UNITED STATES DISTRICT COURT
DISTRICT OF CONNECTICUT

ENZO BIOCHEM, INC., ENZO LIFE SCIENCES, INC. and YALE UNIVERSITY, *Plaintiffs*, *v.* APPLERA CORP. and TROPIX, INC., *Defendants*.	Civil No. 3:04cv929 (JBA) February 22, 2016

RULING ON PLAINTIFFS' MOTION FOR ENTRY OF JUDGMENT AND DEFENDANTS' MOTION FOR SUMMARY JUDGMENT

This twelve-year old case is before this Court after a second remand from the Federal Circuit which vacated this Court's finding of infringement and directed the Court to "determine, consistent with" the Federal Circuit's analysis, "whether the accused product infringes." Plaintiffs Enzo Biochem, Inc., Enzo Life Sciences, Inc. and Yale University ("Enzo") now move [Doc. # 566] for entry of judgment on the current jury verdict, and Defendants Applera Corp. and Tropix, Inc. ("Applera") move [Doc. # 568] for summary judgment. For the following reasons, Plaintiffs' motion is denied and Defendants' motion is granted.

I. Background

The parties' familiarity with the background of this case is presumed. Briefly, Plaintiffs initiated this patent infringement suit in 2004, accusing Defendants of infringement of six patents, including United States Patent Nos. 5,476,928 ("'928 patent"), 5,449,767 ("'767 patent"), and 5,328,824 ("'824 patent"), which cover various techniques and processes for detecting the presence of a particular strand of nucleic acids (i.e., DNA or RNA) in a sample. (*See* Compl. [Doc. # 1].) Relevant here, the '824, '928, and '767

patents disclose the invention of non-radioactive labeling and specify formation of a complex of hybridized[1] nucleotides and a detectable polypeptide.

Specifically, the '767 and '824 patents claim in part: "A method of detecting the presence or absence of a nucleic acid in a sample which comprises the steps of (a) contacting under hybridizable conditions said sample with at least one compound comprising the structure [DIAGRAM] wherein A comprises at least three carbon atoms and represents at least one component of a signaling moiety capable of producing a detectable signal . . . ." (Claim Construction Ruling [Doc. # 137] at 5 (quoting '824 Pat. 30:49–31:29).) The parties disputed whether this language should be read to encompass both direct and indirect identification systems or only indirect systems.[2] On October 13, 2006, following a *Markman* hearing, this Court issued its Claim Construction Ruling [Doc. # 137], finding in Plaintiffs' favor that the patents cover both direct and indirect detection.

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[1] "Hybridization" is "the binding of two separate, complementary strands of nucleic acids to form nucleic acid hybrids." (Claim Constr. Ruling at 1 n.1.)

[2] As the Federal Circuit explained: "[b]ecause hybridization occurs in a predictable manner between complementary strands [of nucleic acids], 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." *Enzo Biochem Inc. v. Applera Corp*. (*Enzo I*), 780 F.3d 1149, 1151 (Fed. Cir. 2015).

Thereafter, on September 6, 2007, the Court entered summary judgment [Doc. # 261] in favor of Defendants. Plaintiffs appealed, and in a March 26, 2010 decision, the Federal Circuit reversed this Court's judgment that the '767, '824, and '928 patents are invalid for indefiniteness and that the '767 and '824 patents are invalid as anticipated, and affirmed the Court's judgment that the '928 patent is invalid as anticipated. *Enzo Biochem Inc. v. Applera Corp*. (*Enzo II*), 599 F.3d 1325 (Fed. Cir. 2010). On remand, this Court denied [Doc. # 418] Applera's motion for summary judgment on infringement and equitable defenses. Plaintiffs waived their claims for infringement of the '824 patent and limited their assertion of the '767 patent to claims 1,[3] 8,[4] 67,[5] 68,[6] and 70,[7] and the case proceeded to trial.

