UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

LIFE TECHNOLOGIES CORPORATION, ET AL.	§	
vs.	§	CASE NO. 2:09-CV-283-TJW-CE
BIOSEARCH TECHNOLOGIES, INC., ET AL.	§	

MEMORANDUM OPINION AND ORDER

I. INTRODUCTION

Plaintiffs Life Technologies Corporation and Applied Biosystems, LLC (collectively, Plaintiffs) brought this action against defendants Biosearch Technologies, Inc. and Eurofins MWG Operon, Inc. (collectively, "Defendants"), alleging infringement of U.S. Pat. No. 5,538,848 (the '848 patent); U.S. Pat. No. 5,723,591 (the '591 patent); U.S. Pat. No. 5,876,930 (the '930 patent); U.S. Pat. No. 6,030,787 (the '787 patent); and U.S. Pat. No. 6,258,569 (the '569 patent) (collectively, the "Livak patents"). The court held a *Markman* hearing on August 23, 2011. After considering the submissions and the arguments of counsel, the court issues the following order concerning the parties' claim construction disputes.

II. THE PATENT-IN-SUIT

All five Livak patents claim priority to the originally filed application, which issued on July 23, 1996 as the '848 patent. The '591 patent and the '930 patent issued from continuation-in-parts of the '848 patent. The applicants filed for the other two Livak patents, the '787 patent and the '569 patent, as successive continuations of the '930 patent.[1]

[1] The specifications of the '591, '930, '787, and '569 patents are essentially identical. Therefore, the citations used herein that reference the '591 patent apply to it as well as the specifications of the '930, '787, and '569 patents.

The ’848 patent is representative of the Livak patents. It is entitled “Method for Detecting Nucleic Acid Amplification Using Self-Quenching Fluorescence Probe” and is directed at a method for “monitoring the progress of nucleic acid amplifications that rely on a nucleic acid polymerase having 5′ → 3′ exonuclease activity.” ’848 patent at Abstract. The Summary of the Invention of the ’848 patent explains as follows:

> Generally the method of our invention relates to monitoring the progress of a nucleic acid amplification reaction that employs a nucleic acid polymerase having 5′ → 3′ exonuclease activity. More particularly, our invention relates to a method of monitoring the amplification of a target polynucleotide by (1) providing an oligonucleotide probe capable of annealing to the target polynucleotide, the oligonucleotide probe having a reporter molecule capable of fluorescing attached to a first end and a quencher molecule attached to a second end such that the quencher molecule substantially quenches any fluorescence of the reporter molecule whenever the oligonucleotide probe is in a single-stranded state and such that the reporter is substantially unquenched whenever the oligonucleotide probe is in a double-stranded state; and (2) extending a primer annealed to the target polynucleotide with a nucleic acid polymerase having 5′ → 3′ exonuclease activity such that the oligonucleotide probe is degraded by the 5′ → 3′ exonuclease activity of the nucleic acid polymerase as it extends the primer.

Id. at 3:29-55. Claim 1 of the ’848 patent, which is representative of the claims of the Livak patents, recites as follows:

> A method for monitoring nucleic acid amplification comprising:
>
> > performing nucleic acid amplification on a target polynucleotide using a nucleic acid polymerase having 5'-3' nuclease activity, a primer capable of hybridizing to said target polynucleotide, and an oligonucleotide probe capable of hybridizing to said target polynucleotide, 3' relative to said primer,
> >
> > said oligonucleotide probe having a fluorescent reporter molecule and a quencher molecule capable of quenching the fluorescence of said reporter molecule,
> >
> > said oligonucleotide probe existing in at least one single-stranded conformation when unhybridized where said quencher molecule quenches the fluorescence of said reporter molecule, said oligonucleotide probe existing in at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched, the fluorescence

> intensity of said reporter molecule being greater than the fluorescence intensity of said quencher molecule when said probe is hybridized to said target; polynucleotide,
>
> said nucleic acid polymerase digesting said oligonucleotide probe during amplification to separate said reporter molecule from said quencher molecule; and
>
> monitoring the fluorescence of said reporter molecule, the generation of fluorescence corresponding to the occurrence of nucleic acid amplification.

Id. at 13:29-56.

III. GENERAL PRINCIPLES GOVERNING CLAIM CONSTRUCTION

"A claim in a patent provides the metes and bounds of the right which the patent confers on the patentee to exclude others from making, using or selling the protected invention." *Burke, Inc. v. Bruno Indep. Living Aids, Inc.*, 183 F.3d 1334, 1340 (Fed. Cir. 1999). Claim construction is an issue of law for the court to decide. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 970-71 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996).

To ascertain the meaning of claims, the court looks to three primary sources: the claims, the specification, and the prosecution history. *Markman*, 52 F.3d at 979. The specification must contain a written description of the invention that enables one of ordinary skill in the art to make and use the invention. *Id.* A patent's claims must be read in view of the specification, of which they are a part. *Id*. For claim construction purposes, the description may act as a sort of dictionary, which explains the invention and may define terms used in the claims. *Id*. "One purpose for examining the specification is to determine if the patentee has limited the scope of the claims." *Watts v. XL Sys., Inc.*, 232 F.3d 877, 882 (Fed. Cir. 2000).

