United States Court of Appeals for the Federal Circuit

LABORATORY CORPORATION OF AMERICA HOLDINGS, LABCORP GENETICS, INC., THE GENERAL HOSPITAL CORPORATION, DBA MASSACHUSETTS GENERAL HOSPITAL,
Plaintiffs-Appellees

v.

QIAGEN SCIENCES, LLC, QIAGEN LLC, FKA QIAGEN, INC., QIAGEN BEVERLY, LLC, FKA QIAGEN BEVERLY, INC., QIAGEN GAITHERSBURG, LLC, FKA QIAGEN GAITHERSBURG, INC., QIAGEN GMBH, QIAGEN N.V., JONATHAN ARNOLD,
Defendants-Appellants

2023-2350

Appeal from the United States District Court for the District of Delaware in No. 1:18-cv-01019-MN, Judge Maryellen Noreika.

Decided: August 13, 2025

EDWARD R. REINES, Jones Day, Palo Alto, CA, argued for plaintiffs-appellees. Also represented by ALEXANDER HORNAT, LEIGH JOHN MARTINSON, WYLEY SAYRE PROCTOR, McCarter & English, LLP, Boston, MA; DANIEL M. SILVER,

Wilmington, DE.

DAVID LEON BILSKER, Quinn Emanuel Urquhart & Sullivan, LLP, San Francisco, CA, argued for defendants-appellants. Also represented by ANDREW EDWARD NARAVAGE; BRIAN C. CANNON, Redwood Shores, CA.

Before LOURIE, DYK, and CUNNINGHAM, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Qiagen Sciences, LLC and others[1] (collectively "Qiagen") appeal from a final judgment of the United States District Court for the District of Delaware following a jury trial. The jury awarded Laboratory Corporation of America Holdings, Labcorp Genetics, Inc., and The General Hospital Corporation (collectively, "Appellees")[2] damages for infringement of its U.S. Patent 10,017,810 ("the '810 patent") and U.S. Patent 10,450,597 ("the '597 patent"). *See* J.A. 73–77. After trial, the district court denied Qiagen's renewed motion for judgment as a matter of law. *ArcherDX, LLC v. Qiagen Scis., LLC*, No. 18-cv-1019,

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[1] The other Defendant-Appellants include Qiagen LLC, fka Qiagen, Inc., Qiagen Beverly, LLC fka Qiagen Beverly, Inc., Qiagen Gaithersburg, LLC, fka Qiagen Gaithersburg, Inc., Qiagen GmbH, Qiagen N.V., and Jonathan Arnold.

[2] On August 30, 2024, ArcherDX, LLC ("Archer") and The General Hospital Corporation, the original plaintiffs, moved unopposed to substitute Laboratory Corporation of America Holdings and Labcorp Genetics, Inc. in place of Archer, noting that while the case was on appeal, Labcorp purchased Archer's interest in the patents in suit and relevant license. ECF No. 45. We granted that motion. ECF No. 49.

2022 WL 4597877 (D. Del. Sep. 30, 2022) ("*Decision*"). Qiagen timely appealed and, as explained below, we *reverse*.

BACKGROUND

I

Appellees' '810 and '597 patents share largely overlapping specifications and are generally directed to methods of preparing DNA samples for sequencing. Because sequencing an entire genome is traditionally expensive and time consuming, researchers developed "enrichment" techniques. Enriching a sample refers to the process of producing copies of the region of interest, as opposed to the entire genome, to make sequencing more efficient. The region of interest, also referred to as the "target area," is often the part of a DNA fragment that a researcher is interested in studying. The target area, for example, may be a section that includes a mutation, or alteration in genetic information, that can lead to disease. Both patents recognize the benefits of target enrichment prior to sequencing. *See* '810 patent col. 1 ll. 38–40 ("Target enrichment prior to next-generation sequencing is more cost-effective than whole genome . . . sequencing[.]"); '597 patent col. 1 ll. 26–28 (same).

