

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)

September 17, 2012

RULING ON CROSS-MOTIONS FOR SUMMARY JUDGMENT

Plaintiffs Enzo Biochem, Inc., Enzo Life Sciences, Inc., and Yale University (collectively, “Enzo”) allege patent infringement under 36 U.S.C. §§ 271, *et seq.*, against Defendants Applera Corp. and Tropix Inc. (collectively “Applera”) with respect to claims 1, 8, 67, 68, and 70 of U.S. Patent No. 5,449,767 (‘767 patent). Plaintiffs move for summary judgment on the basis of infringement [Doc. # 168], and Defendants cross-move for summary judgment of noninfringement as to the ‘767 patent [Doc. ## 176, 315].¹ For the reasons that follow, both motions will be denied.

¹ Defendants’ motion [Doc. # 172] for partial summary judgment of laches has been addressed in a separate ruling. (*See* Ruling on Applera Corp.’s Motion for Partial Summary Judgment of Laches [Doc. # 418].)

Enzo has moved to strike [Doc. # 321] Applera’s summary judgment motion on the ground that it is untimely and improper. However, in the July 12, 2011 status conference, the Court permitted Applera to supplement its briefings on noninfringement (*See* Ex. A to Pl.’s Mot. to Strike [Doc. # 322–1]), and all parties agreed to this disposition. Thus, Plaintiffs’ motion to strike is DENIED.

I. Background

This suit was filed in 2004, and the Court presumes the parties' familiarity with the facts underlying Plaintiffs' claims of patent infringement. Briefly, Enzo's patents-in-suit are directed to various techniques for labeling and detecting nucleic acids such as DNA and RNA. The inventors of the patents-in-suit developed a series of nucleotide probes that do not rely on traditional radioactive labels, which though successful, have "drawbacks," including that radioactive labels are "potentially hazardous," "expensive to purchase and use," and "often very unstable." '824 patent col.1 1134-45. The '824 and '767 patents were directed to the development of non-radioactive labels. The claims of the '824 and '767 patents are directed to a "compound," or a method of using that compound as a detection probe. *Enzo Biochem, Inc. v. Applera Corp.*, 599 F.3d 1325, 1329 (Fed. Cir. 2010). In this compound, a nitrogenous base "B" is covalently attached, either directly or indirectly through a "linkage group" to a chemical moiety, or a functional group within a molecule, "A." *Id.* The Court granted summary judgment in favor of Applera in 2007 (Ruling on Summary Judgment of Invalidity [Doc. # 261]), holding that all asserted claims of the '824 patent, the '767 patent, and the '928 patent were invalid on the basis of indefiniteness or anticipation, and that the '830 patent was not infringed.

In 2010, the Federal Circuit reversed as to the '824 and '767 patents, concluding that their claims were not indefinite, and that genuine issues of material fact existed as to Defendants' anticipation defense. *Enzo Biochem, Inc. v. Applera Corp.*, 599 F.3d 1325 (Fed. Cir. 2010). After the Federal Circuit's ruling the claims that remained in dispute were claims 1, 18, 19, 21, 26, 28, 32, and 33 of U.S. Patent No. 5,328,824 ("the '824 patent") and claims 1, 2, 8, 11, 13, 42, 46-51, 67, 68, and 70 of U.S. Patent No. 5,449,767 ("the '767 patent"). On

May 8, 2012, Plaintiffs advised the Court that they were withdrawing their claim of infringement as to the '824 patent, and withdrawing their infringement claims as to claims 2, 11, 13, 42, 46, 47, 48, 50, 51 of the '767 patent, leaving only claims 1, 8, 67, 68, and 70 of the '767 patent for adjudication. (*See* Joint Motion for Entry of Stipulated Partial Judgment of U.S. Patent No. 5,328,824 [Doc. # 382]; Stipulation Regarding U.S. Patent No. 5,44,767 [Doc. # 383].)