Nonetheless, it is the function of the claims, not the specification, to set forth the limits of the patentee's invention. Otherwise, there would be no need for claims. *SRI Int'l v. Matsushita*

Elec. Corp., 775 F.2d 1107, 1121 (Fed. Cir. 1985) (en banc). The patentee is free to be his own lexicographer, but any special definition given to a word must be clearly set forth in the specification. *Intellicall, Inc. v. Phonometrics, Inc.*, 952 F.2d 1384, 1388 (Fed. Cir. 1992). Although the specification may indicate that certain embodiments are preferred, particular embodiments appearing in the specification will not be read into the claims when the claim language is broader than the embodiments. *Electro Med. Sys., S.A. v. Cooper Life Sciences, Inc.*, 34 F.3d 1048, 1054 (Fed. Cir. 1994).

This court's claim construction decision must be informed by the Federal Circuit's decision in *Phillips v. AWH Corporation*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc). In *Phillips*, the court set forth several guideposts that courts should follow when construing claims. In particular, the court reiterated that "the *claims* of a patent define the invention to which the patentee is entitled the right to exclude." 415 F.3d at 1312 (emphasis added) (*quoting Innova/Pure Water, Inc. v. Safari Water Filtration Systems, Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). To that end, the words used in a claim are generally given their ordinary and customary meaning. *Id*. The ordinary and customary meaning of a claim term "is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Id*. at 1313. This principle of patent law flows naturally from the recognition that inventors are usually persons who are skilled in the field of the invention and that patents are addressed to and intended to be read by others skilled in the particular art. *Id*.

The primacy of claim terms notwithstanding, *Phillips* made clear that "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the

specification." *Id*. Although the claims themselves may provide guidance as to the meaning of particular terms, those terms are part of "a fully integrated written instrument." *Id*. at 1315 (quoting *Markman*, 52 F.3d at 978). Thus, the *Phillips* court emphasized the specification as being the primary basis for construing the claims. *Id*. at 1314-17. As the Supreme Court stated long ago, "in case of doubt or ambiguity it is proper in all cases to refer back to the descriptive portions of the specification to aid in solving the doubt or in ascertaining the true intent and meaning of the language employed in the claims." *Bates v. Coe*, 98 U.S. 31, 38 (1878). In addressing the role of the specification, the *Phillips* court quoted with approval its earlier observations from *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998):

> Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim. The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.

Phillips, 415 F.3d at 1316. Consequently, *Phillips* emphasized the important role the specification plays in the claim construction process.

The prosecution history also continues to play an important role in claim interpretation. Like the specification, the prosecution history helps to demonstrate how the inventor and the PTO understood the patent. *Id.* at 1317. Because the file history, however, "represents an ongoing negotiation between the PTO and the applicant," it may lack the clarity of the specification and thus be less useful in claim construction proceedings. *Id*. Nevertheless, the prosecution history is intrinsic evidence that is relevant to the determination of how the inventor understood the invention and whether the inventor limited the invention during prosecution by narrowing the scope of the claims. *Id.*

Phillips rejected any claim construction approach that sacrificed the intrinsic record in favor of extrinsic evidence, such as dictionary definitions or expert testimony. The *en banc* court condemned the suggestion made by *Texas Digital Systems, Inc. v. Telegenix, Inc.*, 308 F.3d 1193 (Fed. Cir. 2002), that a court should discern the ordinary meaning of the claim terms (through dictionaries or otherwise) before resorting to the specification for certain limited purposes. *Phillips*, 415 F.3d at 1319-24. The approach suggested by *Texas Digital*—the assignment of a limited role to the specification—was rejected as inconsistent with decisions holding the specification to be the best guide to the meaning of a disputed term. *Id*. at 1320-21. According to *Phillips*, reliance on dictionary definitions at the expense of the specification had the effect of "focus[ing] the inquiry on the abstract meaning of words rather than on the meaning of claim terms within the context of the patent." *Id*. at 1321. *Phillips* emphasized that the patent system is based on the proposition that the claims cover only the invented subject matter. *Id.* What is described in the claims flows from the statutory requirement imposed on the patentee to describe and particularly claim what he or she has invented. *Id*. The definitions found in dictionaries, however, often flow from the editors' objective of assembling all of the possible definitions for a word. *Id*. at 1321-22.

Phillips does not preclude all uses of dictionaries in claim construction proceedings. Instead, the court assigned dictionaries a role subordinate to the intrinsic record. In doing so, the court emphasized that claim construction issues are not resolved by any magic formula. The court did not impose any particular sequence of steps for a court to follow when it considers disputed claim language. *Id*. at 1323-25. Rather, *Phillips* held that a court must attach the appropriate weight to the intrinsic sources offered in support of a proposed claim construction, bearing in mind the general rule that the claims measure the scope of the patent grant.