Enrichment methods typically rely on the polymerase chain reaction ("PCR") to amplify (make copies of) a target area in the DNA fragments contained in a DNA sample. *See generally Roche Molecular Sys., Inc. v. CEPHEID*, 905 F.3d 1363, 1366 (Fed. Cir. 2018) (describing PCR); *see also* '810 patent col. 13 l. 20–col. 14 l. 60. To copy the target area of the DNA sample, short pieces of DNA known as "target-specific primers" mark where replication should begin on each denatured DNA strand and serve as the binding site for the polymerase enzyme that performs the replication. *See id.*; *see also* '810 patent col. 77 l. 19–col. 78 l. 16, col. 15 ll. 58–61, col. 16 ll. 33–39, 53–57. By designing target-specific primers so that they anneal to and start the copying between certain sequence locations in the DNA,

researchers can isolate and enrich the regions of sequence that they are interested in analyzing. *See Roche*, 905 F.3d at 1366; '810 patent col. 18 ll. 24–29. Meanwhile, other types of "primers" assist with different functions during the DNA sequencing preparation process. "Adaptor primers" may be designed against the adaptors, which are artificial sequences of DNA ligated to the DNA fragments in the DNA sample, to assist in amplifying only fragments that have ligated adapters. '810 patent col. 16 l. 64–col. 17 l. 8; J.A. 579. "Sequencing primers" enable the library of enriched DNA fragments to be read by the sequencing instrument. '810 patent col. 3 ll. 30–33. The issues in this case involve the design and operation of different types of primers and how they assist in preparing DNA samples for sequencing and analysis.

The claimed method of the '810 patent generally requires first ligating (attaching) an adaptor (a known artificial sequence) to each fragmented piece of DNA, and then conducting two rounds of amplification with two separate pairs of primers: a first adaptor primer and first target-specific primer, and a second adaptor primer and second target-specific primer, each of which has specific definitions in the patent. *See* '810 patent col. 77 l. 19–col. 78 l. 16; *see also id.* at col. 15 ll. 58–61, col. 16 ll. 33–39, col. 16 l. 64–col. 17 l. 8 (defining the terms).

At issue in this appeal are independent claim 16 of the '810 patent and its dependent claims 17 and 19. Exemplary claim 16 recites:

> 16. A method for preparing a nucleic acid for sequencing, the method comprising:
>
> (i) ligating a universal oligonucleotide tail *adaptor* that comprises a first ligatable duplex end and a second unpaired end to a nucleic acid comprising *a known target nucleotide sequence* to produce a ligation product, the universal oligonucleotide tail adaptor comprising an amplification strand and a

> blocking strand, wherein a 3′ duplex portion of the amplification strand and a 5′ duplex portion of the blocking strand are substantially complementary and form the first ligatable duplex end;
>
> (ii) amplifying the ligation product using a first target-specific primer that specifically anneals to the known target nucleotide sequence and a first adaptor primer having a nucleotide sequence identical to a first portion of the amplification strand; and
>
> (iii) amplifying an amplification product of (ii) using a *second target-specific primer* that specifically anneals to the amplification product of (ii) and a second adaptor primer having a nucleotide sequence identical to a second portion of the amplification strand, wherein ligating in step (i) comprises performing an overhang ligation reaction, and wherein the universal oligonucleotide tail adaptor further comprises a barcode portion.

'810 patent col. 77 l. 19–col. 78 l. 16 (emphases added). Relevant here, the district court construed the term "second target-specific primer" to mean "a single-stranded oligonucleotide comprising a 3′ portion comprising a nucleic acid sequence that can specifically anneal to *a portion of the known target nucleotide sequence* comprised by the amplicon resulting from step (b), and a 5′ portion comprising a nucleic acid sequence that is *identical to a second sequencing primer*." *See ArcherDx, Inc. v. QIAGEN Scis., LLC*, No. 18-cv-1019, 2019 WL 6785546, at *1 (D. Del. Dec. 12, 2019) ("*'810 Patent Claim Construction Order*") (emphases added). The court also construed the term "second adaptor primer" to mean "a nucleic acid molecule comprising a nucleic acid sequence *identical to a portion* of the first sequencing primer and is nested with respect to the first adaptor primer." *Id.* (emphasis added).