Following seven days of evidence, the jury returned a verdict finding that Defendants' accused BigDye and dRhodamine dye-terminator products directly

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[3] Claim 1 is an independent claim, which reads in relevant part: "An oligo- or polynucleotide containing a nucleotide having the structure [Diagram] . . . wherein A comprises at least three carbon atoms and represents at least one compound of a signaling moiety capable of producing a detectable signal . . . ." ('767 Pat., Ex. 3 to Stone Decl. in Supp. Def.'s Mot. Summ. J. [Doc. # 568-2] 30:48–68.)

[4] Claim 8 covers: "An oligo- or polynucleotide of claim 1 wherein the linkage group includes the moiety $-CH_2-NH-$." (*Id*. 31:36–37.)

[5] Claim 67 states: "An oligo- or polynucleotide of claim 1 . . . wherein A comprises an indicator model." (*Id*. 36:42–44.)

[6] Claim 68 reads: "An oligo- or polynucleotide of claim 67 wherein said indicator model is fluorescent, electron dense, or is an enzyme capable of depositing insoluble reaction products." (*Id*. 36:44–47.)

[7] Claim 70 covers: ""An oligo- or polynucleotide of claim 68 wherein the fluorescent indicator molecule is selected from the group consisting of fluorescein and rhodamine." (*Id*. 36:51–54.)

infringed, and induced customers to infringe, claims 1, 8, 67, 68, and 70 by Defendants' manufacture, use, or sale of their reagent products and sales of DNA sequencing instruments. (*See* Jury Verdict [Doc. # 476].) The jury rejected Defendants' invalidity defenses of lack of written description, lack of enablement, and anticipation, and issued two advisory findings that (1) Enzo had not unreasonably delayed in filing suit, and (2) ABI was not materially prejudiced by the delay in filing this lawsuit. (*Id.*) The jury awarded Enzo $48,587,500.00 in reasonable royalty damages. (*Id.*) Judgment [Doc. # 544] entered in Plaintiffs' favor on January 7, 2014. Defendants appealed.

On appeal, Defendants raised three issues: (1) "[w]hether the finding of infringement should be reversed because, contrary to the district court's claim construction, the '767 patent does not cover the directly detectable terminator nucleotides of the accused products"; (2) "[w]hether, assuming the '767 patent covers direct detection, the patent is invalid for lack of written description because nothing in the specification describes possession of directly detectable nucleotides, and the only disclosure of such nucleotides is prior art which presented problems overcome by the described indirectly detected nucleotides"; and (3) "[w]hether, assuming the '767 patent covers directly detectable nucleotides, the patent is invalid for lack of enablement because nothing in the specification explains how to make or use a directly detectable nucleotide other than certain prior art detection systems, which presented problems overcome by the enabled indirect detection methods." (Defs.' Opening Br., Ex. 1 to Stone Decl. at 16.[8])

[8] All page numbers cited in this Ruling correspond to ECF's page numbering, found in the header on each page.

The Federal Circuit began by reciting the language of claim 1, which it stated was "representative." *Enzo II*, 599 F.3d at1152. The entirety of the court's discussion then focused on construing the language of claim 1, at the end of which the court concluded that "as claim 1 is limited to indirect detection by its own plain meaning, it would be inappropriate to use the doctrine of claim differentiation to broaden claim 1 to include a limitation imported from a dependent claim, such as direct detection." *Id*. at 1157. The court therefore held that this Court "erred in construing the disputed claims of the patent-in-suit to cover both direct and indirect detection," and reversed this Court's "claim construction, vacate[d]" the Court's "finding of infringement," and "remand[ed]" to the Court "with instruction to determine, consistent with the analysis in this opinion, whether the accused product infringes." *Id.*

II. Discussion

The parties' motions raise several distinct issues pertaining to claims 67, 68, and 70 on the one hand, and claims 1 and 8 on the other. These arguments are discussed in turn below.