The patents-in-suit include claim limitations that Defendants contend fall within the scope of 35 U.S.C. § 112, ¶ 6. "An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure. . . in support thereof, and such claim shall be construed to cover the corresponding structure . . . described in the specification and equivalents thereof." 35 U.S.C. § 112, ¶ 6. The first step in construing a means-plus-function limitation is to identify the recited function. *See Micro Chem., Inc. v. Great Plains Chem. Co.*, 194 F.3d 1250, 1258 (Fed. Cir. 1999). The second step in the analysis is to identify in the specification the structure corresponding to the recited function. *Id.* The "structure disclosed in the specification is 'corresponding' structure only if the specification or prosecution history clearly links or associates that structure to the function recited in the claim." *Medical Instrumentation and Diagnostics Corp. v. Elekta AB*, 344 F.3d 1205, 1210 (Fed. Cir. 2003) (citing *B. Braun v. Abbott Labs*, 124 F.3d 1419, 1424 (Fed. Cir. 1997)). The patentee must clearly link or associate structure with the claimed function as part of the quid pro quo for allowing the patentee to express the claim in terms of function pursuant to § 112, ¶ 6. *See id.* at 1211; *see also Budde v. Harley-Davidson, Inc.*, 250 F.3d 1369, 1377 (Fed. Cir. 2001). The "price that must be paid" for use of means-plus-function claim language is the limitation of the claim to the means specified in the written description and equivalents thereof. *See O.I. Corp. v. Tekmar Co.*, 115 F.3d 1576, 1583 (Fed. Cir. 1997). "If the specification does not contain an adequate disclosure of the structure that corresponds to the claimed function, the patentee will have 'failed to particularly point out and distinctly claim the invention as required by the second paragraph of section 112,' which renders the claim invalid for indefiniteness." *Blackboard, Inc. v. Desire2Learn, Inc.*, 574 F.3d 1371, 1382 (Fed. Cir. 2009) (quoting *In re Donaldson Co.*, 16 F.3d 1189, 1195 (Fed. Cir. 1994) (en banc)). It is important to determine whether one of skill in

the art would understand the specification itself to disclose the structure, not simply whether that person would be capable of implementing the structure. *See Atmel Corp. v. Info. Storage Devices, Inc.*, 198 F.3d 1374, 1382 (Fed. Cir. 1999); *Biomedino*, 490 F.3d at 953. Fundamentally, it is improper to look to the knowledge of one skilled in the art separate and apart from the disclosure of the patent. *See Medical Instrumentation*, 344 F.3d at 1211-12. "[A] challenge to a claim containing a means-plus-function limitation as lacking structural support requires a finding, by clear and convincing evidence, that the specification lacks disclosure of structure sufficient to be understood by one skilled in the art as being adequate to perform the recited function." *Budde*, 250 F.3d at 1376-77

IV. CLAIM TERMS IN DISPUTE

a. "quencher molecule" ('848 patent: 1–24; '591 patent: 1–15; 26–30; '930 patent: 1–17; '787 patent: 1–6; '659 patent: 1–36)

Plaintiffs' Proposed Construction	**Defendants' Proposed Construction**
a molecule capable of absorbing the fluorescence energy of an excited reporter molecule, thereby quenching the fluorescence signal that would otherwise be released from the excited reporter molecule	a molecule that absorbs light at one wavelength and emits light at a different wavelength

The parties' dispute with regard to the term "quencher molecule" is whether the term should be construed as it is expressly defined in the specification of the Livak patents, or instead further limited to only those quenchers that are fluorescent (that is, able to emit light at a different wavelength from the one absorbed). Plaintiff argues that the court should construe this term to mean "a molecule capable of absorbing the fluorescence energy of an excited reporter molecule, thereby quenching the fluorescence signal that would otherwise be released from the excited reporter molecule." Plaintiffs' proposed construction appears verbatim in the

specifications of four out of the five asserted patents, all of which are related. *See, e.g.*, '591 patent at 1:36-41. Furthermore, Plaintiffs argue that the claims and specifications of the Livak patents repeatedly use the term "quencher molecule" to reference the quenching or absorbing of the detectable fluorescence signal from the excited reporter molecule. *See, e.g.*, '848 patent at Abstract; 1:66-2:12; 3:37–44, 3:64-4:1; 5:46–58, claims 1, 14, 24. As such, Plaintiffs contend that their proposed construction is consistent with the Livak patents' explicit definition and general teachings regarding the claimed "quencher molecule."

Defendants' proposed construction, on the other hand, limits the claimed "quencher molecules" to those that absorb light at one wavelength and emit light at a different wavelength. Defendants argue that the "quencher molecule" must be limited to quenchers that "emit light" to prevent various claims of the patents-in-suit from becoming nonsensical. According to Defendants, because some claims of the Livak patents require a ratio of fluorescence intensities of the reporter and quencher molecules, the quencher molecule must be limited to a molecule that actually emits light. For example, claim 24 of the '848 patent recites:

> … the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is hybridized to said target polynucleotide being at least about a factor of 6 greater than the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is single-stranded ….

'848 patent at 16:22-28. Defendants argue that a quencher molecule that does not emit light has a fluorescence intensity of zero, making this claim term, and those similar to it, nonsensical.

Defendants also argue that the prosecution history supports their argument that the quencher molecule must emit light. During prosecution of the '848 patent, the examiner rejected claim language requiring quenchers that "substantially quench" any florescence as indefinite under 35 U.S.C. § 112(2). The patentees subsequently removed "substantially" from the claim

language, but did not seek to replace this language with "totally quenched" or some variation thereof. As such, Defendants argue that the prosecution history demonstrates that the patentees intended to cover only quencher molecules that emitted some measure of light.

Defendants, however, admit that the specifications of the Livak patents disclose quenchers that emit light and quenchers that do not. For example, the '848 patent explains:

> The probe contains a fluorescent "reporter" molecule and a "quencher" molecule such that the [sic] whenever the reporter molecule is excited, the energy of the excited state nonradiatively transfers to the quencher molecule where it *either dissipates nonradiatively or is emitted at a different emission frequency than that of the reporter molecule*.

