLOGIES, INC.,
OXFORD NANOPORE TECHNOLOGIES, LTD.,
Defendants-Appellees

2020-2155, 2020-2156

Appeals from the United States District Court for the District of Delaware in Nos. 1:17-cv-00275-LPS, 1:17-cv-01353-LPS, Chief Judge Leonard P. Stark.

Decided: May 11, 2021

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

MICHAEL HAWES, Baker Botts, LLP, Houston, TX, argued for defendants-appellees. Also represented by ELIZABETH FLANNERY; STEPHEN M. HASH, Austin, TX.

Before LOURIE, TARANTO, and STOLL, *Circuit Judges*.

TARANTO, *Circuit Judge*.

Pacific Biosciences of California, Inc. (PacBio) sued Oxford Nanopore Technologies, Inc. and Oxford Nanopore Technologies, Ltd. (collectively, Oxford), accusing Oxford of infringing several of its patents, including U.S. Patent Nos. 9,546,400 and 9,772,323. A jury found all asserted claims infringed but also determined that they are invalid under 35 U.S.C. § 112 for lack of enablement. The district court denied PacBio's motion for judgment as a matter of law (and for a new trial) on enablement. The district court also denied PacBio's request that the court grant a new trial because of Oxford's improper remarks during opening, remarks that included references to the potential applications of its accused products to the then-emerging global COVID-19 crisis. PacBio argued that the remarks caused prejudice that could not be remedied by the curative instruction the district court gave at PacBio's request. We affirm.

I

PacBio owns the '400 and '323 patents, which share a specification, so we generally cite only the '400 patent's specification. The patents describe methods for sequencing a nucleic acid, such as deoxyribonucleic acid (DNA). The methods use nanopore technology, described in one form as follows: nucleic acids are drawn through nanometer-sized holes formed in a substrate, and while they transit the holes, their sequences of nucleotides are identified or characterized based on changes in electric current passing through the substrate. *See* '400 patent, col. 1, lines 25–27; *id.*, col. 8, lines 55–61. The '323 patent issued from a continuation of a continuation of the application that issued as the '400 patent; and both claim priority to a provisional application filed on April 10, 2009.

The patents, in discussing the prior art, explain that "rapid determination of the nucleotide sequence . . . is a major goal of researchers seeking to obtain the sequence

for the entire genome of an organism." *Id.*, col. 1, lines 19–22. The patents' solution includes a system with "upper and lower fluidic regions" above and below a membrane having a nanopore passage from one region to the other, with electrodes that permit application of a voltage to create a potential difference that causes molecules to "translocate" between the two regions. *Id.*, col. 8, lines 35–38, 48–61; *id.*, col. 9, lines 6–15, 47–53; *id.*, col. 10, line 64 through col. 11, line 5. The membrane in which the nanopores are formed, as described by the patents, can use lipid or solid-state materials and may include "hybrid" nanopores, formed by treating substrate material with organic molecules, such as proteins, that serve as "spacers" to narrow the nanopores so that only single strands of DNA (ssDNA) or ribonucleic acid (ssRNA) pass through, "in a sequential, single file order." *Id.*, col. 1, lines 28–31; *id.*, col. 14, lines 1–60; *id.*, col. 15, lines 3–10; *id.*, col. 17, lines 42–53; *see also id.*, Fig. 5.

The patents further describe using "processive DNA-binding enzyme[s] to enzymatically regulate the rate of ssDNA translocation through the nanopore." *Id.*, col. 25, lines 11–13; *see also id.*, col. 24, lines 53–54 ("In certain embodiments, polymerases are used to modulate the passage of a nucleic acid strand through a nanopore."). Too fast a rate may impair accuracy, and enzymes can "promote efficient sequence detection, e.g., by allowing a reaction to proceed at a rate that provides for a desirable balance between accuracy and throughput." *Id.*, col. 25, lines 3–10. The patents state that enzymes can bind to ssDNA in the fluid, then combine with the protein "spacer" in the nanopore to "act as a plug," but that "[a]pplying a strong enough [electric] potential can rip the ssDNA from the tightly bound exonuclease, advancing the ssDNA through the nanopore." *Id.*, col. 25, lines 29–34; *see also id.*, Fig. 25(A) & (B). Pulses that alternate large and small potential differences, when used in connection with the enzyme, "can pull the ssDNA through the nanopore in steps, for

example one base at a time. The rate and duty cycle of the pulses could be altered to optimize the translocation rate and measurement duration." *Id.*, col. 25, lines 34–40.