II. Legal Standard

Summary judgment is appropriate when, after opportunity for discovery and upon motion, there is no genuine dispute of material fact for trial and one party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c). Summary judgment must be granted against a party who has failed to introduce evidence sufficient to establish the existence of an essential element of that party's case, on which the party will bear the burden of proof at trial. *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986). The summary judgment movant, however, has the initial responsibility of identifying the legal basis of its motion, and of pointing to those portions of the record that it believes demonstrate the absence of a genuine issue of material fact. *Id.* at 323. Once the movant has made this showing, the burden shifts to the nonmovant to designate specific facts showing that there is a genuine issue for trial. *Id.* at 324.

In an action for patent infringement, literal infringement of a claim is found only “when every limitation recited in the claim appears in the accused device, i.e., when ‘the properly construed claim reads on the accused device exactly.’” *DeMarini Sports, Inc. v. Worth, Inc.*, 239 F.3d 1314, 1331 (Fed. Cir. 2001). As to indirect, “induced infringement,” “[w]hoever actively induces infringement of a patent shall be liable as an infringer.” 35

U.S.C. § 271(b). To prove liability for induced infringement, a plaintiff must show the existence of direct infringement by some party, *see Golden Blount, Inc. v. Robert H. Peterson Co.*, 438 F.3d 1354, 1362 (Fed. Cir. 2006), and that the accused inducer intended to encourage another's infringement, *DSU Med. Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006).

“Since the ultimate burden of proving infringement rests with the patentee, an accused infringer seeking summary judgment of noninfringement may meet its initial responsibility either by providing evidence that would preclude a finding of infringement, or by showing that the evidence on file fails to establish a material issue of fact essential to the patentee's case.” *Novartis Corp. v. Ben Venue Laboratories, Inc.*, 271 F.3d 1043, 1046 (Fed. Cir. 2001) (citing *Vivid Tech., Inc. v. American Sci. & Eng'g, Inc.*, 200 F.3d 795, 807 (Fed. Cir.1999)). “Summary judgment of noninfringement may only be granted if, after viewing the alleged facts in the light most favorable to the nonmovant and drawing all justifiable inferences in the nonmovant's favor, there is no genuine issue whether the accused device is encompassed by the patent claims.” *Id.* (citing *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1304 (Fed. Cir.1999)).

III. Discussion

Both parties have moved for summary judgment as to the '767 patent: Plaintiffs move on the basis of infringement, and Defendants cross-move on the basis of noninfringement, arguing that the Federal Circuit's 2010 decision requires Plaintiffs to come forward with additional evidence of no substantial interference to succeed on their infringement claim.²

² It bears noting that because Plaintiffs filed their motion for summary judgment of infringement in 2007, they obviously did not have the benefit of the Federal Circuit's 2010

The Court first addresses the relevant claim limitations of the '767 patent and Plaintiffs' motion for summary judgment of infringement prior to addressing the 2010 ruling and Defendants' motion for summary judgment of noninfringement on the "not interfering substantially" claim limitation.

A. The Claims Limitations of the '767 Patent

Plaintiffs argue that both of Defendants' dye terminators read on the following "representative" claim limitations of the '767 patent, which are the sole claims that remain for adjudication:

1. An oligo- or polynucleotide containing a nucleotide having the structure: [diagram]

wherein B represents a 7-deazapurine or a pyrimidine moiety covalently bonded to the C1'-position of the sugar moiety, provided that whenever B is a 7-deazapurine, the sugar moiety is attached at the N9 -position of the 7-deazapurine, and whenever B is a pyrimidine, the sugar moiety is attached at the N1-position of the pyrimidine;

wherein A comprises at least three carbon atoms and represents at least one component of a signaling moiety capable of producing a detectable signal; wherein B and A are covalently attached directly or through a linkage group that does not substantially interfere with the characteristic ability of the oligo- or polynucleotide to hybridize with a nucleic acid and does not substantially interfere with formation of the signalling moiety or detection of the detectable signal, provided also that if B is 7-deazapurine, A or the linkage group is attached to the 7-position of the deazapurine, and if B is pyrimidine, A or the linkage group is attached to the 5-position of the pyrimidine;

ruling and reasoning.

wherein one of x and y represents [diagram]; and the other of x and y is absent or represents —OH or —H; and wherein z represents H— or HO—.