The district court further construed the term "known target nucleotide sequence," which appears in the

construction of "second target-specific primer," as "a portion of a target nucleic acid for which the sequence (e.g. the identity and order of the nucleotide bases comprising the nucleic acid) is known." *Id.* Later, the district court clarified that the term "portion of the known target nucleotide sequence," which also appears in the definition of "second target-specific primer," must be "a portion of the same known target nucleotide sequence that is referenced in step (i) of claim 16." *See* J.A. 808–09 (revisiting claim construction of "second target-specific primer").

The '597 patent is said to be an improvement over the earlier '810 patent. *See* J.A. 512–13; *see also* Appellee Br. 8. Instead of adding adaptors to both ends of the DNA fragments as in the '810 patent, the '597 method generally uses several random primers in their place. Thus, unlike the '810 patent, which uses PCR primers for known sequences on both ends of a DNA fragment, the '597 patent uses a target-specific primer on one end and random primers on the other.

At issue in this appeal are independent claim 1 of the '597 patent and its dependent claims 5 and 19. Exemplary claim 1 recites:

> 1. A method of preparing nucleic acids for analysis, the method comprising:
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> (a) contacting a first nucleic acid template comprising a sequence of a first strand of a double-stranded target nucleic acid with a complementary *target-specific primer* that comprises a target-specific hybridization sequence, under conditions to promote template-specific hybridization and extension of the target-specific primer;
>
> (b) contacting a second nucleic acid template comprising a sequence of a second strand that is complementary to the sequence of the first strand of the double-stranded target nucleic acid with a

> plurality of different primers that share a common sequence that is 5′ to different hybridization sequences, under conditions to promote template-specific hybridization and extension of at least one of the plurality of different primers, wherein the different hybridization sequences have different 3′ ends, and wherein each primer of the plurality of different primers does not anneal to the same sequence of the double-stranded target nucleic acid as any other primer of the plurality of different primers,
>
> wherein, following (a) and (b), an extension product is generated to contain both a sequence that is characteristic of the target-specific primer and a sequence that is characteristic of the at least one of the plurality of different primers; and
>
> (c) subjecting the extension product to an amplification reaction comprising successive rounds of polymerase extension of i) a tail primer that comprises a 3′ sequence that specifically anneals to the complement of the common sequence and that comprises a 5′ tail sequence, and ii) a primer that specifically anneals to the complement of the target-specific hybridization sequence.

'597 patent col. 77 ll. 12–48 (emphasis added). Relevant here, the district court construed the term "target-specific primer" to mean "a primer that has a level of complementarity between the primer and the target such that . . . the primer will anneal to and mediate amplification of the *target nucleic acid* and will not anneal to or mediate amplification of *non-target sequences* present in a sample." *ArcherDX, Inc. v. QIAGEN Scis., LLC*, No. 18-cv-1019, 2020 WL 3316055, at *1 (D. Del. June 18, 2020) ("*'597 Patent Claim Construction Order*") (emphases added).

II

On July 10, 2018, Appellees sued Qiagen, alleging that Qiagen infringed the '810 patent. *Decision*, at *1. Later, after the '597 patent had issued, Appellees filed an amended complaint, adding a claim for infringement of the '597 patent. *Id.* Specifically, Appellees alleged that various Qiagen kits, containing materials used to prepare a DNA sample for sequencing, infringe the asserted patents. *Id.* To use those kits, a user first obtains and fragments a DNA sample. Then, according to Qiagen, identical artificial sequences (adaptors) are ligated to the ends of each DNA fragment. Those adaptors, Qiagen explains, are common to all Qiagen accused kits and contain sequences that enable the DNA to attach to, and be sequenced by, a sequencing machine. Qiagen further explains that its accused kits contain three types of primers that are used in its DNA preparation process. Forward ("FP") and universal ("UP") primers are designed to anneal to the complement of the adaptor sequence; a gene specific primer ("GSP") is designed to anneal to a sequence in the gene that one seeks to analyze; and a sample index primer ("SIP") anneals to a sequence that the GSP adds on by way of a tail.

