NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

ENZO BIOCHEM INC, ENZO LIFE SCIENCES, INC, YALE UNIVERSITY,
Plaintiffs-Appellants

v.

APPLERA CORP., TROPIX INC,
Defendants-Appellees

2016-1881

Appeal from the United States District Court for the District of Connecticut in No. 3:04-cv-00929-JBA, Judge Janet Bond Arterton.

Decided: August 2, 2017

L. GENE SPEARS, Baker Botts, LLP, Houston, TX, argued for plaintiffs-appellants. Also represented by MICHAEL HAWES.

ROBERT N. HOCHMAN, Sidley Austin LLP, Chicago, IL, argued for defendants-appellees. Also represented by CARTER GLASGOW PHILLIPS, JENNIFER J. CLARK, Washington, DC; NICHOLAS P. GROOMBRIDGE, JENNIFER H. WU,

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Before PROST, *Chief Judge,* O'MALLEY, and WALLACH, *Circuit Judges.*

O'MALLEY, *Circuit Judge.*

Enzo Biochem, Inc., Enzo Life Sciences, Inc., and Yale University (collectively, "Enzo") appeal from the District of Connecticut's entry of summary judgment in favor of Applera Corp. and Tropix, Inc. (collectively, "Applera"). *See Enzo Biochem, Inc. v. Applera Corp.* (*District Court Decision*), No. 3:04cv929 (JBA), 2016 U.S. Dist. LEXIS 20904 (D. Conn. Feb. 22, 2016). Because the district court accurately interpreted this court's decision regarding the proper construction of the claims in U.S. Patent No. 5,449,767 ("the '767 patent") and correctly analyzed Enzo's doctrine of equivalents argument, we *affirm*.

I. BACKGROUND

With this appeal, this court now has considered this infringement action on three separate occasions over the course of thirteen years of litigation between these parties. We assume the parties are familiar with the background facts, and we therefore recite only those facts relevant to our decision in this appeal.

A. DNA and RNA Sequencing and the '767 Patent

As explained in the previous appeals, DNA and RNA are composed of a series of units called "nucleotides." *Enzo Biochem, Inc. v. Applera Corp.* (*Enzo II*), 780 F.3d 1149, 1150 (Fed. Cir. 2015) (quoting *Enzo Biochem, Inc. v. Applera Corp.* (*Enzo I*), 599 F.3d 1325, 1328 (Fed. Cir. 2010)). Each nucleotide is composed of a nitrogenous base, a pentose sugar, and a phosphate group. *Id.* at 1150–51 (quoting *Enzo I*, 599 F.3d at 1328). Two strands of DNA or RNA having complementary nitrogenous bases

will "hybridize" to form a double-stranded complex. *Id.* at 1151 (quoting *Enzo I*, 599 F.3d at 1328).

The technology at issue in this case deals with the use of nucleotide probes to detect the presence of a particular DNA or RNA sequence in a sample or to identify an otherwise unknown DNA sequence. In our previous opinions, we explained how hybridization can be used to detect the presence of a nucleic acid:

> Because hybridization occurs in a predictable manner between complementary strands, it is possible to detect the presence of a nucleic acid of interest in a sample. For example, a chemical entity, called a "label," can be attached to or incorporated into a nucleic acid strand of a known sequence, called a "probe," which will hybridize with a complementary sequence of interest, called a "target." Once the probe is hybridized with the target, a detectable signal is generated either from the label itself (referred to as "direct detection") or from a secondary chemical agent that is bound to the label (referred to as "indirect detection"). If a signal is detected from the sample after all unhybridized probes have been removed, detection of the signal implies the presence of a target in that sample.

Id. (quoting *Enzo I*, 599 F.3d at 1328).

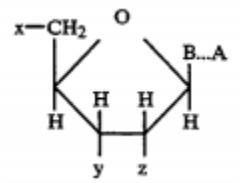
The '767 patent explains that "[m]any procedures employed in biomedical research and recombinant DNA technology rely heavily on the use of" radioactive labels, such as isotopes of hydrogen, phosphorus, carbon, or iodine. '767 patent, col. 1 ll. 23–27. When used as labels, these radioactive compounds provide "useful indicator probes that permit the user to detect, monitor, localize, or isolate nucleic acids and other molecules of scientific or clinical interest, even when present in only extremely small amounts." *Id.* at col. 1 ll. 27–32. But the '767

patent notes that the use of these radioactive materials has "serious limitations and drawbacks." *Id.* at col. 1 ll. 35–37. For example, elaborate safety precautions are necessary for the preparation, utilization, and disposal of the isotopes to avoid potentially hazardous levels of exposure to the radioactive material. *Id.* at col. 1 ll. 27–41. The radioactive material also is expensive to use and purchase. *Id.* at col. 1 ll. 41–46. And it is often unstable, with a short shelf-life. *Id.* at col. 1 ll. 46–52.