67. An oligo- or polynucleotide of claim 1 or 48 wherein A comprises an indicator molecule.
68. An oligo- or polynucleotide of claim 67 wherein said indicator molecule is fluorescent, electron dense, or is an enzyme capable of depositing insoluble reaction products.
70. An oligo- or polynucleotide of claim 68 wherein the fluorescent indicator molecule is selected from the group consisting of fluorescein and rhodamine.

'767 Patent, Claims 1, 67, 68, 70.

In Applera's method of automated DNA sequencing using dye terminators, each of the four terminators is tagged with a different fluorescent dye. ("Automated DNA Sequencing," Ex. 12 to Perez Decl. at AP0002487.) During the amplification phase (i.e., cycle sequencing), the growing chain is simultaneously terminated and labeled with the dye that corresponds to that base. (*Id.*) Applera's DNA sequencing instruments detect fluorescence from four different dyes that are used to identify the A, C, G, and T extension reactions, and each dye emits light at a different wavelength when excited by an argon ion laser. (*Id.* at AP0002485.) Applera's dye terminators are incorporated into polynucleotide extension productions (*see* Declaration of Dr. Sinden [Doc. # 170] ¶ 86), and this incorporation permits the detection of the polynucleotides during the separation and detection phase of DNA sequencing (*id.* ¶ 105; "Automated DNA Sequencing" at 0002485).

Plaintiffs appear to have provided an undisputed record as to each limitation of Claim 1 of the '767 patent, except the "not substantially interfere" limitation of claim 1,

which Defendants dispute is met by their products. (*See* Def.'s Loc. R. 56(a)2 Stmt [Doc. # 219) ¶¶ 2, 4.]

In support of their argument for infringement, Plaintiffs have pointed to statements made by Defendants' experts describing the Defendants' products. Dr. Stephen Menchen testified that:

When we went through the screening process to evaluate these, we were trying to optimize the peak patterns in the activity based on the structural changes in the dye, the linker, and the base. And what we found was that when we left the EO out on the ddA, we got a better pattern and better activity with that dye compared to having the EO there. . . . [I]n order to determine DNA sequence, you have to have a signal at every base, at every extension product. And the signal that you get has to be roughly equivalent to the signal that came before and came after in order to evaluate those peaks. Sometimes we'll see cases where we see no signal at all so that we need even peak heights in order to determine the sequence. And the more even the peak heights, well, that's what we're after. And that's how these were designed, to optimize that.

(Menchen Dep. at 70:3–25.) Dr. Menchen also testified that “three of the four dRhodamine terminators use the new ethylene oxide EO linker to attach the dye to the dideoxy nucleotide. This improves incorporation of the dye–label terminators.” (*Id.* at 73:4–12.)

Defendants' expert Dr. David Cassel testified:

So we had been evaluating some number of chemical linkages, covalent linkages between the heterocyclic base of the dideoxy nucleoside triphosphate and the fluorescent dye. And the choice of that linker strongly affects sequencing performance. . . . When you take a dideoxy nucleotide triphosphate and hang a linker and dye off of it covalently, and incorporate that into a piece of DNA, that has a significant impact on the electrophoretic mobility of that piece of DNA, so that in your analysis at the end when you're running a DNA sequencer and these fragments are moving past the detector, there can be big, big shifts in how fast the different fragments moved.

(Cassel Dep., Ex. 10 to Perez Decl. at 96:18-98:21).