After a five-day trial held in August 2021, the jury found that Qiagen willfully infringed claims 16, 17, and 19 of the '810 patent under the doctrine of equivalents and willfully and literally infringed claims 1, 5, and 19 of the '597 patent. *Id.* at *1–2. The jury also found that Appellees failed to establish that any one of those claims was invalid. *Id.* at *2. The jury awarded Appellees roughly $4.7 million in damages. *Id.* Following trial, Qiagen renewed its motion for judgment as a matter of law ("JMOL") on the jury's findings of infringement, no invalidity, and damages, and, in the alternative, moved for a new trial. *Id.* The court denied those motions. *See id.* at *3–13. Qiagen timely appealed, and we have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

Qiagen argues that the district court erred by not granting its renewed motion for JMOL of non-infringement of both patents, invalidity of the '810 patent, and no damages for both patents. For the following reasons, we reverse the district court's denial of JMOL of non-infringement of both patents because insufficient evidence supported the jury's findings. We therefore need not reach the validity and damages issues.[3]

We review a district court's JMOL decision under the law of the regional circuit. *Steuben Foods, Inc. v. Shibuya Hoppmann Corp.*, 127 F.4th 348, 353 (Fed. Cir. 2025). The Third Circuit reviews a JMOL decision *de novo*, applying the same standard as the district court. *Id.* "Such a motion should be granted only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of every fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find liability." *Id.* (citation omitted).

Infringement is a question of fact that we review for substantial evidence when tried to a jury. *Syngenta Crop Prot., LLC v. Willowood, LLC*, 944 F.3d 1344, 1355 (Fed. Cir. 2019). "A factual finding is supported by substantial evidence if a reasonable jury could have found in favor of the prevailing party in light of the evidence presented at trial." *Provisur Techs., Inc. v. Weber, Inc.*, 119 F.4th 948, 952–53 (Fed. Cir. 2024), *cert. denied*, 145 S. Ct. 1181 (2025) (citation omitted). We review claim construction

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[3] Qiagen's invalidity argument for the '810 patent is contingent on the court affirming the district court's denial of JMOL of non-infringement. *See* Appellant Br. 5; 39. Because we reverse the district court's denial of JMOL of non-infringement, we need not reach Qiagen's invalidity argument.

determinations based on intrinsic evidence *de novo*, but, when extrinsic evidence is considered, we review any subsidiary factual findings for clear error. *TomTom, Inc. v. Adolph*, 790 F.3d 1315, 1322 (Fed. Cir. 2015).

I

We begin with the '810 patent. The jury found that Qiagen's accused kits infringe claims 16, 17, and 19 under the doctrine of equivalents. *Decision*, at *5. Qiagen raises two arguments on appeal. First, it contends that it was error to "[a]llow[] the jury to apply 'plain meaning' to conclude that one sequence being *identical* to another, had the exact same meaning as the one sequence being *identical to a portion* of the other sequence." Appellant Br. 31 (emphases added). Specifically, it argues that the accused "second target-specific primer," *i.e.*, Qiagen's SIP, is not "identical" to the claimed "second sequencing primer," *i.e.*, Qiagen's Read2 primer, simply because they share an overlapping "portion" of a sequence. *See id.* at 28–31. Second, Qiagen argues that its accused SIP cannot be a "second target-specific primer" under the doctrine of equivalents because insufficient evidence supports that it meets any prong of the function-way-result test. *See* Appellant Br. 31–41. We agree with Qiagen that there was insufficient evidence from which a reasonable jury could have concluded that Qiagen's accused products infringe the '810 patent. We discuss each argument in turn.