A. Claims 67, 68, and 70

With respect to claims 67, 68, and 70, the parties' briefs attempt to reason through the Federal Circuit's somewhat cryptic mandate and its effect on claims 67, 68, and 70. The confusion arises because while Defendants raised the issue on appeal of whether *any of the claims* of the '767 patent cover direct detection (in Defendants' words, whether the "'767 patent . . . cover[s] the directly detectable terminator nucleotides of the accused products" (Defs.' Opening Br. at 16)), the Federal Circuit's opinion analyzes only the language of claim 1, before concluding that "[t]he district court erred in construing the

disputed claim**s** of the patent-in-suit to cover both direct and indirect detection," *Enzo II*, 599 F.3d at 1157 (emphasis added).

Plaintiffs contend that the Court should enter judgment in its favor on claims 67, 68, and 70 because the jury already found that the accused products infringed those claims, and that finding is not affected by the Federal Circuit's decision. (*See* Pls.' Mem. Supp. Mot. for Entry of J. [Doc. # 567] at 13.) According to Plaintiffs, the Federal Circuit construed only claim 1, leaving the scope of claims 67, 68, and 70 unchanged. (*See id.*) Although Plaintiffs acknowledge that under this theory, claims 67, 68, and 70 are broader than claim 1,[9] from which they depend, in violation of 32 U.S.C. § 112 ¶ 4,[10] they argue that Defendants have waived this defense by not raising it earlier, and that if the Federal Circuit thought otherwise, it would have remanded for a determination of invalidity rather than of infringement. (*See id.* at 14–16.) Indeed, Plaintiffs assert, in light of the Federal Circuit's mandate to determine "whether the accused product infringes," *Enzo II*, 599 F.3d at 1157, this Court does not have the discretion to take up invalidity (Pls.' Mem. Supp. at 23–27).

As further support for their reading of the Federal Circuit's decision, Plaintiffs note that while the Federal Circuit took issue with this Court's finding "that dependent claims 67, 68, and 70 . . . involved direct detection and therefore independent claim 1

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[9] The Federal Circuit construed claim 1 to cover indirect detection while under Plaintiffs' construction, claims 67, 68, and 70 cover direct detection.

[10] Under § 112 ¶ 4, "a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers."

must not be limited to indirect detection," *Enzo II*, 599 F.3d at 1156, on the grounds that "dependent claims cannot broaden an independent claim from which they depend," *id.*, under Defendants' interpretation, the Federal Circuit will have "'construe[d] away' that very limitation from the dependent claims it cited as having it" (Pls.' Reply [Doc. # 571] at 2–3).

Plaintiffs argue that their reading best comports with Federal Circuit precedent, citing *Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, in which the Federal Circuit held that where a dependent claim and the claim upon which it depends "deal with non-overlapping subject matter," the dependent claim should be held invalid, rather than be construed to cover the same subject matter as the claim upon which it depends. 457 F.3d 1284, 1291–92 (Fed. Cir. 2006). As Plaintiffs put it, "[i]nstead of holding that a circle is a square, the Court accepted that a circle is indeed a circle and held the claim invalid for improper dependency." (Pls.' Reply at 5.)

Defendants, for their part, urge the Court to "enter judgment of non-infringement" in their favor because "[t]he Federal Circuit held that none of 'the claims at issue' in this case covers direct detection" and there is no dispute that the accused products do not infringe a claim limited to indirect detection. (Defs.' Mem. Supp. Mot. Summ. J. [Doc. # 568-1] at 7.) In support of their reading of the Federal Circuit's decision, Defendants note that "[f]rom the first page of the Federal Circuit's decision to the last, the court treated the asserted claims collectively" (*id.* at 15), and discussed the language of claim 1 only after "explaining that '[c]laim 1 is representative' of the asserted claims'" (*id.* at 12 (quoting *Enzo II*, 599 F.3d at 1152); *see* Defs.' Opp'n Mot. for Entry J. [Doc. # 570] at 8–9). Moreover, in its conclusion, the court specifically held that "'[t]he

district court erred in construing the disputed claims of the patent-in-suit to cover both direct and indirect detection,'" again using the plural. (Defs.' Mem. Supp. at 15 (quoting *Enzo II*, 599 F.3d at 1157) (emphasis in Defs.' Mem. Supp. but not in original).)