In Applera's d-Rhodamine and BigDye terminators, the base and signalling moiety are covalently attached through an ethylene oxide (EO) linkage group. (Sinden Decl. at ¶ 71; B.B. Rosenblum, *et al.*, "New dye-labeled terminators for improved DNA sequencing patterns," *Nucleic Acids Research* (1997), Ex. 13 to Perez Decl. at AP049693–694; Menchen Dep. at 85:21–87:3.) Plaintiffs assert that as it functions, the EO linkage group does not substantially interfere with hybridization or detection of the fluorescent signal, pointing to the *Nucleic Acids Research* article as evidence, which states: "[a]gain, we chose the dye set which maximized the evenness of the peaks in the sequencing pattern and minimized the dye-related mobility effects." (Rosenblum, Ex. 13 to Perez Decl. at AP049693–694.) Defendants, in opposition, contend that while it is critical that their terminators "have similar performance attributes and that these attributes remain constant throughout the sequence; *it is not critical that none of them affect incorporation or hybridization.*" (Menchen Decl. ¶ 9 (emphasis added).) Dr. Menchen also opines that "the addition of linkers . . . does in fact interfere with the ability of these terminators to be incorporated into nucleotide chains as well as affect the ability of polynucleotides incorporating the modified nucleotides to hybridize with complementary nucleotides." (*Id.* ¶ 7.)

Neither Plaintiffs nor Defendants, nor their experts, explain whether functioning "at similar and constant levels" (Menchen Decl. ¶ 4) means "no substantial interference," thereby satisfying the claim limitation, or whether the degree to which Menchen opines that the linkers "interfere" would be substantial or not.

B. Infringement of the No Substantial Interference Claim Limitation

The relevant portion of claim 1 specifies, "wherein B and A are covalently attached directly or through a linkage group that *does not substantially interfere* with the characteristic

ability of the oligo– or polynucleotide to hybridize with a nucleic acid and *does not substantially interfere* with formation of the signalling moiety or detection of the detectable signal.” (’67 Patent, claim 1 (emphasis added).) The Court construed this term to mean that “the linkage group neither substantially interferes with the ability of the compound to hybridize with the nucleic acid nor substantially interferes with the ability of A to be detected.” Claim Construction, 2006 WL 2927500, at *6. Plaintiffs’ infringement argument is that BDT’s nitrogenous base B is covalently attached to the A moiety through a linkage group that does not substantially interfere. Defendants respond that the BDT and dRT do in fact “affect” the incorporation of nucleotides during hybridization, and therefore do not satisfy the limitation, and further, that based on Applera’s interpretation of the Federal Circuit’s 2010 ruling, they are entitled to summary judgment of noninfringement.

In support of their motion for summary judgment of infringement, Enzo’s expert Dr. Sinden opined that the linkage group connecting the BigDye moiety (“A”) to the 5–position of the pyrimidine base (“B”) “is *designed so that it does not interfere with the ability of the oligo– or polynucleotide containing the labeled nucleotide to hybridize with a complementary nucleic acid or with detection of the detectable signal.*” (Sinden Decl. ¶ 67 (emphasis added).)

Enzo claims infringement based on the propargyl ethoxyamino (EO) linker used in the BDT and drT terminators, which it asserts was designed and proved not to substantially interfere with hybridization or detection of the signal. The Rosenblum article in *Nucleic Acids Research* describing the BDT states that Applera “chose the dye set which maximized the evenness of the peaks in the sequencing pattern and minimized the dye–related mobility effects.” (Rosenblum at AP049694.)

As was discussed in the Rosenblum article, Defendants' experts also emphasized the importance of optimizing the evenness of the "peak patterns" in their depositions. Dr. Steven Menchen, who worked on developing the Applera products, testified that the ddA terminator was not paired with the EO linker because Applera was:

trying to optimize the peak patterns in the activity based on the structural changes in the dye, the linker, and the base. And what we found was that when we left the EO out of the ddA, we got a better pattern and better activity with that dye compared to having the EO there.

(Menchen Dep. at 70.) He also stated that "in order to determine DNA sequence, . . . the signal that you get has to be roughly equivalent to the signal that came before and came after in order to evaluate these peaks." (*Id.*) Jonathan Cassel, who like Menchen worked on developing Applera's terminator products, further testified that the choice of which linker to pair with a dye terminator has a "profound effect on sequencing performance" and "effects [sic] electrophoretic mobility significantly," thereby affecting the overall DNA sequencing process. (Cassel Dep., Pls. Ex. 10, at 96–98.) Testing by Applera researchers revealed that the "better peak evenness" of the dRT and BDT resulted in improved DNA "sequencing accuracy." (Rosenblum at AP049695.)