A

First, Qiagen argues that the district court erred in denying JMOL of non-infringement by allowing the jury to conclude that "identical" could mean "identical to a portion." Appellant Br. 28–29. As noted above, the "second target-specific primer" requires "a 5′ portion comprising a nucleic acid sequence that is *identical* to a second sequencing primer." *See '810 Patent Claim Construction Order*, at *1 (emphasis added). But here, it is undisputed that the accused "second target-specific primer"—Qiagen's SIP—

contains 19 nucleotides, while the accused "sequencing primer" called Read2 contains 34 nucleotides. Despite that difference in sequence length, Appellees accused the SIP of satisfying the "second target-specific primer" limitation of claim 16 because the sequence of the SIP is identical to a portion of the sequence of Read2 and because identical to a portion can include identical to the whole. The district court agreed. Just before trial, it determined that "identical is an issue of fact for the jury." J.A. 400. On that basis, the district court in its JMOL decision concluded that although Appellees had to show that the accused SIP contained a sequence *identical* to Read2, "[t]he jury was not precluded from finding that 'identical' may include identical to a portion," and thus the jury's infringement finding was supported. *Decision*, at *6. We disagree.

It was error for the district court to turn a matter of claim construction over to the jury to decide as a factual dispute. *See O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008) ("When the parties raise an actual dispute regarding the proper scope of these claims, the court, not the jury, must resolve that dispute."). As a matter of claim construction, "identical" cannot mean "identical to a portion" because "identical" means the same. *See, e.g.*, *identical*, Webster's New World College Dictionary (4th ed. 2009) ("1 the very same 2 exactly alike or equal"); *identical*, Merriam-Webster's Collegiate Dictionary (11th ed. 2003) ("1 being the same . . . 2 having such close resemblance as to be essentially the same").

Furthermore, the specification and claims differentiate the two terms according to their degree. *See Seachange Int'l, Inc. v. C-COR, Inc.*, 413 F.3d 1361, 1368 (Fed. Cir. 2005) ("[D]ifferent words or phrases used in separate claims are presumed to indicate that the claims have different meanings and scope" (internal quotation marks and citation omitted). In particular, where two claim terms differ by a matter of degree, perhaps by use of a modifier for one term and not the other, a proper construction should

give effect to that difference. *See, e.g.*, *Arlington Indus., Inc. v. Bridgeport Fittings, Inc.*, 632 F.3d 1246, 1254–55 (Fed. Cir. 2011) ("Reading a [modified version of the spring metal adaptor] limitation into the [unmodified version of the] term 'spring metal adaptor' would render these additional modifiers superfluous, which weighs against doing so.").

Here, the "second target-specific primer" must be "*identical* to a second sequencing primer." *'810 Patent Claim Construction Order*, at *1 (emphasis added); *id.* at *5 (noting that the parties do not dispute that the '810 patent defines "second target-specific primer" as having this requirement (citing '810 patent col. 16 ll. 33–39)). In contrast, the "adaptor primer" of claim 16 need only be "*identical to a portion* of the first sequencing primer," *id.* (emphasis added); '810 patent col. 78 ll. 6–8, where a "portion" of a DNA molecule is defined as comprising all or a subset of a sequence, *see* '810 patent col. 9 ll. 1–5. As Qiagen explains and as the specification makes clear, the difference in specificity is important—the number of complementary nucleotides impacts the conditions under which primers anneal to particular sequences. Appellant Br. 29 (citing '810 patent col. 13 ll. 58–61 ("Conditions for primer-target nucleic acid annealing vary with the length and sequence of the primer[.]")). Reading the modifier, "a portion," into the unmodified term "identical" would render the modifier language superfluous. *See Arlington Indus.*, 632 F.3d at 1254–55. Thus, "identical to a portion" cannot have the same degree of claim scope as "identical." The district court therefore erred in allowing the jury to consider that "identical" can mean "identical to a portion," and in further denying JMOL to Qiagen on this issue.

B

Next, Qiagen argues that the district court erred in denying JMOL of non-infringement because no reasonable jury could have found that the accused SIP satisfies the

"second target-specific primer" limitation of claim 16. Specifically, Qiagen argues that the accused SIP does not infringe under the doctrine of equivalents because it fails all three prongs of the function-way-result test. Again, we agree.