For the sequencing of ssDNA (identifying the sequence of its individual nucleotides), the patents describe use of "an array of electrical/CMOS [complementary metal-oxide-semiconductor] components (amplifiers)" that measure aspects of a current through the substrate—*e.g.*, amplitude and duration of "current blockage," and "interpulse duration"—as ssDNA moves through the nanopore. *Id.*, col. 20, lines 6–9; *id.*, col. 29, lines 43–46; *id.*, col. 41, lines 46–56. The patents note, however, that such measurements "can overlap significantly" between different nucleotides, creating "miscall errors." *Id.*, col. 29, lines 46–50; *see also id.*, col. 41, lines 60–63 ("Thus, if the probability distribution of current blockage (likely Gaussian-like) for a nucleotide is highly overlapping with that of a different nucleotide, then there may be a large probability of miscall if only this metric is used."). This problem, the patents state, prevented prior art systems from "achiev[ing] single nucleotide resolution, especially in embodiments that might be scaled to a commercially viable DNA sequencing system." *Id.*, col. 39, lines 49–51.

The patents state a reason for the resolution troubles: "[T]he amplitude of electric current passing through the nanopore (which constitutes the signal) depends on the identity of several bases that reside in the pore throughout the duration of the current measurement." *Id.*, col. 39, lines 52–55. Given that there are four different nucleotides, there are 4^N possibly different current levels if "N=the number of bases that affect the current measurement." *Id.*, col. 39, lines 55–60; *see also id.*, col. 41, lines 46–56. But, the patents note, there may not be 4^N distinct current levels for the 4^N possible N-long nucleotide sequences ("some of [the possibilities] may be degenerate"). *Id.*, col. 39, lines 59–60.

The sole independent claim of the '400 patent, claim 1, recites:

> 1. A method for sequencing a nucleic acid template comprising:
>
> a) providing a substrate comprising a nanopore in contact with a solution, the solution comprising a template nucleic acid above the nanopore;
>
> b) providing a voltage across the nanopore;
>
> c) measuring a property which has a value that varies for N monomeric units of the template nucleic acid in the pore, wherein the measuring is performed as a function of time, while the template nucleic acid is translocating through the nanopore, wherein N is three or greater; and
>
> d) determining the sequence of the template nucleic acid using the measured property from step (c) by performing a process including comparing the measured property from step (c) to calibration information produced by measuring such property for 4 to the N sequence combinations.

'400 patent, col. 47, line 37 through col. 48, line 6. Dependent claim 4 of the '400 patent includes the additional requirement that "the translocation rate through the pore is enzymatically controlled." *Id.*, col. 48, lines 11–12. The sole independent claim of the '323 patent, claim 1, is similar to claim 1 of the '400 patent, but not identical: for example, it requires a "plurality of template nucleic acids above the nanopore" and includes an "enzymatically controlled" limitation (as in dependent claim 4 of the '400 patent). *See* '323 patent, col. 47, lines 13–34. PacBio asserted claims 1, 4, and 15 of the '400 patent, and claims 1, 4, and 18 of the '323 patent. The parties agree that the patents and the asserted claims are materially similar for purposes

of the issues on appeal. *See* PacBio Opening Br. 22 n.3; Oxford Br. 3 n.1.

B

PacBio sued Oxford in the District of Delaware in 2017, asserting in two separately filed cases that Oxford infringed the '400 and '323 patents, as well as two other patents (U.S. Patent Nos. 9,678,056 and 9,738,929) that are not at issue on appeal. Before trial, the district court granted a PacBio motion in limine (MIL) "to prevent [Oxford] from using 'pejorative' terms (such as 'non-practicing entity,' 'NPE,' and 'paper patents') and from presenting evidence about the consequences of this litigation." J.A. 27 (MIL Order). The court's order continued, "it would be inappropriate to put before the jury evidence or argument about the potential impact of a verdict in favor of PacBio—such as higher prices or slower medical research—as these issues are not for the jury to decide . . . ." *Id.*