'848 patent at 2:1-5 (emphasis added). The patentee expressly contemplated that the quencher molecule taught in the Livak patents could either release energy absorbed from the reporter molecule by emitting light, or, instead, release the energy by dissipating it nonradiatively. *See also* '848 patent at 5:46-58. Furthermore, Defendants' attempt to limit the claimed quencher to a molecule that emits light ignores the fact that the patentee knew how to define the scope of the quencher molecule when he chose to do so. For example, claim 1 of the '930 patent requires an "oligonucleotide probe including a fluorescent reporter molecule and a *quencher molecule* capable of quenching the fluorescence of said reporter molecule." Claim 16 of the '930 patent, however, requires an "oligonucleotide probe including a fluorescent reporter molecule and a *fluorescent quencher molecule* capable of quenching the fluorescence of said reporter molecule." As is evident from the claim language, claim 16 requires that the quencher molecule be fluorescent, whereas claim 1 does not. And, finally, although some of the claims of the Livak patents require a ratio of fluorescence intensities of the reporter and quencher molecules, not all of the claims require this. *Compare* '848 patent at claim 1 *with* '838 patent at claim 14. Considering this, the court rejects Defendants' argument that the "quencher molecule" must, in

all instances, be fluorescent. Although the claims of the Livak patent require, in some instances, that the quencher molecule emit light so that a certain ratio might be determined, the court will not read such a limitation into all of the claims of the Livak patents. The court also rejects Defendants' contention that the prosecution history on which it relies rises to the level of a clear disclaimer of claim scope. The prosecution shows no intention on the part of the patentee to disavow quenchers that do not emit light.

b. "a hairpin structure" ('591 patent: 1–15; 26–30; '930 patent: 1–17; '787 patent: 1–6; '569 patent: 1–36)

Plaintiffs' Proposed Construction	**Defendants' Proposed Construction**
where the probe hybridizes to itself to form a loop such that the quencher molecule is brought into proximity with (next to) the reporter molecule in the absence of a complementary nucleic acid sequence to prevent the formation of the hairpin structure	a single stranded oligonucleotide sequence that is hybridized with itself to form a double stranded duplex of 3 or more contiguous basepairs at the detection temperature of the assay

Plaintiffs propose the following construction for the term "a hairpin structure": "where the probe hybridizes to itself to form a loop such that the quencher molecule is brought into proximity with (next to) the reporter molecule in the absence of a complementary nucleic acid sequence to prevent the formation of the hairpin structure." Plaintiffs' proposed construction is derived from the patentees' express description of this term in the specifications of four out of the five Livak patents. *See, e.g.*, '591 patent at 1:48-54. Furthermore, during the prosecution of the Livak patents, the patentees confirmed that the specification's description of "a hairpin structure" was consistent with their understanding of the meaning of the term:

In the Specification, Applicants teach that

> probes containing a reporter molecule – quencher molecule pair have been developed for hybridization assays where the probe forms a hairpin structure, i.e., where the probe hybridizes to itself to form a loop such that the quencher molecule is brought into proximity with the reporter

> molecule in the absence of a complementary nucleic acid sequence to prevent the formation of the hairpin structure. W090/03446; European Patent Application No. 0 601 889 A2.
>
> Specification, page 2, lines 13-19. The Specification thus clearly defines what is intended by the term "hairpin structure." This definition for the term "hairpin structure" is consistent with other art references which employ the term "hairpin structure."

Ex. G. at 2, attached to Plaintiff's Opening Claim Construction Brief, Dkt. No. 180.

Defendants, on the other hand, argue that the court should construe "a hairpin structure" to mean "a single stranded oligonucleotide sequence that is hybridized with itself to form a double stranded duplex of 3 or more contiguous basepairs at the detection temperature of the assay." Defendants' proposed construction imports the following two limitations: (1) three or more contiguous basepairs; and (2) at the detection temperature of the assay. With regard to the first limitation, Defendants argue that because the embodiments disclosed in WO/9003446, the European patent application to which the Livak patents cite to support the proposed definition of a hairpin structure, show a hairpin structure of three or more contiguous pairs, the hairpin structures of the Livak patents must be likewise limited. *See* '591 patent at 1:46-54; *see also* Ex. B at Fig. 4, attached to Defendants' Responsive Claim Construction Brief, Dkt. No. 192. The court may not, however, import embodiments from the intrinsic record into the claims. Consequently, the court rejects Defendants' proposed "3 or more contiguous basepairs" limitation.

With regard to the second proposed limitation, Defendants argue that the main condition contributing to the ability of an oligonucleotide to form the double-strand necessary for a hairpin structure is temperature. *See, e.g.*, '591 patent at 3:43-47. As such, Defendants argue that the correct construction of "a hairpin structure" must include reference to the temperature at which

the presence or absence of the hairpin structure is determined. The claims of the Livak patents, however, recite:

> monitoring the fluorescence of said reporter molecule fluorescence intensity of said reporter molecule indicating the presence of said [sic] *under conditions* where said oligonucleotide probe does not hybridize with itself to form a hairpin structure in order to detect the hybridization of said target polynucleotide to said oligonucleotide probe.