In opposition to Plaintiffs' motion, Applera maintains that there is a difference between "evenness" of terminator performance, as required for DNA sequencing, and the question of "interference" with DNA hybridization and incorporation. Defendants explain that their terminator products are each comprised of a set of four dye-labeled dideoxynucleotides (ddA, ddC, ddT, ddG) (corresponding to the four DNA bases (A, C, T, and G)), and that while the latter three use an EO linker group, the ddA terminator uses a propargyl amino ("PA") linker group in order to maintain evenness of peak patterns. (Def.

Opp'n Mem. at 13 n.5; Kricka Non-Infr. Decl. ¶ 17.) Applera also asserts that “Enzo fails to explain, under its theory, how the EO linker meets the claim limitation given that this linker was shown to be unsuitable for at least one of the four dye-labeled terminators,” (Def. Opp'n at 15), citing to the same excerpts of the Menchen and Cassel depositions, *supra*, as referring to only sequencing.

Dr. Menchen also opines that “it is entirely permissible for the terminators to affect both hybridization and incorporation as long as they do so equally as compared to one another” to facilitate DNA sequencing. (Menchen Decl. ¶ 9.) He contends that while evenness is required to perform sequencing reactions, the addition of the linkers in BDT and drT “interfere with the ability of these terminators to be incorporated into nucleotide chains as well as affect the ability of polynucleotides incorporating the modified nucleotides to hybridize with complementary nucleotides.” (*Id.* ¶¶ 7, 13, 14; Shaheer H. Khan, “Dye Terminator Chemistry: Effects of Substrate Structure on Sequencing Analysis,” at AP170368 (“[W]e have studied the effects of combinations of base, dye, and dye linkage on terminator incorporation during sequencing”).) Dr. Menchen further states:

[I]n my experience the addition of groups linking fluorescent dyes to nucleotides *generally interferes* with the ability of those nucleotides to be recognized and incorporated by DNA polymerases and also affects hybridization of oligonucleotides prepared with the modified nucleotides to a complementary polynucleotide.

(Menchen Decl. ¶¶ 4, 9 (emphasis added).) Defendants note that the difference between these linkers is not discussed by Dr. Sinden, and argue that his statements are conclusory and cannot prove the “not interfering substantially” limitation.³

³ Plaintiffs attack Defendants' linkage group-based argument as made “too late in the game,” given that Applera has supplemented its non-infringement contentions three times,

As discussed above, in rebuttal to Dr. Sinden’s conclusion of no substantial interference, Dr. Menchen states that use of linkers like the EO and PA used in Applera’s terminator products “does in fact interfere with the ability of these terminators to be incorporated into nucleotide chains as well as *affect[s]* the ability of polynucleotides incorporating the modified nucleotides to hybridize with complementary nucleotides.” (Menchen Decl. ¶ 7 (emphasis added).) Thus, Plaintiffs’ argument that “Applera’s dye terminators contain a nitrogenous base, B, covalently attached to the A moiety through a linkage group which does not substantially interfere with hybridization or detection of the signal” (Pl.’s Mem. Supp. [Doc. # 169] at 27 (citing Sinden Decl. ¶ 67; Menchen Dep., Ex. 9 to Perez Decl. at 70:3–25, 73:4–12)), while stating their conclusion, does not show an absence of a material factual dispute. Indeed, as support for their argument, Plaintiffs cite to Dr. Menchen’s deposition testimony that they were “trying to optimize the peak patterns in the activity based on the structural changes in the dye, the linker, and the base” (Menchen Dep. at 70:3–8), and “in order to determine DNA sequence, you have to have a signal at every base, at every extension product” (*id.* at 70:15–17). However, Dr. Menchen’s testimony does