The trial began on March 9, 2020, as concerns about the new coronavirus SARS-CoV-2, causing COVID-19, were already rampant but had not yet produced the large-scale shutdowns that would occur in a matter of days. The opening statements from both parties acknowledged COVID-19 and the relevance of the DNA-sequencing technology at issue to dealing with this virus and others; and it is undisputed that Oxford told PacBio the night before the openings that it would mention such relevance, and that PacBio did not object in advance. PacBio, in its opening, mentioned the new coronavirus in passing. J.A. 1073 (Tr. 120:24–121:11 (PacBio mentioning coronavirus and sequencing can "[m]aybe help develop a vaccine")). Then Oxford did so much more extensively (than PacBio did and than prefigured in Oxford's pre-opening notice to PacBio) and with specific factual assertions. *See* J.A. 1079 (Tr. 145:4–12), 1081–82 (Tr. 153:3–156:25 (Oxford discussing "infectious disease monitoring" and telling a story about sending products to Wuhan, China, at the outset of the

coronavirus outbreak)). Oxford made those remarks as part of its references to PacBio seeking to exclude Oxford's products and to previous litigation between the parties on other patents. J.A. 1079 (Tr. 143:2–145:12), 1084 (Tr. 165:9–12), 1085 (Tr. 169:2–17).

PacBio objected to Oxford's opening, mentioning both the reference to previous litigation and the statement that PacBio was "attempting to exclude it from the market, which [the MIL Order] said that the effect of the case and the possible ramifications was clearly an implication." J.A. 1084–85 (Tr. 165:13–166:11); *see also* J.A. 1089 (Tr. 185:3–9 (preserving objection)). The next day, PacBio argued in favor of its motion for two curative instructions to counteract "the exploitation of the violation of the MIL [Order]." J.A. 1153 (Tr. 279:2–3).[1] The district court

---

[1] *See* J.A. 1153 (Tr. 279:2–19) ("The issue is the clear vio—that is the exploitation of the violation of the MIL. I mean, it's so cynical. The violation of the MIL is not the mention of coronavirus. I knew they were going to do. We did it. We've done that same work. We weren't flamboyant about it. They were. Over the top, one might say. [¶] But leaving that aside, that's just exploiting the violation. The violation is we specifically said they shouldn't be stating that we're trying to exclude nanopore sequencing. That is exactly what the Court ordered. That is exactly what [Oxford's counsel] knowingly, intentionally, and willfully did to the jury, knowing, like we all know, the bell can't be unrung. Presumably, a happy client somewhere. And that that is what they did. [¶] And the media [in a report of the previous day's opening] said that the trial is about PacBio trying to take the coronavirus technology off the market. Why? Because that is the only way to understand the transcript."); J.A. 1155 (Tr. 287:23–288:3) ("Your Honor, there was a clear violation of the order and the statement of exploiting it for the Coronavirus is very different. It's not a

criticized Oxford for violating the MIL Order, recognizing that the COVID-19 references were part of that violation, and agreed to give the curative instructions that PacBio had requested. J.A. 1156–57 (Tr. 292:17–294:12).

One instruction addressed the reference to other proceedings. J.A. 1159 (Tr. 303:10–15). The other stated:

> In opening statement, [Oxford] argued that this isn't the first time that PacBio has tried to use its patents to exclude nanopore sequencing. However, if you find [Oxford] liable for patent infringement, you are not—you are only being asked to award monetary compensation to PacBio. You are not being asked to exclude any [Oxford] product from the market or to stop any research work being performed on [Oxford] products.

J.A. 1159 (Tr. 303:17–24). Before giving the instructions, the court also warned both parties about "turn[ing] this really into a trial about an ongoing global health crisis that has to be on the minds of the jury," which would be "unfair" and "improper" and would "inflam[e] the jury" and "would create a real risk of a verdict" not based on the evidence. J.A. 1157 (Tr. 293:22–294:5). The court required the parties, from then on, to disclose to each other "any reference, any evidence, any suggestion that you think you're going to make to Coronavirus" and bring any disputes to the court's attention "before the witnesses take the stand." J.A. 1157 (Tr. 294:6–12).