'930 patent at 3:51-56 (emphasis added); *see also* '787 patent at 23:53-56. Although there are multiple "conditions" identified in the specification (*see* '591 patent at 3:42-46), Defendants ask the court to import only one of those "conditions" into the claim language – that is, the detection temperature of the assay. In essence, Defendants ask the court to import a limitation into the claim language without providing any evidence that the patentees intended the claimed "conditions" to be limited solely to the detection temperature of the assay. Accordingly, the court rejects Defendants' second proposed limitation.

As discussed above, Plaintiffs' proposed construction parrots the definition given in the specifications of the Livak patents, except that it adds the words "(next to)." Plaintiffs argue that the "(next to)" language will assist the jury in understanding what the phrase "into proximity with" means. The court, however, concludes that the phrase "next to" is too limiting. *See, e.g.*, '591 patent at 7:10-14 (As further illustrated in FIG. 2, when the probe is hybridized to a target sequence, the probe adopts at least one conformation where the quencher molecule *is not positioned close enough* to the reporter molecule to quench the fluorescence of the reporter molecule.") (emphasis added)); Ex. G. at 3, attached to Plaintiffs' Opening Claim Construction Brief, Dkt. No. 181 ("As shown in figure 2, the oligonucleotide backbone of the probe adopts a conformation where the quencher is *sufficiently close* to the reporter molecule to quench the reporter molecule without forming a hairpin.") (italic emphasis added)). Rather, the court

concludes that the phrase "nearby" accurately captures the meaning of "into proximity with" when the phrase is read in light of the specification.[2]

In conclusion, the court adopts the following construction of "a hairpin structure": "where the probe hybridizes to itself to form a loop such that the quencher molecule is brought into proximity with (nearby) the reporter molecule in the absence of a complementary nucleic acid sequence to prevent the formation of the hairpin structure."

c. "said reporter/quencher molecule is separated from said quencher/reporter molecule by at least 15 nucleotides" ('848 patent: 4, 6, 15; '591 patent: 2, 4, 27, 32; '930 patent: 3, 5; '787 patent: 3, 5)

Plaintiffs' Proposed Construction	**Defendants' Proposed Construction**
one member of a reporter-quencher pair is attached to a nucleotide of the probe and the other member to a nucleotide at least 15 nucleotides away. This construction will be applied to other claims with different numbers of nucleotides.	the reporter and quencher molecules are at least 15 nucleotides apart, inclusive of the nucleotides to which the reporter and quencher molecules are attached. The interpretation will be applied to other claims with different numbers of nucleotides.

Plaintiffs argue that the court should construe the phrase "said reporter/quencher molecule is separated from said quencher/reporter molecule by at least 15 nucleotides," and other similar phrases with different numbers of nucleotides, to mean "one member of a reporter-quencher pair is attached to a nucleotide of the probe and the other member to a nucleotide at least 15 nucleotides away." Plaintiffs' proposed construction is derived from descriptions of this phrase in the specifications of all five of the Livak patents. The specifications explain that "a separation of about 6–16 nucleotides … is typically achieved by attaching one member of a reporter-quencher pair to the 5′ end of the probe and the other member to a base 6–16

[2] During the claim construction hearing, Defendants indicated that they considered the term "nearby" to be an appropriate explanation of the meaning of "in proximity with." *See* Dkt. No. 209 at 46 ("*words like proximity, nearby*, make a lot of sense in connection with the -- the probes we're talking about" and "Number one, the base or the stem, they are *proximately nearby*, but that's not necessarily next to or touching.")

nucleotides away." '848 patent at 2:55–57; *see also* '591 patent at 3:62-4:5. Furthermore, Plaintiffs argue that this definition is consistent with the prosecution history of the Livak patents. For example, in the prosecution history of the '591 patent, the applicants explained that Table 1 of the Lee reference (s*ee* Ex. F, attached to Plaintiffs' Opening Claim Construction Brief, Dkt. No. 180), "teaches an energy transfer probe where the donor and acceptor are separated by 7 nucleotides." Ex. K, at 12, attached to Plaintiffs' Opening Claim Construction Brief, Dkt. No. 180. Plaintiffs argue that the applicants' description of the donors and acceptors in these probes as "separated by 7 nucleotides," inclusive of only the nucleotide to which the acceptor (or quencher) is attached, follows the description of separation in the Livak patents, and thus follows Plaintiffs' proposed construction.

Defendants, on the other hand, argue that the court should construe this phrase to mean "the reporter and quencher molecules are at least 15 nucleotides apart, *inclusive of the nucleotides to which the reporter and quencher molecules are attached*.). Defendants' argument that the separation between the two molecules must be inclusive, is based on a discussion in the Livak patents concerning probe naming and nucleotide position conventions. *See* '591 patent at 7:14-28. The section relied on does not state that the separation between the reporter and quencher molecules must be inclusive of the two nucleotides to which they are attached. Furthermore, Defendants admitted during the claim construction hearing that the examples disclosed in the Lee reference do not conform to their proposed definition. Considering this, the court rejects Defendants' proposed construction.

The court agrees with Plaintiffs that that their proposed construction of "said reporter/quencher molecule is separated from said quencher/reporter molecule by at least 15 nucleotides" is consistent with the use of the phrase throughout the intrinsic record.