and not once has it ever contended that its linkage groups did not meet the ‘not substantially interfering’ claim limitation.” (Pls. Reply Mem. at 3.) The cases Plaintiffs cite in support of this undue delay argument, however, come from the Federal Circuit on appeal from the Northern District of California, which has local rules specifically requiring disclosure within certain a timeframe of infringement arguments. See *Safeclick, LLC v. Visa Int’l Serv. Ass’n*, 2006 WL 3017347 (Fed. Cir. 2006); *02 Micro Int’l Ltd. v. Monolithic Power Sys, Inc.*, 467 F.3d 1355 (Fed. Cir. 2006). The local rule–specific holdings of these cases, therefore, are not binding authority in this district, where no such rules were in effect. However, Plaintiffs’ argument fails even if cast in terms of generalized delay, for Defendants represented to Plaintiffs on February 26, 2007 in their Third Supplemental Response to Interrogatory No. 4: “Enzo has provided no evidence, nor can it, that the linkers utilized in Applera’s BigDye and dRhodamine terminators meet the claim limitation of having no ‘substantial interference’ with hybridization and/or detection.” (Def. Third Supplem. Resp., Ex. 2 to Pls.’ Reply at 9.) Thus, over Plaintiffs’ objection, the Court will consider Defendants’ argument.

not provide evidence that would enable a reasonable juror to conclude, without more, that “optimizing the peak patterns” and “having a signal at every base” in the accused products means that such products do not substantially interfere with hybridization or detection of the signal, thus satisfying the claim limitation.

Viewing the record in the light most favorable to the non-moving party, Defendants’ evidence that the linkers used in its products were designed at least in part to even out interactions for purposes of DNA *sequencing* (and not hybridization) may be found to contradict Dr. Sinden’s opinion that the linkage group does not substantially interfere with hybridization or detection, such that Plaintiffs are not entitled to judgment as a matter of law. Plaintiffs’ motion, and Defendants’ opposition, both suffer from a certain obscurity in their experts’ opinions, such that the Court cannot determine whether “peak patterns” or Defendants’ desire to “even[] out interactions” could satisfy the “no substantial interference” claim limitation. Therefore, Plaintiffs’ motion for summary judgment of infringement as to Claim 1 of the ‘767 Patent must be denied. Claims 8, 67, 68, and 70 depend on Claim 1, therefore Plaintiffs’ motion for summary judgment of infringement is also denied as to these dependent claims.

C. Impact of the 2010 Federal Circuit Ruling and Applera’s Motion for Summary Judgement of Noninfringement

In its 2007 opposition to Enzo’s summary judgment motion on infringement, and in support of its current summary judgment motion, Defendants maintained that the claims of the ‘767 patent were indefinite and this Court agreed. (*See* Defs.’ Opp’n at 2.) On appeal, the Federal Circuit rejected this conclusion and found that the targeted limitation, “not interfering substantially,” was sufficiently definite to support an infringement claim. Relying on that opinion, Defendants now assert that because Plaintiffs have not offered any evidence

showing the accused products' lack of "substantial interference" in "view of the guidance provided by the Federal Circuit's decision" (*See* Defs.' Mem. Supp. [Doc. # 315–1] at 1), Defendants are entitled to summary judgment as to the '767 patent on non–infringement grounds.

"Indefiniteness requires a determination whether those skilled in the art would understand what is claimed," applying general principles of claim construction. *Enzo*, 599 F.3d at 1332. The Federal Circuit disagreed that a person of ordinary skill in the art would not know how to determine whether a linkage group substantially interferes with hybridization:

As used in the phrase "not interfering substantially," the word "substantially" denotes language of magnitude because it purports to describe *how much* interference can occur during hybridization, i.e., an insubstantial amount of interference. . . . The claims in this case provide at least some guidance as to how much interference will be tolerated.