PacBio did not seek a new trial at that time. During closing, Oxford used words such as "exclude" and "block," borrowing words from PacBio testimony or documents, *see* J.A. 1105 (Tr. 247:3–6), 1503 (Tr. 1225:11–1226:3), and the

---

violation of any order to mention the word, although it may come to that if this continues. And so that's confusing, that they're mushing the two things together.").

closing was not found to be improper. *See* J.A. 1686–88 (Tr. 1612:21–1618:21), 1689 (Tr. 1622:3–25); *see also* J.A. 1989–90, 1996–97. Moreover, PacBio has not identified any post-opening COVID-19 comment made by Oxford to the jury, and the district court noted that Oxford did not violate the MIL Order after the opening. *See* J.A. 53 (7/30/20 Tr. 17:9–14); *Pac. Biosciences of Cal., Inc. v. Oxford Nanopore Techs., Inc.*, Nos. 1:17-cv-00275, 1:17-cv-01353, 2020 WL 4699049, at *5 (D. Del. Aug. 13, 2020) (*Post-Trial Decision*).

The case went to the jury on March 17, 2020, J.A. 1706, and the jury returned its verdict on March 18, 2020, J.A. 1741–43; *see* J.A. 399–414 (verdict). The jury found all asserted claims of the '400 and '323 patents infringed, and also supported by the written description, but also determined that all of the asserted claims are invalid for lack of enablement. J.A. 401–03, 407–08. The district court entered judgment for Oxford based on the jury's verdict on March 31, 2020.

After trial, PacBio renewed its motion for judgment as a matter of law (JMOL) on enablement lodged during trial under Federal Rule of Civil Procedure 50. J.A. 27,435–60. PacBio also moved for a new trial under Rule 59, arguing that the jury's enablement verdict was unsupported and that Oxford's statements regarding COVID-19 violated the MIL Order and were so prejudicial that the case should be retried. *Id.* The district court denied PacBio's motion. *Post-Trial Decision*, 2020 WL 4699049, at *1.

For JMOL on the enablement verdict, the court noted a statement by Oxford's expert, Dr. Nick Goldman, on cross examination, that a relevant artisan, having a particular piece of prior art, could perform the method of claim 1 of the '400 patent in 2009, and the court also noted Dr. Goldman's statement that he did not know the factors specified in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). *Post-Trial Decision*, 2020 WL 4699049, at *1. But the court concluded that the record "as a whole" did "contain substantial

evidence to support the verdict" of non-enablement. *Id.* at *2. The district court identified evidence beyond Dr. Goldman's testimony that was relevant to the *Wands* factors and could support the jury's verdict; and the court noted Dr. Goldman's testimony that the claims at issue were not enabled and stressed that the jury was free to consider Dr. Goldman's credibility and all the evidence. *Id.* at *2–3.

The court similarly rejected PacBio's motion for a new trial based on references to COVID-19 made in Oxford's opening statement. Acknowledging that such references implicated the possible consequences of the jury's verdict in violation of the MIL Order, the court explained, "[t]here is just no indication . . . that this jury was inflamed, that it was not careful," or that the jury otherwise failed to properly consider the evidence because of the mentions of COVID-19. *Id.* at *8–9 (alteration in original).

The court entered final judgment on August 13, 2020. *Id.* at *1. PacBio timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

II

On appeal, PacBio argues that the jury's verdict finding that the '400 and '323 patents lack enabling disclosure is unsupported by the evidence, requiring JMOL in its favor. *See* PacBio Opening Br. 21–41. PacBio also argues summarily for a new trial based on the enablement evidence. *Id.* at 42. Much more fully, PacBio argues for a new trial based on Oxford's statements about COVID-19. *Id.* at 42–60. We reject these challenges.