As an alternative to the use of radioactive labels, the '767 patent explains that "a series of novel nucleotide derivatives that contain biotin, iminobiotin, lipoic acid, and other determinants attached covalently to the pyrimidine or purine ring have been synthesized." *Id.* at col. 2 ll. 63–68. These nucleotide derivatives interact "specifically and uniquely with proteins such as avidin or antibodies." *Id.* at col. 3 ll. 2–3. "If avidin is coupled to potentially demonstrable indicator molecules, including fluorescent dyes, . . . electron-dense reagents, . . . or enzymes capable of depositing insoluble reaction products, . . . the presence, location, or quantity of a biotin probe can be established." *Id.* at col. 1 ll. 61–67.

The '767 patent asserts that the use of this modified detection approach provides "detection capacities equal to or greater than procedures which utilize radioisotopes and [it] often can be performed more rapidly and with greater resolving power." *Id.* at col. 3 ll. 9–13. The '767 patent further describes these new nucleotide derivatives as providing an approach to detection that is "relatively inexpensive[]," does not require "elaborate safety procedures," uses "chemically stable" derivatives, and allows for "the development of safer, more economical, more rapid, and more reproducible research and diagnostic procedures." *Id.* at col. 3 ll. 14–28.

Claim 1 of the '767 patent covers an oligo- or polynucleotide containing a nucleotide having the following structure:



See id. at col. 30 l. 48–col. 31 l. 21. The disputed language of claim 1 involves the following limitation: "wherein A comprises at least three carbon atoms and represents at least one component of a signaling moiety capable of producing a detectable signal . . . ." *Id.* at col. 30 ll. 66–68.

All other asserted claims of the '767 patent depend, directly or indirectly, from claim 1. Claim 8 depends from claim 1 and claims, "[a]n oligo- or polynucleotide of claim 1 wherein the linkage group includes the moiety –CH2–NH–." *Id.* at col. 31 ll. 36–37. Claim 67 depends from claim 1 and claims, "[a]n oligo- or polynucleotide of claim 1 or 48 wherein A comprises an indicator molecule." *Id.* at col. 36 ll. 42–43. Claim 68 depends from claim 67 and claims, "[a]n oligo- or polynucleotide of claim 67 wherein said indicator molecule is fluorescent, electron dense, or is an enzyme capable of depositing insoluble reaction products." *Id.* at col. 36 ll. 44–47. Claim 70 depends from claim 68 and claims, "[a]n oligo- or polynucleotide of claim 68 wherein the fluorescent indicator molecule is selected from the group consisting of fluorescein and rhodamine." *Id.* at col. 36 ll. 51–53.

B. Procedural History

This litigation began in 2004, when Enzo filed suit against Applera alleging infringement of six patents, including the '767 patent, that generally cover various techniques and processes for detecting the presence of a particular strand of DNA or RNA in a sample. In 2006, the district court construed the claims of all six patents.

After multiple years of litigation and an appeal to this court regarding invalidity issues decided on summary judgment, *see Enzo I*, 599 F.3d at 1332–43, Enzo and Applera went to trial in October 2012. Enzo limited its infringement contentions during the jury trial to claims 1, 8, 67, 68, and 70 of the '767 patent. The jury found Applera infringed the claims at issue and awarded $48.6 million in damages.

After the district court entered final judgment, Applera appealed. Applera argued that the district court erred in its claim construction because the claims of the '767 patent only cover indirect detection. In the alternative, Applera argued that, if the claims cover direct detection, they are invalid for lack of written description and lack of enablement. We agreed with Applera and reversed the district court's claim construction because we concluded that "the inventors were claiming only indirect detection." *Enzo II*, 780 F.3d at 1156. Given that conclusion, we held that "[t]he district court erred in construing the disputed claims of the patent-in-suit to cover both direct and indirect detection." *Id.* at 1157. We treated claim 1 as representative, *id.* at 1152, and specifically stated that "claim 1 is limited to indirect detection," *id.* at 1157. We then remanded the case to the district court to determine whether the accused product infringes under the proper claim construction. *Id.*

On remand, Enzo moved for entry of judgment on the jury verdict, and Applera moved for summary judgment of noninfringement. *District Court Decision*, 2016 U.S. Dist. LEXIS 20904, at *3. The district court agreed with Applera that our decision in *Enzo II* covered all claims of the '767 patent, not just claim 1 as argued by Enzo, and rejected Enzo's doctrine of equivalents argument relating to claims 1 and 8. *Id.* at *13–14, 20–22. The district court therefore denied Enzo's motion for judgment on the jury verdict and granted Applera's motion for summary judgment. *Id.* at *22–23. Enzo appealed. We possess subject

matter jurisdiction pursuant to 28 U.S.C. § 1295(a) (2012).