"The doctrine of equivalents provides a limited exception to the principle that claim meaning defines the scope of the exclusivity right in our patent system." *VLSI Tech. LLC v. Intel Corp.*, 87 F.4th 1332, 1341 (Fed. Cir. 2023). Liability under the doctrine, therefore, "is the exception" and "not the rule." *Id.* at 1342 (cleaned up). "[P]roof of equivalents must be limitation specific, not focused only on the claim as a whole." *Id.* To determine whether the accused element is an equivalent to a claim limitation, we ask "whether a substitute element matches the function, way, and result of the claimed element." *Id.* (quoting *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 40 (1997)). "Such matching requires that each of function, way, and result be substantially the same." *VLSI*, 87 F.4th at 1342 (cleaned up). And the "patentee must provide particularized testimony and linking argument as to the insubstantiality of the differences between the claimed invention and the accused device." *Id.* (cleaned up).

For each prong of the function-way-result test, the district court recounted the parties' arguments and expert testimony before summarily concluding that the jury had heard sufficient evidence that it was entitled to credit. *Decision*, at *6–7 ("In the face of conflicting testimony about whether Qiagen's products perform substantially the same function, in substantially the same way, to achieve substantially the same result, the jury was entitled to credit Plaintiffs' evidence."). But, as we explain below, the evidence provided by Appellees is not exceptional and does not rise to the level of "particularized testimony and linking argument" showing substantial similarity between the accused products and asserted claims in function, way, or

result. *VLSI*, 87 F.4th at 1342 (cleaned up). We discuss each prong of the function-way-result test in turn.

We begin with the "function" prong. The district court concluded that substantial evidence supported the jury's finding that Qiagen's SIP performs substantially the same function as the claimed "second target-specific primer." *See Decision*, at *6. We disagree. As Qiagen explains, "[t]he function of a target-specific primer in the '810 patent is to anneal to the known target nucleic sequence to provide a second specificity step to achieve the desired specificity." Appellant Br. 34. Put simply, its function "is to increase enrichment for the target sequences over non-target sequences," *i.e.*, achieve specificity. *Id.* Those assertions are supported by the specification, which explains that the second target specific primer "*specifically* anneals to a portion of the known target nucleotide sequence." '810 patent col. 16 ll. 35–37 (emphasis added). The specification further explains that "'specific' when used in the context of a primer specific for a target nucleic acid refers to a level of complementarity between the primer and the target such that there exists an annealing temperature at which the primer will anneal to and mediate amplification of the target nucleic acid and will not anneal to or mediate amplification of non-target sequences present in a sample." '810 patent col. 8 ll. 49–55. Thus, the claimed "second-target specific primer" is used to facilitate specificity during the amplification process.

The accused SIP's function is different. It does not enrich the target sequence or provide specificity. Instead, it ensures that the DNA fragment is compatible with the sequencer so that it may be sequenced. J.A. 587. Appellees' own expert stated as much, explaining that the SIP binds to a "common sequence" that the GSP adds on by way of a tail, *see* J.A. 581, and thus it does not bind to the native DNA fragment containing the "target" sequence. For that reason, Appellees' expert admitted that there was no literal infringement. *See* J.A. 581. Nonetheless, the expert went

on to testify that there was still infringement under the doctrine of equivalents because, in his view, the SIP works together with another Qiagen primer, its UP, to perform substantially the same function as the "second target-specific primer." *See* J.A. 581. But the Qiagen UP is an adaptor primer with its own function. *See* J.A. 592. And while the '810 patent's specification explains that the second target-specific primer and second adaptor primer work together, it also explains that the second target-specific primer performs its own function of enriching the target sequence, *i.e.*, creating specificity. '810 patent col. 16 ll. 46–50 (disclosing that second target-specific primers "can serve to suppress primer dimers," *i.e.*, the unwanted off-target byproduct in PCR); col. 18 ll. 24–29 (describing target specificity rates). Based on the evidence, no reasonable jury could have found substantial similarity between the function of the claimed "second target-specific primer" and the accused SIP.