A

We review a district court's decision on a JMOL motion de novo, following the law of the regional circuit, here the Third Circuit. *Leader Techs., Inc. v. Facebook, Inc.*, 678 F.3d 1300, 1305 (Fed. Cir. 2012). "[V]iewing the record in the light most favorable to the verdict winner and drawing all reasonable inferences in its favor," *id.*, we ask whether

"a reasonable jury would not have a legally sufficient evidentiary basis to find for the party," Fed. R. Civ. P. 50(a)(1). *See also In re Lemington Home for the Aged*, 777 F.3d 620, 626 (3d Cir. 2015) (JMOL may be granted "only if, as a matter of law, the record is critically deficient of that minimum quantity of evidence from which a jury might reasonably afford relief" to the verdict winner). "[W]hether a patent satisfies the enablement requirement is a question of law based on underlying factual findings." *McRO, Inc. v. Bandai Namco Games America Inc.*, 959 F.3d 1091, 1096 (Fed. Cir. 2020). Here, "we review the factual underpinnings of enablement for substantial evidence." *Idenix Pharms. LLC v. Gilead Sciences Inc.*, 941 F.3d 1149, 1154 (Fed. Cir. 2019) (internal quotation marks omitted). With no greater detail in the verdict, we treat the jury as having made all verdict-supporting factual findings that are supported by substantial evidence. *See Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1378 (Fed. Cir. 2009) (describing "implicit factual findings" approach); *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1359–60 (Fed. Cir. 2012) (same for obviousness).

"The requirement of enablement, stated in 35 U.S.C. § 112, enforces the essential '*quid pro quo* of the patent bargain' by requiring a patentee to teach the public how 'to practice the full scope of the claimed invention.'" *McRO*, 959 F.3d at 1099–100 (quoting *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003)); *see also J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 142 (2001). A claim is not enabled if (as it is the challenger's burden to prove by clear and convincing evidence) a relevant artisan would not be able to practice the claimed invention "without undue experimentation," *Amgen Inc. v. Sanofi*, 987 F.3d 1080, 1084 (Fed. Cir. 2021) (internal quotation marks omitted), a determination typically guided by the following "factual considerations": "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims," *id.* (quoting *Wands*, 858 F.2d at 736–37). "[A] patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012); *Amgen*, 987 F.3d at 1084; *Idenix*, 941 F.3d at 1154; *Trustees of Boston Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1362 (Fed. Cir. 2018); *Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1378–79 (Fed. Cir. 2002); *Nat'l Recovery Techs. Inc. v. Magnetic Separation Systems, Inc.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999).

Although PacBio seems to suggest otherwise at some points, it is not enough for enablement here that relevant artisans knew how to perform *some* "nanopore sequencing" before the priority date of the '400 and '323 patents. What matters is the scope of the asserted claims, which (taken as a whole, as PacBio does) claim methods of "determining the sequence of the template nucleic acid," without limiting the character of that "template nucleic acid," by measuring certain properties (in particular, electric current properties) as the nucleic acid passes through a nanopore, using a determination of the number of nucleotides that affect the current (N), and using enzymes to control the rate of passage through the nanopore. *See supra* pp. 5–6. Notably, PacBio acknowledges that the '400 and '323 patents do not differentiate between "particular types of DNA." PacBio Opening Br. 39.

In arguing for JMOL, PacBio places principal reliance on the following exchange from the deposition of Oxford's expert, Dr. Goldman, introduced at trial during cross-examination of Dr. Goldman:

> 'Question: A person of ordinary skill in the art in 2009 with the Akeson grant in front of them you

> believe would be able to successfully perform the method of claim 1 of the '400 patent?
>
> 'Answer: Yes.'

J.A. 1480 (Tr. 1134:2–6). The "Akeson grant" was a grant application to the National Institutes of Health filed by another Oxford witness, Dr. Mark Akeson, before 2009. *See* J.A. 1836. PacBio asserts that, in the quoted exchange, "Dr. Goldman admitted on cross-examination that the claims of the '400 and '323 Patents were enabled." PacBio Opening Br. 14; *see also id.* at 22 & n.3 ("Dr. Goldman squarely admitted that a person skilled in the art in 2009 would be able to ***successfully*** perform the method of claim 1 of the '400 Patent."; footnote attached, stating: "For purposes of enablement, there is no difference between the '400 and '323 Patent[s]."); *id.* at 18.