II. DISCUSSION

We review a district court's grant of summary judgment under the law of the regional circuit. *Teva Pharm. Indus. Ltd. v. AstraZeneca Pharm. LP*, 661 F.3d 1378, 1381 (Fed. Cir. 2011). The Second Circuit reviews the grant of summary judgment de novo. *Major League Baseball Props., Inc. v. Salvino, Inc.*, 542 F.3d 290, 309 (2d Cir. 2008). Summary judgment is proper when, drawing all justifiable inferences in the non-movant's favor, "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a); *see also Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242 (1986).

In addressing the parties' arguments, we first address the scope of *Enzo II* and its effect on claims 67, 68, and 70. We then consider Enzo's doctrine of equivalents argument regarding claims 1 and 8.[1]

A. The Scope of *Enzo II*

Enzo argues that the district court incorrectly interpreted our decision in *Enzo II*. Enzo asserts that *Enzo II* only dealt with claim 1 and left intact the previously-construed scope of claims 67, 68, and 70, covering both direct and indirect detection. Based on its view of our decision in *Enzo II*, Enzo contends that we should reverse the current judgment on claims 67, 68, and 70, and reinstate the jury's finding of infringement and damages award.

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[1] Enzo does not contest that claims 1 and 8 are not literally infringed under our claim construction in Enzo II. See District Court Decision, 2016 U.S. Dist. LEXIS 20904, at *15.

We conclude that, after carefully parsing our decision, the district court correctly interpreted *Enzo II*. As the district court explained, *Enzo II* consistently refers to the "claims" at issue in that appeal, which extended beyond claim 1 to include claims 8, 67, 68, and 70. *See District Court Decision*, 2016 U.S. Dist. LEXIS 20904, at *14. For example, our opinion in *Enzo II*, after acknowledging that Enzo had asserted claims 1, 8, 67, 68, and 70, states that the district court "erred in its claim construction by finding that the *claims at issue* covered direct detection." *Enzo II*, 780 F.3d at 1150 (emphasis added). We reiterated this statement in the conclusion, where we stated, "[t]he district court erred in construing *the disputed claims* of the patent-in-suit to cover both direct and indirect detection." *Id.* at 1157 (emphasis added). The opinion also looks to the specification to consider whether it includes any teaching of direct detection applicable to the claims and concludes that the specification does not "support[] the inclusion of direct detection." *Id.* at 1156. As noted by the district court, it would have been illogical for us to recognize the existence of five claims in the appeal and then repeatedly refer to the "claims at issue" or the "disputed claims" when referring only to claim 1 and not to claims 67, 68, and 70. *See District Court Decision*, 2016 U.S. Dist. LEXIS 20904, at *14.

The district court also correctly noted that our decision in *Enzo II* acknowledged Applera's alternative invalidity arguments regarding lack of written description and lack of enablement, but did not address the merits of those arguments. *Id.* We did not need to address Applera's alternative arguments because our analysis found that the scope of the claims at issue, including claims 67, 68, and 70, did not extend beyond indirect detection.

Because Enzo does not contend that Applera infringes claims 67, 68, and 70 under the proper reading of the claims we provided in *Enzo II*, we affirm the district court's judgment as to claims 67, 68, and 70.

B. Doctrine of Equivalents for Claims 1 and 8

Enzo concedes that Applera does not literally infringe claims 1 and 8 under our claim construction in *Enzo II*. *See id.* at *15. But Enzo argues that Applera infringes these claims under the doctrine of equivalents. Enzo contends that the district court erred in granting summary judgment of noninfringement because there is a genuine dispute of material fact regarding whether Applera's accused products infringe under the doctrine of equivalents.

"[A] product or process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997). "What constitutes equivalency must be determined against the context of the patent, the prior art, and the particular circumstances of the case." *Id.* at 24 (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 609 (1950)).

A party can show infringement under the doctrine of equivalents if every limitation of the asserted claim, including a limitation's "equivalent," is found in the accused product, "where an 'equivalent' differs from the claimed limitation only insubstantially." *Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp.*, 149 F.3d 1309, 1315 (Fed. Cir. 1998). "Whether a component in the accused subject matter performs substantially the same function as the claimed limitation in substantially the same way to achieve substantially the same result may be relevant to this determination." *Id.*

But we also have explained that "the concept of equivalency cannot embrace a structure that is specifically excluded from the scope of the claims." *Dolly, Inc. v. Spalding & Evenflo Cos.*, 16 F.3d 394, 400 (Fed. Cir.