Regarding the "way" prong, the "second target-specific primer" enriches the DNA sample and provides specificity by being designed against, annealing to, and amplifying a known target sequence, while specifically not facilitating the amplification of non-target sequences. '810 patent col. 16 ll. 33–39; *see also '810 Patent Claim Construction Order*, at *1. The accused SIP does not act in this way; it binds to a "common sequence" that the GSP adds on by way of a tail, and not to any target sequence. *See* J.A. 581. Thus, no reasonable jury could have found that the SIP acts in a substantially similar way as the claimed "second target-specific primer."

Regarding the "results" prong, the accused SIP also does not achieve substantially the same "result" as the "second target-specific primer." As Qiagen explains, the SIP amplifies any DNA with the common sequence from the first round of PCR, rather than selectively enriching the target sequence. Appellant Br. 38. For example, if first target-specific primers (*i.e.*, Qiagen's GSPs) mis-prime on a

non-target sequence or otherwise interact to produce primer dimers, the SIP cannot eliminate those off-target amplicons from the final pool. *Id.*; *see also* '810 patent col. 16 l. 65–col l. 5. (explaining that target-specific primers "can interact with each other in an undesired off-target manner"). We therefore conclude that no reasonable jury could have found that the accused SIP and claimed "second target-specific primer" produce substantially similar results based on the evidence.

Thus, the district court erred in denying Qiagen's renewed motion for JMOL of non-infringement under the doctrine of equivalents for the '810 patent. Even when viewing the evidence in the light most favorable to Appellees, there was insufficient evidence from which a reasonable jury could have found liability.

II

Turning to the '597 patent, the jury found that Qiagen's accused products literally infringe claims 1, 5, and 19. *Decision*, at *3. Qiagen argues on appeal that the district court erred in denying its renewed motion for JMOL of non-infringement because no reasonable jury could have found that the accused kits include the claimed "target-specific primer." It raises two arguments on appeal. First, Qiagen argues that insufficient evidence supports the jury's finding that the accused FP is a "target-specific primer." Appellant Br. 44–48. Second, it argues that insufficient evidence established that sequences in the claimed DNA interacted with the accused primers to satisfy steps (a) and (b) of claim 1. *Id.* at 49–57. We agree that the district court erred in not granting the renewed JMOL of non-infringement of the '597 patent. Because we conclude so on the basis of Qiagen's first argument, we need not address its second.

The district court relied on two primary pieces of evidence to conclude that there was substantial evidence supporting the jury's finding that the accused FP satisfied the

"target-specific primer" limitation. *Decision*, at *4. First, it explained that the jury heard expert testimony that "'the FP primer in the Qiagen workflow, targets the ligated adaptor' and thus satisfies the Court's construction of 'target-specific primer.'" *Id.* (quoting J.A. 591). Second, it explained that the jury also heard testimony that "the FP binds to 'a very small proportion of the molecules' in a sample," *id.* (quoting J.A. 620), because it only binds to the adaptor's compliment.

Appellees' theory, which relies on the evidence discussed above and was adopted by the district court, was accurately described by Qiagen as being "that because adaptor sequences are added to the *DNA fragment that contains the target sequence*, then the FP primer that anneals to those newly-added adaptor sequences is annealing to the *same molecule* as the actual target sequence." Appellant Br. 46 (emphases added); *see* Appellee Br. 36–38. But the evidence underlying that theory, even when viewed in the light most favorable to Appellees, is not substantial evidence supporting the jury's infringement finding. While we agree with Appellees that a DNA fragment and its ligated adaptor may, as a combination, contain target and common sequences, it is not the case that any primer that simply anneals to any portion of that combined product automatically satisfies the "target-specific primer" limitation as construed in the '597 patent. We discuss the district court's errant reliance on such evidence below.