The jury was not required to give Dr. Goldman's answer, even understood in isolation, the broad meaning PacBio now gives it. It is enough to say that, in the absence of further elaboration of the point, the jury could have understood Dr. Goldman to be saying no more than that a relevant artisan could have "perform[ed] the method of claim 1 of the '400 patent," J.A. 1480, on the particular subset of nucleic acids addressed in the Akeson grant, namely, "DNA hairpins," which were synthesized nucleic acids used to test the viability of such sequencing technologies. J.A. 1836–54. Especially in light of other evidence about the difference between the synthetic nucleic acids Akeson addressed and biological DNA, the jury could properly understand the specific answer to the specific question on which PacBio relies not to be conceding that a skilled artisan could make and use the full scope of the invention (even of claim 1 of the '400 patent, let alone all the asserted claims), including the full range of "nucleic acid templates." In fact, just before that question and answer, the jury heard Dr. Goldman answer "no" to the question whether "a person of ordinary skill in the art with the '400 patent in front of

them trying to use the claim 1 method, including adding everything, if they had access to the Akeson grant, . . . would have been able to use the invention[,] . . . [t]o be able to successfully perform the method . . . of the '400 and '323 [patents]." J.A. 1480 (Tr. 1133:1–9).

The jury's task was not to view one portion of Dr. Goldman's testimony in isolation, but to consider all the evidence, including any portion of the evidence that might clarify how to understand other portions. And there was substantial evidence that supported non-enablement. Dr. Goldman himself testified that the asserted claims of the '400 and '323 patents lack enablement because of the required element of determining "N" (how many nucleotides affect the current measurement during transit of a nucleic acid through the nanopore). J.A. 1475 (Tr. 1113:1–23).

Even aside from the "N" claim limitation, the jury had substantial evidence of non-enablement of the full claim scope. For example, Dr. Akeson testified that his research, leading to the "Akeson grant," was limited to "DNA hairpin[s]," *see* J.A. 1406–07 (Tr. 934:17–935:16); J.A. 1405 (Tr. 930:1–13), and that the first successful nanopore sequencing of biological DNA molecules, to his knowledge, did not occur until 2011, *see* J.A. 1408 (Tr. 940:3–941:12); J.A. 1421 (Tr. 992:9–17); and there is no indication, or argument by PacBio, that the 2011 success was made possible by the disclosure in the '400 and '323 patents, *see Everlight Elecs.*, 896 F.3d at 1363–64. Another of Oxford's witnesses, Dr. James Clarke, testified that "nobody was" able to use nanopore sequencing to sequence biological DNA until 2011. J.A. 1423 (Tr. 1001:23–1002:4); *see also* J.A. 1293 (Tr. 674:2–6) (Dr. Willcocks); J.A. 1491–92 (Tr. 1180:25–1182:3) (Dr. Ha). There also was evidence that, when Oxford announced its success in 2012 at a large meeting of scientific professionals in the field, three years after the priority date of the patents at issue here, the audience of 700 reacted in a way that suggests that the advance

regarding nanopore sequencing with biological DNA was a major one. *See* J.A. 1409 (Tr. 943:1–944:14).

We therefore conclude that there was ample evidence to support a finding that, before the 2009 priority date of the '400 and '323 patents, relevant artisans did not know how to perform nanopore sequencing for more than a narrow range of the full scope of nucleic acids covered by the asserted claims. *See Idenix*, 941 F.3d at 1161 ("Where, as here, working examples are present but are 'very narrow, despite the wide breadth of the claims at issue,' this factor weighs against enablement." (quoting *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1374 (Fed. Cir. 1999))); *cf. Union Carbide Chems. & Plastics Tech. Corp. v. Shell Oil Co.*, 308 F.3d 1167, 1186 n.9 (Fed. Cir. 2002).

Notably, PacBio had no evidence of actual reduction to practice of its own that would undermine Oxford's evidence of non-enablement. As PacBio acknowledged, its reduction to practice was constructive only, *i.e.*, took the form of its description in patent applications, without any accompanying real-world reduction to practice. *See* Oral Arg. 0:35–0:55. The jury heard from named inventor Dr. Turner that PacBio never performed nanopore sequencing in 2009, J.A. 1104 (Tr. 244:10–15), and also heard stipulations of uncontested facts that PacBio had never performed the claimed methods, J.A. 1501 (Tr. 1217:7–1219:6); J.A. 5013–14. The jury had evidence, as well, that conveyed an intent by PacBio to "tangle . . . up" and "fool" competitors with its patents, language that might be understood to point away from PacBio's having achieved an enabled method. J.A. 1989; J.A. 1105 (Tr. 247:12–13).