1994). The doctrine of equivalents also cannot "render[] a claim limitation inconsequential or ineffective." *Akzo Nobel Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1342 (Fed. Cir. 2016). And, as the Supreme Court has stated, "if a theory of equivalence would entirely vitiate a particular claim element, partial or complete judgment should be rendered by the court, as there would be no further *material* issue for the jury to resolve." *Warner-Jenkinson*, 520 U.S. at 39 n.8.

Enzo claims that the district court "misconstrued" its expert declaration and improperly drew inferences in favor of Applera, rather than Enzo, when ruling on the motion for summary judgment. Appellant's Br. 25. According to Enzo, the district court could not have granted summary judgment on the doctrine of equivalents in the face of its expert's "reasoned and reasonable function/way/result comparison of the accused products with the invention of claim 1." *Id.* at 26. Enzo also argues that its "asserted equivalent" was not disclaimed through the '767 patent's criticism of radioactive labeling. *Id.* at 29. Enzo acknowledges that it critiqued radioactive labels for "their hazards, inconvenience, cost and shelf life," but it argues that the district court did not explain the relevance of these issues to the doctrine of equivalents theory put forward by Enzo. *Id.* Enzo asserts that it is not "asserting a scope of equivalents broad enough to encompass all directly detectable labels including radioactive ones"; instead, it focused on a particular subset of direct detection. *Id.*

We conclude that the district court correctly granted summary judgment in favor of Applera. The district court explained that the patent "describes its method of indirect detection as a superior means of detection as compared to direct detection, with 'detection capacities equal to or greater than products which utilize' direct detection." *District Court Decision*, 2016 U.S. Dist. LEXIS 20904, at *21 (quoting *Enzo II*, 780 F.3d at 1155). As the district

court aptly concluded after its analysis, "[Enzo] cannot now claim that indirect and direct detection are insubstantially different, and no jury could so find." *Id.* at *22.

Indeed, Enzo's attempt to reframe its infringement case under the doctrine of equivalents runs headfirst into our decision in *Enzo II*. In that decision, we reviewed the claims and the specification to find that the claims covered only indirect detection. *Enzo II*, 780 F.3d at 1154–55. We explained that "[t]he specification provides additional support that claim 1 covers only indirect detection." *Id.* at 1155. We also stated that the specification does not "support[] the inclusion of direct detection, even when extrinsic expert testimony is considered." *Id.* at 1156. And the specification's "only discussion of direct detection . . . was exclusively in the context of discussing how indirect detection is a superior method." *Id.* at 1155. Based on these facts, we were "persuaded that the inventors were claiming only indirect detection." *Id.* at 1156.

Our decision in *Enzo II*, therefore, focused entirely on the conclusion that the asserted claims do not include direct detection in part because they *excluded* direct detection. Enzo's attempt to incorporate direct detection methods now through the doctrine of equivalents fails. In *Dolly*, we concluded that "the concept of equivalency cannot embrace a structure that is specifically excluded from the scope of the claims." 16 F.3d at 400. Applying this concept to that case, we noted that "[a] stable rigid frame assembled from the seat and back panels is not the equivalent of a separate stable rigid frame which the claim language specifically limits to structures exclusive of seat and back panels." *Id.* Indeed, we found that the district court erred by "failing to give effect to this claim limitation in applying the doctrine of equivalents." *Id.* The same principle applies in this case; the concept of equivalency cannot embrace direct detection because it is "specifically excluded from the scope of the claims," *id.*, as we found in *Enzo II*. Including direct detection as an

equivalent of indirect detection would render meaningless the claim language on which we based our decision in *Enzo II*; direct detection cannot be an equivalent of indirect detection in relation to these patent claims. *See Akzo Nobel Coatings*, 811 F.3d at 1342 ("Under the doctrine of equivalents, an infringement theory thus fails if it renders a claim limitation inconsequential or ineffective."); *Am. Calcar, Inc. v. Am. Honda Motor Co.*, 651 F.3d 1318, 1338–39 (Fed. Cir. 2011) (concluding that a theory of equivalence was "legally insufficient" because it "would vitiate [the] claim limitation by rendering it meaningless" to find that "a signal from one source" was equivalent to "signals from a plurality of sources").

As the district court correctly held, no reasonable jury could find, even under the doctrine of equivalents, that Applera's accused products using direct detection infringe Enzo's patent claiming indirect detection.

III. CONCLUSION

For the foregoing reasons, we affirm the district court's judgment in this case.

AFFIRMED