Accordingly, the court construed this phrase to mean "one member of a reporter-quencher pair is attached to a nucleotide of the probe and the other member to a nucleotide at least 15 nucleotides away." This construction will be applied to similar claim phrases with different numbers of nucleotides.

d. "terminal nucleotide" ('848 patent: 8–13; 17–22; '591 patent: 6–11; '930 patent: 7–12)

Plaintiffs' Proposed Construction	**Defendants' Proposed Construction**
No construction is required for this term.	a terminal nucleotide unit that comprises a base, a ribose or deoxyribose structure and a phosphate or modified phosphate structure

Defendants' proposed construction of the term "terminal nucleotide" seeks to import numerous limitations. Defendants, however, make no attempt to support their proposed limitations. Furthermore, Plaintiffs argue that Defendants' construction ignores the modified base and sugar moieties explicitly contemplated by the description of nucleosides in the specification. *See* '848 patent at 4:29-5:8. Defendants do not answer this criticism of their proposed construction. The court, therefore, rejects Defendants' proposed construction. The court agrees with Plaintiffs that this term needs no further construction.

e. "monitoring the fluorescence" ('848 patent: 1–24; '930 patent: 1–15; '787 patent: 1–6)

Plaintiffs' Proposed Construction	**Defendants' Proposed Construction**
No construction is required for this term.	monitoring the generation of fluorescence at a particular wavelength only at the conclusion of an amplification reaction

Plaintiffs argue that the term "monitoring the florescence" does not require construction. Defendants, on the other hand, argue that this term must be construed because the Livak patents are necessarily limited to monitoring polymerase chain reactions ("PCR") using dual-labeled probes "at the conclusion of an amplification reaction." Defendants contend that "real time"

monitoring of PCR was not publicly available at the time of the invention – that is, the filing date of the '848 patent – November 16, 1994. The Livak patents, however, cite to 1992 and 1993 publications disclosing monitoring fluorescence during reactions in "real time." *See* '848 patent at 1:37-38. For example, the 1992 article explains a method by which "amplification can be continuously monitored in order to follow its progress." Ex. Y at 415, attached to Plaintiffs' Reply Brief, Dkt. No. 201. The 1993 article discloses "a simple, quantitative assay for any amplifiable DNA sequence that uses a video camera to monitor multiple polymerase chain reactions (PCRs) simultaneously over the course of thermocycling. " Ex. Z at 1026, attached to Plaintiffs' Reply Brief, Dkt. No. 201. These two references show that a skilled artisan, reading the intrinsic record, would understand "monitoring the fluorescence" to refer to checking the fluorescence as the reaction progressed using either of the above referenced systems for doing so.

Defendants argue that an extrinsic publication shows that one of the inventors, Dr. Livak, did not consider real time PCR monitoring to be within the scope of the original invention because he came up with it only after having access to the ABI Prism machine. The cited reference, however, does not give rise to such an inference. The article cited by Defendants explains that "[r]esearchers have developed several methods of quantitative PCR and RT-PCR," and describes different methods that measure product during PCR reactions. Ex. C at 986, attached to Defendants' Responsive Claim Construction Brief, Dkt. No. 192. This article states that its "goal was to develop a high-throughput" methodology for such real time measurements. *Id*. at 987. The mere fact that, as Defendants note, the paper discloses "a novel 'real time' quantitative PCR method ... resulting in much faster and higher throughput assays," does not mean that there were no other real time quantitative PCR methods already in existence. In fact,

the article specifically cites the 1992 article discussed above as disclosing another method by which real-time PCR can be performed. *Id.* at 992. The court, therefore, rejects Defendants' contention that the inventors did not intend to include methods of real-time monitoring in the Livak patents.

In conclusion, the court rejects Defendants' attempt to exclude real-time monitoring from the scope of the Livak patents. Furthermore, the court agrees with Plaintiffs that the term "monitoring the fluorescence" needs no further construction.

f. "said oligonucleotide probe/sequence existing in/is capable of adopting at least one single-stranded conformation when unhybridized/not hybridized to said target polynucleotide where said quencher molecule quenches the fluorescence of said reporter molecule, said oligonucleotide probe/sequence existing in/is capable of adopting at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched" ('848 patent: 1–24; '591 patent: 1–15; 26–30; '930 patent: 1–17; '787 patent: 1–6)

Plaintiffs' Proposed Construction	**Defendants' Proposed Construction**
No construction is required for this term.	**§112, ¶ 6 Applies:** This is a functional limitation for which there is no corresponding structure in the claims sufficient to give this function. As such, the claim term is indefinite.

The parties dispute whether the following phrase, and others similar to it, are subject to construction under § 112, ¶ 6:

> said oligonucleotide probe existing in at least one single-stranded conformation when unhybridized where said quencher molecule quenches the fluorescence of said reporter molecule, said oligonucleotide probe existing in at least one conformation when hybridized to said target polynucleotide where the fluorescence of said reporter molecule is unquenched

'848 patent at 13:41-47. "[A] claim term that does not use [the word] 'means' will trigger the rebuttable presumption that § 112 ¶ 6 does not apply." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1369 (Fed. Cir. 2002). The presumption that a limitation lacking the term