Like Plaintiffs, Defendants call the Court's attention to the Federal Circuit's decision in *Pfizer*, but in support of the opposite conclusion. (*Id*. at 19.) Defendants maintain that if anything, *Pfizer* "demonstrate[s] the rigidity of the rule" that "'a dependent claim cannot be broader than the claim from which it depends'" (*id*. (quoting *Alcon Research Ltd. v. Apotex, Inc*., 687 F.3d 1362, 1367 (Fed. Cir. 2012)), even if "the dependent claim covers 'what might otherwise have been patentable subject matter" (*id*. (quoting *Pfizer*, 457 F.3d at 1292)). For this reason, Defendants argue, the Federal Circuit would not have interpreted the dependent claims in a way that made them broader than the claim upon which they depend. (*Id*. at 18; *see* Defs.' Opp'n at 9.)

Finally, Defendants argue that the Federal Circuit never addressed their alternative argument that if the '767 patent covers direct detection, it is invalid for lack of written description or for lack of enablement, indicating to them that the court was not holding that the patent covers direct detection. (Defs.' Mem. Supp. at 16; Defs.' Opp'n at 9–10.)

Although neither party's arguments successfully eliminate all ambiguity from the Federal Circuit's ruling, the Court finds Defendants' interpretation to be the more plausible of the two. It would be odd indeed for the Federal Circuit to continuously use the plural "claims" if it intended to refer only to claim 1. Further, although the conclusion Defendants urge does seem to be in tension with *Pfizer*'s warning that courts "should not rewrite claims to preserve validity," 457 F.3d at 1292 (internal quotation marks omitted),

the Court can conceive of no reason why the Federal Circuit would not have addressed Defendants' alternative arguments if its holding was not that all of the claims cover solely indirect detection. The Court therefore adopts Defendants' interpretation of the Federal Circuit's opinion, holding that the Federal Circuit intended its ruling to construe all of the claims at issue to cover only indirect detection. Because there is no dispute that the accused products utilize direct detection, and Plaintiffs do not claim infringement under a doctrine of equivalents theory with respect to claims 67, 68, and 70, judgment is entered in Defendants' favor on those claims.[11]

B. Claims 1 and 8

Turning to claims 1 and 8, both parties agree that "there is no literal infringement under the Federal Circuit's construction." (Pls.' Opp'n Defs.' Mot. Summ. J. [Doc. # 569] at 5.) Nonetheless, "Plaintiffs submit . . . that those claims are—even under that construction—infringed under the doctrine of equivalents." (*Id.*)

As a preliminary matter, the parties dispute whether Plaintiffs waived this argument by "drop[ping] [their] infringement theory that the accused products could be covered by claims limited to indirect detection" after the Court issued the Claim Construction Ruling. (Defs.' Mem. Supp. at 8.) Defendants contend that "[i]f Enzo believed . . . that direct detection was an equivalent of indirect detection, it could have disclosed its view, compiled any evidence in support, offered expert testimony, and sought to moot the claim-construction issue that it knew was heading for post-trial appellate review." (*Id.*) However, as Plaintiffs argue in response, and as Defendants

[11] For this reason, the Court does not reach Defendants' contention that the claims are invalid, nor Plaintiffs' assertion that Defendants have waived this defense.

appear to acknowledge in their Reply,[12] when the Federal Circuit addressed this very issue in *Exxon Chemical Patents, Inc. v. Lubrizol Corp*., 137 F.3d 1475 (Fed. Cir. 1998), it held that in circumstances similar to these, the plaintiff was not barred from raising a doctrine of equivalents argument, writing:

> Contrary to Lubrizol's suggestion, Exxon cannot be charged with having abandoned its doctrine-of-equivalents theory of liability by not submitting it to the jury or raising it on the previous appeal. Once the district judge construed the claim language in Exxon's favor, the doctrine-of-equivalents issue in the case became moot. Exxon could not realistically be expected to request alternative jury instructions asking for an advisory verdict on whether the patent would be infringed under the doctrine of equivalents on Lubrizol's proposed claim construction. Nor could Exxon, as appellee, have been expected to defend the judgment in its favor on the basis of a theory of liability that was never given to the jury. The question whether there could be doctrine-of-equivalents infringement under the claim construction adopted by this court became a critical issue in the case only after this court's decision on appeal. For that reason, this court did not address the merits of Exxon's claim that it is entitled to a new trial on infringement under the doctrine of equivalents, and the district court therefore erred in concluding that it was barred by this court's mandate from considering Exxon's new trial motion.

Id. at 1478–79 (internal citations omitted). For substantially the same reasons as recited by the Federal Circuit in *Exxon*, this Court finds that Plaintiffs are not barred from asserting a doctrine of equivalents theory.

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[12] In their Reply, rather than continuing to pursue the theory that Plaintiffs waived the doctrine of equivalents argument by failing to raise it earlier, Defendants contend that "[t]he Court should bar Enzo from asserting the doctrine of equivalents because Enzo waived that argument by not asserting it in its own motion." (*See* Defs.' Reply [Doc. # 572] at 9.) This argument, however, for which Defendants cite no authority, does not appear to have any basis in law. The Court is aware of no rule of law prohibiting a party from arguing that summary judgment should not be entered in its opponent's favor on a particular issue while not seeking judgment in its own favor on that issue.

To infringe by equivalence, an accused product or process must "contain elements identical or equivalent to each claimed element of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 40 (1997). "A finding of infringement under the doctrine of equivalents requires a showing that the difference between the claimed invention and the accused product or method was insubstantial or that the accused product or method performs the substantially same function in substantially the same way with substantially the same result as each claim limitation of the patented product or method." *AquaTex Indus., Inc. v. Techniche Sols.*, 479 F.3d 1320, 1326 (Fed. Cir. 2007). The "function, way, result inquiry focuses on an examination of the claim and the explanation of it found in the written description of the patent." *Id.* (internal quotation marks omitted).

Plaintiffs contend that summary judgment should not be granted in Defendants' favor as to claims 1 and 8 because there is a genuine dispute of material fact as to whether indirect and direct detection are insubstantially different such that the accused products infringe the '767 patent by equivalence. (*See* Pls.' Opp'n at 5, 11–12.) Relying on the declaration of their expert, Dr. Richard Sinden, Plaintiffs argue that:

> among the problems addressed in the '767 patent are those directed to signal strength and amplification. To detect labeled nucleotides, the "signal" from the label must be strong enough to come within the detection threshold of whatever method is applied to detect it. In order to do that, these signals are typically "amplified" by a variety of techniques, several of which are disclosed in the patent. One of these techniques is indirect detection, i.e., reacting the "A" of claim one with something that yields a stronger signal. Examples of that "something" include antibodies and avidin, the latter of which was known to form strong complexes with biotin, a preferred example of indirectly detection "A." . . .

> Much like the patent's proposed addition of avidin to amplify the signal of a biotinated nucleotide, the accused products also employ materials extraneous to the labeled nucleotides to amplify their signal yield. All of the accused BigDye and dRhodamine kits include polymerase chain reaction (PCR) enzymes. These enzymes amplify the fluorescent signal from DNA sequences labeled with the dye terminators by increasing the concentration of those sequences. The differences between this amplification and the avidin/biotin amplification of the patent's preferred example is that it works by increasing the concentration of molecules producing the signal rather than the signal strength for an individual molecule. . . . As to the indirectly-detectable "A" of claim one, the use of PCR to amplify the signal of DNA sequences labeled by the fluorescent dye terminators in the accused products serves the same function (to make the signal detectable by the methodology employed), in ways that differ insubstantially (increasing concentration vs. increasing strength), to yield the identical result (a detectable signal).