Id. at 1333–34 (emphasis in original) (internal citations omitted). The "guidance" provided by the '767 claim limitation includes: the specific language of the structure recited in the dependent claim, e.g., "the term 'not interfering substantially' in the independent claims allows for at least as much interference as that exhibited when the linkage group has the structure specified in the dependent claims," *id.* at 1334 (citing '767 patent col.31 ll.38–40); the examples provided in the specification of "suitable linkage groups," *id.* (citing '767 patent col.9 ll.1–5); the polynucleotides' "thermal denaturation profiles and hybridization properties," which "can be used to measure the degree to which a linkage group interferes

with hybridization,” *id.* at 1334–35 (citing ‘767 patent col.19 ll.9–14); and the prosecution history of the ‘767 patent.⁴ *id.*

Considering this intrinsic evidence, the Federal Circuit concluded that there was “a general guideline and examples sufficient to enable a person of ordinary skill in the art to determine the scope of these claims,” *id.* (citing *In re Marosi*, 710 F.2d 799, 803 (Fed. Cir. 1983)), and that “the claims are not indefinite even though the construction of the term ‘not interfering substantially’ defines the term without reference to a precise numerical measurement.” *Id.* In Defendants’ motion for summary judgment of noninfringement, they argue that the Federal Circuit had specified that there was an additional “requirement” that Plaintiffs must perform a “comparison between the accused product and the examples in the patent specification.” (Defs.’ Mem. Supp. at 3.) However, contrary to Defendants’ contention, the Federal Circuit did not expressly hold that any specific test or evidence is required in order to show whether the “not interference substantially” claim limitation is met. The Federal Circuit opinion stated that “when a ‘word of degree’ is used, the court must determine whether the patent provides ‘some standard for measuring that degree,’” *Enzo*

⁴ The Federal Circuit also considered the prosecution history of the Ward Patents as part of its examination of the “intrinsic evidence,” and found it relevant to its conclusion that the “not interfering substantially” limitation was not indefinite:

Before the U.S. Patent and Trademark Office (“PTO”), Enzo overcame an indefiniteness rejection over the “not interfering substantially” language by submitting a declaration under 37 C.F.R. § 1.132, which was signed by its vice president, Dr. Engelhardt . . . , listing eight specific linkage groups that Enzo declared did not substantially interfere with hybridization or detection. Among the named linkage groups was –CH=CH–CH₂–NH (the same group recited in the patents’ dependent claims) . . . [b]ased on this submission, the examiner withdrew the indefiniteness rejection.

Id. at 1335.

Biochem, Inc. v. Applera Corp., 599 F.3d 1325, 1332 (Fed. Cir. 2010) (citing *Seattle Box Co., Inc. v. Indus. Crating & Packing, Inc.*, 731 F.2d 818, 826 (Fed. Cir. 1984)), and concluded, while not providing an exhaustive list, that there were, in fact “standards for measuring [the] degree” of “not interfering substantially” with respect to the ‘824 and ‘767 patent language. It seems unlikely that the Federal Circuit intended that any particular standard for measuring the degree of interference, of the several enumerated in the opinion, would be a requirement for proving satisfaction of that claim limitation, absent any language in the opinion to that effect. Thus, the Federal Circuit’s decision is not read to require any specific type of proof in order to satisfy the “not interfering substantially” claim limitation of the ‘767 patent. Defendants argue that Plaintiffs had to have proffered evidence of the “thermal denaturation profiles and hybridization properties” that the Federal Circuit said “can be used to measure the degree to which a linkage group interferes with hybridization,” *see* 599 F.3d at 1334, and that Plaintiffs’ failure to show evidence of the degrees of interference is fatal to their claims of infringement. (Defs’ Mem. Supp. [Doc. # 315–1] at 11–12.) However, this ground for Applera’s motion for summary judgment of noninfringement of the “no substantial interference” claim limitation depends on its reading of the 2010 Federal Circuit opinion which the Court rejects; that is, that the Federal Circuit required a “comparative test” in order to determine substantial interference. (Defs.’ Mem. Supp. at 14.)