"means" is not subject to § 112, ¶ 6 can be overcome if it is demonstrated that "the claim term fails to 'recite sufficiently definite structure' or else recites 'function without reciting sufficient structure for performing that function.'" *Id*. (quoting *Watts v. XL Sys., Inc.*, 232 F.3d 877, 880 (Fed. Cir. 2000)); *see also Lighting World, Inc. v. Birchwood Lighting, Inc*., 382 F.3d 1354, 1358 (Fed. Cir. 2004). The Federal Circuit, however, has made clear that "the presumption flowing from the absence of the term 'means' is a strong one that is not readily overcome." *Lighting*, 382 F.3d at 1358; *see also Al-Site Corp. v. VSI Int'l, Inc.*, 174 F.3d 1308, 1318-19 (Fed. Cir. 1999); *Personalized Media Communications, LLC v. Int'l Trade Comm'n*, 161 F.3d 696, 703 (Fed. Cir. 1998). Furthermore, in considering whether a claim term recites sufficient structure to avoid application of § 112, ¶ 6, it is not necessary that the claim term denote a specific structure. *Lighting World, Inc.*, 382 F.3d at 1358-60. Instead, the Federal Circuit has explained that "it is sufficient if the claim term is used in common parlance or by persons of skill in the pertinent art to designate structure, even if the term covers a broad class of structures and even if the term identifies the structures by their function." *Id*. (citations omitted).

Here, Defendants argue that the claim limitations at issue recite the following function: existing in/is capable of adopting at least one single-stranded conformation when unhybridized/not hybridized to said target polynucleotide where the quencher quenches the fluorescence of the reporter molecule, and existing in/capable of adopting at least one conformation when hybridized to said target polynucleotide where the fluorescence of the reporter is unquenched. More specifically, Defendants argue that the function of these claims relates to existing in or adopting different conformations such that each conformation has an effect on quenching. Defendants admit that the means for this function is the recited "oligonucleotide probe/sequence." But Defendants argue that, because an oligonucleotide

probe/sequence can encompass a variety of different sequences, a person of ordinary skill in the art would be unable to identify what sequences are needed to perform the recited function. As such, Defendants argue that these claim limitations are indefinite.

The court is not convinced that Defendants have overcome the heavy presumption that these claim limitations are not subject to §112, ¶ 6. Defendants' alleged "functions" appear to merely be the recited properties of the alleged oligonucleotide probe/sequence. Furthermore, Defendants have provided the court with no evidence that one of ordinary skill in the art would be incapable of understanding the structural arrangements of the probe/sequence. And, finally, both the Federal Circuit and this court have recognized that the fact that a claim term is broad and might include almost an infinite number of structures does not render the limitation subject to § 112, ¶ 6. *See Crane Co. v. Sandenvendo Am.*, No. 07-CV-42-CE, 2009 WL 1586704 at *15-16 (E.D. Tex. June 5, 2009); *see also Lighting World*, 382 F.3d at 1361-62. In sum, the court rejects Defendants' argument that these claim limitations are subject to § 112, ¶ 6 and concludes that these limitations need no further construction.

g. Measuring Florescence Terms

Term	Plaintiffs' Proposed Construction	Defendants' Proposed Construction
"the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is hybridized to said target polynucleotide is at least a factor of 6 greater than the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is not hybridized to said target polynucleotide" ('591 patent: 1–14)	No construction is required for this term.	§112, ¶ 6 Applies: The only structure identified by the patentees as corresponding to this limitation is probe P2-27, a specific probe of 27 nucleotides with a 5' FAM (reporter) and a 3' TAMRA (quencher). Therefore, the claims containing this term are limited to the use of the P2-27 probe. Alternative Interpretations: In the event that this clause is not found to invoke § 112, ¶ 6, alternative interpretations are proposed: 1. The claim term is too indefinite and ambiguous to interpret. 2. (FIR)hybridized > 6(FIR)unhybridized "FIR" is the "fluorescence intensity of the reporter." The only conditions outlined in the patent are for the data generated in Table 2 ('848 patent) as follows. The FIR measurements are done in a solution of 10 mM Tris-HCl (pH 8.3), 50 mM KCl and 4 μM MgCl2. The FIR measurement is done by exciting the complex at the reporter's excitation maxima and detecting at the reporter's emission maxima. The measurements are done in this solution with 50 nM of the probe, and then with the addition of 100 nM target sequence.
"the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is hybridized to said target polynucleotide being at least about a factor of 6/is at least 6 times greater than the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is single-stranded/said oligonucleotide sequence is not hybridized to said target polynucleotide" ('848 patent: 24; '591 patent: 15; '930 patent: 17)	No construction is required for this term.	§112, ¶ 6 Applies: The only structure corresponding to this limitation is probe A1-26, a specific probe of 26 nucleotides with a 5' FAM (reporter) and a 3' TAMRA (quencher). Therefore, the claims containing this term are limited to the use of the A1-26 probe. Alternative Interpretations: In the event that this clause is not found to invoke § 112, ¶ 6, alternative interpretations are proposed: 1. The claim term is too indefinite and ambiguous to interpret. 2. [FIR/FIQ]hybridized > 6([FIR/FIQ]unhybridized) "FIR" is the "fluorescence intensity of the reporter", and "FIQ" is the "fluorescence intensity of the quencher" The only conditions outlined in the patent are for the data generated in Table 2 ('848 patent) as follows. The measurements are done in a solution of 10 mM Tris-HCl (pH 8.3), 50 mM KCl and 4 μM MgCl2. The FIR measurement is done by exciting the complex at the reporter's excitation maxima and detecting at the reporter's emission maxima. The FIQ measurement is done by exciting the complex at the reporter's excitation maxima and detecting at the quencher's emission maxima. The measurements are done in this solution with 50 nM of the probe, and then with the addition of 100 nM target sequence.