(*Id*. at 11–12 (internal citations omitted).)

Defendants respond that no reasonable jury could find that indirect detection is insubstantially different from direct detection, and summary judgment should therefore be granted in their favor. Specifically, they argue that: (1) Dr. Sinden's theory is "scientific gibberish," as the biotin in the invention "gives off no signal;" rather, "[i]t is the avidin that is detected, after complexing with biotin," and therefore, contrary to Dr. Sinden's declaration, avidin does not "amplify a detectable signal from biotin" (Defs.' Reply at 9–10); (2) the '767 patent does not claim and did not invent signal-amplification techniques (*id*.); and (3) there are fundamental differences between direct and indirect detection (*id*. at 11).

The Court finds Defendants' arguments persuasive. Consistent with the Federal Circuit's understanding of the patent as describing "how 'A,' a biotin, iminobiotin, or lipoic acid, forms a detectable unit, i.e., a signaling moiety, upon interaction with avidin

or antibodies," *Enzo II*, 599 F.3d at 1155, Dr. Sinden himself testified that "[b]iotin in itself doesn't generate a signal that's detectable" (Sinden Dep., Ex. 1 to Defs.' Reply at 7). Because that is so, it would not be accurate to describe indirect detection as a method of signal amplification.

Nor does the patent describe it this way. Rather, 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. *Enzo II*, 599 F.3d at 1155 (quoting '767 Pat. 3:5–13). Although the specification does mention signal amplification in a few places (*see, e.g.*, '767 Pat. 22:23–54), as Dr. Sinden acknowledged in his deposition, the patent does not disclose techniques for signal amplification, but rather "utilize[s] technologies that have been around that do amplify signal" (Sinden Dep. at 9). In Dr. Sinden's words, the claimed invention is not directed so much at improving the "strength of the signal" as improving methods of "signal generation and detection." (*Id.*)

As Defendants aptly note, "[a]n alternative to the claimed invention specifically criticized in the specification for problems that the invention purports to overcome cannot be an 'equivalent' to the invention itself." (Defs.' Mem. Supp. at 28.) Indeed, the Federal Circuit has left no doubt that methods or structures "[s]pecifically identified, criticized, and disclaimed" in a specification cannot later be relied upon as equivalents. *Gaus v. Conair Corp.*, 363 F.3d 1284, 1291 (Fed. Cir. 2004) (internal quotations marks omitted). Because "the specification's only discussion of direct detection, here radioactive labeling, was exclusively in the context of discussing how indirect detection is a superior method," and "[t]he specification not only discusses the limitations and drawbacks of

using radioactive labeling, but states that the claimed compounds can be used 'as an alternative to radioisotopes for detection and localization,'" *Enzo II*, 599 F.3d at 1155 (quoting '767 Pat. 3:5–13), Plaintiffs cannot now claim that indirect and direct detection are insubstantially different, and no jury could so find.[13] Summary judgment is therefore granted in Defendants' favor on claims 1 and 8.

III. Conclusion

For the foregoing reasons, Plaintiffs' Motion [Doc. # 566] for Entry of Judgment on the Current Jury Verdict is DENIED, and Defendants' Motion [Doc. # 568] for Summary Judgment is GRANTED. Judgment is entered in Defendants' favor. The Clerk is directed to close this case.

IT IS SO ORDERED.

/s/
Janet Bond Arterton, U.S.D.J.

Dated at New Haven, Connecticut this 22nd day of February 2016.

[13] Because the Court grants Defendants summary judgment on claims 1 and 8, it does not reach Defendants' contention that claim 1 does not cover mononucelotides. (*See* Defs.' Mem. Supp. at 27–30.)