As discussed *supra*, the Court concludes that evidence of “thermal denaturation profiles and hybridization properties,” while something that “a person of ordinary skill would likely look to,” 599 F.3d at 1325, is not required to prove infringement. Thus, the fact that Plaintiffs have not come forward with this particular type of evidence does not entitle

Defendants to judgment as a matter of law.⁵ The degree to which the accused products do or do not “substantially interfere” with hybridization or detection, while performing as intended, remains a triable issue of fact for the jury. Accordingly, Defendants’ motion for summary judgment of non–infringement is denied.

D. Indirect Infringement

Plaintiffs move for summary judgment on the basis of indirect infringement, arguing that Defendants induced their customers to infringe Claims 1, 67, 68, and 70 of the ‘767 patent by selling kits containing dye terminator. (Pls’ Mem. at 35.) Defendants also cross–move for summary judgment of non–indirect–infringement, asserting that the sale of non–dye terminator products cannot constitute indirect infringement of the ‘767 patent.

Because the Court has determined that summary judgment on the Plaintiffs’ claim of infringement is not warranted, the issue of induced infringement also must be left for trial. *See Met–Coil Sys. Corp. v. Korners Unltd., Inc.*, 803 F.2d 684, 687 (Fed. Cir. 1986) (“Absent direct infringement of the patent claims, there can be neither contributory infringement, nor inducement of infringement.”) (internal citations omitted).

As to Defendants’ 2007 cross–motion asserting non–indirect–infringement as to the related product lines of “thermal cycling device[s],” “software, filter sets, run modules, dye set/primer (mobility) files, instrument (matrix) files, sequencing standards, matrix standards, separating polymers, filter wheels, protocols, user manuals, and the like” (‘767

⁵ In addition, Applera’s in–house counsel, as early as 1995, apparently acknowledged that the ‘767 patent covered DNA sequencing technology, in his letter to the Patent Trade Office in which he stated that claim 195 of Patent Application No. 886,660 (ultimately, Claim 1 of the ‘767 patent) “covers fluorescently labeled DNA sequencing fragments . . . a key component *in all presently and foreseeably available automated DNA sequencing procedures and instruments*—that is, a fundamental technology upon which *all genome sequencing projects rely*.” (Ex. 8 to Perez Decl. at GT0008335 (emphasis added).)

Patent Infringement Charts, Defs.' Mot. Ex. 4–D), Applera states that “DNA sequencers and other laboratory equipment cannot be covered by [the ‘767] patent,” which is “limited on [its] face to ‘[a]n oligo– or polynucleotide’ having a defined structure” (*id.* (citing ‘767 Patent Claim 1)).

So long as “purposeful, culpable expression and conduct” is evinced by the infringer, steps taken “to encourage direct infringement, such as advertising an infringing use or instructing how to engage in an infringing use, show an affirmative intent that the product be used to infringe.” *DSU Med. Corp. v. JMS Co., Ltd.*, 471 F.3d 1293, 1305–06. Thus, as it is undisputed that the “related software, filter sets, run modules,” etc., are made and sold by Applera specifically for use with the BDT and rDT kits, they could be the basis for liability based on induced infringement, provided that direct infringement is proven. As the question of infringement remains open, the question of Defendants’ intent to induce infringement must be left for the fact–finder. Thus, Defendants’ Motion of non–infringement [Doc. # 176] is also denied with respect to the reagent–related products and the ‘767 patent.

IV. Conclusion

For the reasons discussed above, Plaintiffs' motion [Doc. # 168] for summary judgment of infringement is DENIED. Defendants' 2007 motion for summary judgment of noninfringement as to their assertions of non-indirect infringement [Doc. # 176] as to the '767 patent is DENIED, and their motion for summary judgment of noninfringement as to the "no substantial interference limitations" as to the '767 patent [Doc. # 315] is also DENIED. The parties' joint motion [Doc. # 382] for entry of stipulated partial judgment of the '824 patent is GRANTED.

The following issues remain for adjudication at trial:

- i. Infringement (direct and induced/indirect infringement)
- ii. Non-infringement of the "no substantial interference limitations"
- iii. Laches
- iv. Anticipation

IT IS SO ORDERED.

/s/

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

Dated at New Haven, Connecticut this 17th day of September, 2012.