First, the district court's reliance on the testimony that the FP "targets the ligated adaptor" is misplaced. *Decision*, at *4. As noted earlier, the district court construed "target-specific primer" to mean "a primer that has a level of complementarity between the primer and the target such that . . . the primer will anneal to and mediate amplification of the *target nucleic acid* and will not anneal to or mediate amplification of *non-target sequences* present in a sample." *'597 Patent Claim Construction Order*, at *1 (emphases added). The district court further construed "target

nucleic acid" as a "a nucleic acid molecule of interest (e.g., a *nucleic acid to be analyzed*)." *Id.* (emphasis added). Thus, the '597 patent differentiates between target and non-target sequences. The "target" refers to that which is "analyzed" or studied, *e.g.*, the genetic mutation sequence area, *id.*, whereas a type of non-target sequence is a "common sequence," or sequence that is universally present in all DNA fragments in the sample, *see* '597 patent col. 16 ll. 59–61.

Here, the FP targets and anneals to an adaptor—an artificial sequence "common" to every DNA fragment in the sample. *See* J.A. 611 ("All the molecules in the soup have the adaptor added to it[.]"). That artificial adaptor sequence is never "analyzed" because it is a common, artificial sequence that does not correspond to the "targeted" genetic mutation sequence. *See, e.g.*, J.A. 522 (explaining that, based on an inventor's knowledge and experience, adaptor sequence is "never" analyzed); *see also* J.A. 575 (explaining that PCR "assist[s] folks like clinicians in . . . looking for the mutations"). In other words, the FP targets the ligated adaptor, which is not the "nucleic acid to be *analyzed*." *'597 Patent Claim Construction Order*, at *1 (emphasis added). Rather, it is merely an artificial component that attaches to the ends of that molecule of interest to support sequencing operations.

Second, the district court's reliance on testimony that the FP binds to "a very small proportion of the molecules" is also misplaced. *See Decision*, at *4 (quoting J.A. 620). The FP *can* be ligated to adaptor sequence regardless of whether target or non-target sequences are contained by the sample. *See* J.A. 532 (Inventor Long Phi Le was asked "[i]f you have an adapter primer that binds to the universal oligonucleotide tail adapter, it binds to that adapter if the adapter is ligated to off-target sequences; right?," and he responded, "Correct."). That the FP binds to "a very small proportion of the molecules," then, does not mean that it cannot or does not bind to molecules that happen not to

contain target sequence. Thus, the FP is not a "target-specific primer" because it fails to "*not* anneal to or mediate amplification of *non-target sequences* present in a sample." *See '597 Patent Claim Construction Order*, at *1 (emphases added).

Appellees' response that the FP works in concert with the GSP to target and amplify sequences and that nothing in the court's construction precludes the target-specific primer from mediating amplification of the target nucleic acid in concert with another primer is unpersuasive. *See* Appellee Br. 37. As discussed, the district court's construction requires that the "target-specific primer . . . will anneal to and mediate amplification of the target nucleic acid and will not anneal to or mediate amplification of non-target sequences present in a sample." *See '597 Patent Claim Construction Order*, at *1. It does not allow or suggest, let alone require, that the "target-specific primer" work in conjunction with another primer to perform its required functions. On the contrary, the construction specifically requires the "target-specific primer" to perform the required functions. Thus, the GSP cannot assist the accused FP in fulfilling the function of the "target-specific primer." *See In re Power Integrations, Inc.*, 884 F.3d 1370, 1377 (Fed. Cir. 2018) (rejecting an argument that permitted two circuit elements to work in concert to "cause" an action because "[a]lthough the [subject] patent does not expressly exclude" the assistance of the second element, "the plain claim language . . . specifically requires the counter—not some other circuit element—to 'caus[e]' the converter to adjust the control input" (citation omitted)). Appellees' reliance on Qiagen's GSP is incorrect because it runs counter to the requirements of the claimed "target-specific primer."

The district court therefore erred in denying Qiagen's renewed motion for JMOL of non-infringement for the '597 patent. Even when viewing the evidence in the light most favorable to Appellees, there was insufficient evidence from which a reasonable jury could have found liability.

CONCLUSION

We have considered Appellees' remaining arguments and find them unpersuasive. For the foregoing reasons, we *reverse* the district court's denial of JMOL of non-infringement for both patents at issue. The district court should therefore on remand grant JMOL of non-infringement on the '810 and '597 patents.

REVERSED