Viewing the facts most favorably to Oxford, we think that the record supports the legal conclusion that the disclosures of the '400 and '323 patents, even when combined with knowledge of relevant artisans, required undue experimentation to enable the full scope of the relevant claims.

B

We review a decision denying a motion for a new trial for abuse of discretion, following the law of the regional circuit, here, the Third Circuit. *See Vectura Ltd. v GlaxoSmithKline LLC*, 981 F.3d 1030, 1035 (Fed. Cir. 2020); *see also Jester v. Hutt*, 937 F.3d 233, 238 (3d Cir. 2019). "Under Third Circuit law, a district court should grant a new trial only if the jury's verdict is against the great weight of evidence and either is a miscarriage of justice or cries out to be overturned." *Vectura*, 981 F.3d at 1035; *Leonard v. Stemtech Int'l Inc.*, 834 F.3d 376, 386 (3d Cir. 2016). The district court has broad discretion in not setting the verdict aside. *Leonard*, 834 F.3d at 386.

1

PacBio first seeks a new trial based on the jury's verdict that the asserted claims are invalid for lack of enablement. *See* PacBio Opening Br. 42. PacBio's two-sentence argument summarily asserts, as a basis for a new trial, that Dr. Goldman "offered only 'general and vague' statements regarding enablement" and "admitted that" he could not recall specific examples showing a lack of enablement. *Id.* For the reasons explained above, Dr. Goldman's testimony does not stand alone, and the jury could reasonably rely on the evidence as a whole to determine that the claims at issue were not enabled. We draw no different conclusion when asking if the district court abused its discretion in deeming the evidence sufficient for purposes of the new-trial standard.

2

PacBio also argues that a new trial is necessary based on Oxford's references to COVID-19 and the possible consequences of an infringement verdict for COVID-19. *See* PacBio Opening Br. 44–53. A new trial based on improper remarks is proper if "the appellee made prejudicial remarks and it is 'reasonably probable' those prejudicial

remarks influenced the jury's verdict." *Vectura*, 981 F.3d at 1042 (quoting *Draper v. Airco, Inc.*, 580 F.2d 91, 97 (3d Cir. 1978)). "On the issue of the impact of improper conduct at trial, the views of the judge who supervised the trial proceedings are entitled to considerable weight." *Vectura*, 981 F.3d at 1044. We see no abuse of discretion in the district court's determination that the opening remarks were not sufficiently likely to have influenced the jury to create a miscarriage of justice.

As described above, PacBio, which presented its opening statement to the jury first, itself mentioned the possible connection between COVID-19 and the technology at issue. And despite knowing that Oxford would mention COVID-19 in its opening, PacBio did not object in advance. When Oxford, in its opening, made a considerably more extended mention of COVID-19 in connection with references to earlier litigation and PacBio's alleged effort to exclude Oxford's products, PacBio objected that the references to earlier litigation and the purported effort to exclude Oxford's products violated the MIL Order. The next day, before testimony commenced, PacBio and the court treated the references to COVID-19 as related to the MIL Order violation, and the court gave exactly the curative instruction that PacBio requested. The court also required that the parties "carefully disclose to one another any reference, any evidence, any suggestion that" they might make to COVID-19 later in the trial and bring any disputes to the court's attention before the subject was mentioned to the jury. J.A. 1157 (Tr. 294:6–12). The court used that procedure later during trial to prevent evidence from reaching the jury that it deemed prejudicial. *See* J.A. 1339–40 (Tr. 860:3–864:15). Not until after the verdict did PacBio request a new trial based on the remarks Oxford made in its opening. After the opening, Oxford did not refer to COVID-19 or violate the MIL Order.

In denying the motion for a new trial, the district court did not consider the request for a new trial to have been

forfeited. Rather, the court addressed and rejected it on its merits, considering all the circumstances. *See Post-Trial Decision*, 2020 WL 4699049, at *8. The court determined that there was not a high enough likelihood, in light of the curative instructions, that Oxford's improper opening tainted the jury's consideration of the issues to justify ordering a new trial. *Id.* at *8–9.