The court will address the parties' claim construction disputes with regard to the following two claim limitations together: (1) "the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is hybridized to said target polynucleotide is at

least a factor of 6 greater than the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is not hybridized to said target polynucleotide"; and (2) "the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is hybridized to said target polynucleotide being at least about a factor of 6/is at least 6 times greater than the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is single-stranded/said oligonucleotide sequence is not hybridized to said target polynucleotide."

The parties first dispute whether these limitations are subject to construction under § 112, ¶ 6. Defendants argue that both of these limitations are functional in nature and that their function is changing the fluorescence intensity of a reporter molecule. Defendants admit that the "oligonucleotide probe/sequence" is the structure that accomplishes this alleged function. Defendants, however, again argue that the "oligonucleotide probe/sequence" is not sufficient structure for performing the alleged function because a variety of oligonucleotide sequences can be used to accomplish the function. As discussed immediately above, the court has rejected Defendants' argument that the mere fact that a claim term might encompass many structures renders the limitation subject to § 112, ¶ 6. *See Crane*, 2009 WL 1586704 at *15-16; *see also Lighting World*, 382 F.3d at 1361-62. The court, therefore, also rejects Defendants' contention that these claim limitations are subject to § 112, ¶ 6.

Second, Defendants contend that these limitations are indefinite because fluorescence intensities vary widely with different conditions, and, without specifying such conditions, these limitations are indefinite. "Only claims 'not amenable to construction' or 'insolubly ambiguous' are indefinite." *Halliburton Energy Servs., Inc. v. M-I LLC*, 514 F.3d 1244, 1249 (Fed. Cir. 2008) (quoting *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed. Cir.

2005)). "A claim is not indefinite merely because parties disagree concerning its construction." *See Haemonetics Corp. v. Baxter Healthcare Corp.*, 607 F.3d 776, 783 (Fed. Cir. 2010). "An accused infringer must thus demonstrate by clear and convincing evidence that one of ordinary skill in the relevant art could not discern the boundaries of the claim based on the claim language, the specification, the prosecution history, and the knowledge in the relevant art." *Id*.

Defendants fail to address Plaintiffs' evidence indicating that optimization of oligonucleotide hybridization conditions were routine and well known in the art at the time the Livak patents were issued. In fact, in making their indefiniteness argument, Defendants actually rely on a journal article cited in the prosecution history of the Livak patents, which demonstrates that skilled artisans knew how to optimize such reactions using different techniques. Considering this, the court is not convinced that one of ordinary skill in the art would be unable to determine the boundaries of these limitations. Accordingly, the court rejects Defendants' contention that these claim limitations are indefinite.

Finally, Defendants offer two constructions for these limitations, which Defendants argue incorporate all of the elements of the claim terms in a mathematical formula and limit the claim limitations to the conditions, such as salt and probe concentrations, disclosed in the specification for achieving the recited reactions. The court, however, cannot import limitations from the specifications of the Livak patents into the claims. *See Phillips,* 415 F.3d at 1312–13, 1323; *Linear Tech. Corp. v. ITC*, 566 F.3d 1049, 1058 (Fed. Cir. 2009). As such, the court rejects Defendants' proposed constructions for these limitations.

Although it is improper to import the exact formula (described in the specification) for achieving the recited reactions into the claims of the Livak patents, the court concludes (and Plaintiffs agree) that the claim language must be limited to the methods used to achieve the

reactions as of November 16, 1994 – that is, the methods used as of the filing date of the '848 patent. *See PC Connector Solutions LLC v. SmartDisk Corp.*, 406 F.3d 1359, 1363 (Fed. Cir. 2005) ("A claim cannot have different meanings at different times; its meaning must be interpreted as of its effective filing date."). The court, therefore, construes these terms as follows:

(1) "the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is hybridized to said target polynucleotide is at least a factor of 6 greater than the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is not hybridized to said target polynucleotide" means "when measured in accordance with the methods used as of November 16, 1994, the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is hybridized to said target polynucleotide is at least a factor of 6 greater than the fluorescence intensity of said reporter molecule when said oligonucleotide sequence is not hybridized to said target polynucleotide"; and

(2) "the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is hybridized to said target polynucleotide being at least about a factor of 6/is at least 6 times greater than the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is single-stranded/said oligonucleotide sequence is not hybridized to said target polynucleotide" means "when measured in accordance with the methods used as of November 16, 1994, the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is hybridized to said target polynucleotide being at least about a factor of 6/is at least 6 times greater than the ratio of the fluorescence intensities of said reporter molecule to said quencher molecule when said probe is single-stranded/said oligonucleotide sequence is not hybridized to said target polynucleotide."

V. CONCLUSION

The court adopts the constructions set forth in this opinion for the disputed terms of the patents-in-suit. The parties are ordered that they may not refer, directly or indirectly, to each other's claim construction positions in the presence of the jury. Likewise, the parties are ordered to refrain from mentioning any portion of this opinion, other than the actual definitions adopted by the court, in the presence of the jury. Any reference to claim construction proceedings is limited to informing the jury of the definitions adopted by the court.

It is so ORDERED.

SIGNED this 22nd day of September, 2011.

CHARLES EVERINGHAM IV
UNITED STATES MAGISTRATE JUDGE