The court reasonably found support for that determination in PacBio's own conduct and contemporaneously expressed views about references to COVID-19 before the jury, including PacBio's mention of the subject in its opening and its request for no more than curative instructions (which the court gave). *See Post-Trial Decision*, 2020 WL 4699049, at *6–7. It reasonably found no improper conduct beyond the opening statement. *Id.* at *5. The court also reasonably concluded that there was "no indication of any sort that the jury did anything other than what it was supposed to do." *Id.* at *8. The district court noted the jury's care in its deliberations, reflected in the questions the jury asked of the court before reaching its verdict. *Id.* The court further noted that, after receiving the case on March 17 and deliberating through the afternoon, the jury was offered the option of continuing for a few hours or instead returning to the courthouse the next day, and it opted to return on March 18, which it did, deliberating for two hours in the morning before returning its verdict. *Id.* Finally, the court reasoned that the jury's careful substantive focus was reflected in the fact that the jury, though giving Oxford a bottom-line victory of invalidity, distinguished the written-description challenge (which it rejected) from the enablement challenge (which it accepted). *Id.* at *6. Although PacBio asserts that the distinction shows confusion, we see no basis for such a conclusion, as the legal standards are different, and the evidence allowed a conclusion that the problem with PacBio's patents was not that their specification failed to describe the combined elements of their claims so as to indicate PacBio's invention of the

combination but, rather, that the specification, together with relevant artisans' knowledge, did not enable the actual performance of the claimed methods in their full scope. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1345 (Fed. Cir. 2010) (en banc) (distinguishing the two standards)

Given all the circumstances, we do not see a basis for disturbing the district court's assessment that there was an insufficient likelihood that the improper opening remarks had an adverse impact on the ultimate verdict to justify a new trial in this case. A contrary conclusion is not supported by the cases on which PacBio chiefly relies. In *Fineman v. Armstrong World Industries, Inc.*, the Third Circuit affirmed the district court's own assessment of prejudice as warranting a retrial where, during closing (just before deliberations), plaintiff's counsel "improperly testified to his own truthfulness and trustworthiness, supplied 'facts' not in evidence about the credibility of [defendant's] witnesses, accused [defendant's] witnesses of being 'liars' and 'perjurers,' and levied 'an unadorned, disparaging attack' upon defense counsel throughout his summation." 980 F.2d 171, 207 (3d Cir. 1992); *see also id.* at 208–09. In *Blanche Road Corp. v. Bensalem Township*, another affirmance by the Third Circuit of a district court's own assessment that a retrial was needed, counsel accused the trial judge, in front of the jury, of not treating him fairly, vouched for the credibility of witness testimony, and referred to documents not in the record during closing arguments. 57 F.3d 253, 264 (3d Cir. 1995). In *Draper v. Airco, Inc.*, the Third Circuit reversed the district court's rejection of a new-trial motion and required a new trial, but it did so based on an exceptional combination of improper actions by plaintiff's counsel during closing: "(1) he attempted to prejudice the jurors through repeated inappropriate references to the defendants' wealth; (2) he asserted his personal opinion of the justness of his client's cause; (3) he prejudicially referred to facts not in evidence; and (4)

without provocation or basis in fact, he made several prejudicial, vituperative[,] and insulting references to opposing counsel." 580 F.2d at 95; *see also id.* at 96–97 (concluding that counsel's "closing address to the jury contains such numerous and serious violations of so many rules of proper argument" that curative instructions were not enough). The present case, in the timing and isolated character of the improper statements, along with the other circumstances we have described, materially differs from PacBio's authorities. *See Fineman*, 980 F.2d at 208 (noting cases where "isolated" improper remarks did not warrant a new trial).

In sum, we see an inadequate basis here to substitute our judgment about prejudice for the judgment of the district court. "Because the trial judge was present and able to judge the impact of counsel's remarks, we defer to his assessment of the prejudicial impact." *Leonard*, 834 F.3d at 399 (citation omitted). Therefore, we affirm the denial of PacBio's motion for a new trial on this ground.

III

For the foregoing reasons, we affirm the judgment of the district court.

AFFIRMED