IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

LIFE TECHNOLOGIES CORPORATION; APPLIED BIOSYSTEMS, LLC; INSTITUTE FOR PROTEIN RESEARCH; ALEXANDER CHETVERIN; HELENA CHETVERINA; and WILLIAM HONE,	)	
Plaintiffs/Counterclaim Defendants,	)	C.A. No. 09-706 (RK)
v.	)	
ILLUMINA, INC. and SOLEXA, INC.,	)	
Defendants/Counterclaim Plaintiffs.	)	

PLAINTIFFS' RESPONSIVE CLAIM CONSTRUCTION BRIEF

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LEGEND

The following citation conventions are used in this brief:

- D.I. # = Docket Item number
- JA## = page number in the Joint Appendix
- ’478 patent = U.S. Patent No. 5,616,478
- ’568 patent = U.S. Patent No. 6,001,568
- ’698 patent = U.S. Patent No. 5,958,698
- ’994 patent = U.S. Patent No. 6,831,994
- ’505 patent = U.S. Patent No. 6,654,505
- ’656 patent = U.S. Patent No. 7,232,656
- ’035 patent = U.S. Patent No. 7,598,035
- XX:YY = column number:line number(s) of referenced patent
- All emphases to quotations in this brief have been added to the original, except where indicated otherwise.

INTRODUCTION

This is the responsive claim construction brief of Life Technologies Corp. and Applied Biosystems, LLC (together, "Life"), the Institute for Protein Research, Alexander Chetverin, Helena Chetverina, and William Hone (collectively, "Plaintiffs"). Plaintiffs' Opening Brief (D.I. 67) provided constructions for 24 terms from seven different patents (from four patent families), each driven by intrinsic evidence and the governing canons of claim construction. Illumina and Solexa's Opening Brief (D.I. 65), in contrast, repeatedly ignored the intrinsic evidence (including its own contradictory statements in the pending reexamination proceedings on its patents) in favor of cherry-picked language from the patents, prosecution histories, and myriad dictionaries. Plaintiffs explain these errors below and show that Plaintiffs' positions should be adopted.

I. PLAINTIFFS' CHETVERIN PATENTS: DISPUTED CLAIM TERMS

1. "Amplification system" ('478 patent, all claims; '698 patent, all claims; '568 patent, claim 16)

"Polymerase enzyme system" ('568 patent, claims 1, 2, 4, 10)

Term(s)[1]	Plaintiffs' Construction	Illumina's Construction
"amplification system" "polymerase enzyme system"	a set of components that together can amplify a nucleic acid	a set of components (including a buffer, a nucleic acid amplification enzyme, nucleotide substrates, and, where required, oligonucleotide primers) that together can amplify a nucleic acid

The parties agree that the amplification system is a set of components that together can amplify a nucleic acid; this language is in both parties' proposed constructions. Plaintiffs' view is that no further construction is required. In contrast, Illumina asks the Court to read into the claims a requirement that the amplification system must contain specific components as set forth in the parenthetical portion of its construction. As shown in Plaintiffs' opening brief, the

[1] The parties agree these two terms should be construed the same way, and this brief refers to both terms as "amplification system."

intrinsic evidence strongly demonstrates that the narrowing proposed by Illumina would be inappropriate. *See* D.I. 67 at 8. Illumina's brief does not refute this showing. Instead, Illumina argues that the jury will require such further construction "to discern what these terms mean." D.I. 65 at 10. But Plaintiffs' construction is already sufficiently precise for the jury to understand and apply: if the amplification system employed by Illumina is capable of amplifying nucleic acids, the requirement is met.[2] Indeed, Illumina's proposed construction would only confuse the jury by introducing complexity and scientific terminology about primers, enzymes, buffers, and nucleotide substrates.

Illumina's two citations to the patent also do not support its proposed narrowing. Its cite from the background section (which is the only one that lists all of Illumina's proposed limiting components) is merely illustrative of the prior art, and so cannot limit the claimed invention. *See* D.I. 65 at 10 (citing JA7 at 1:24-27). Illumina's cite from the patent regarding enzyme systems similarly does not limit the claimed invention because it is also merely illustrative of the prior art and, further, is not relevant because enzyme systems are only a subset of amplification systems.[3] *See id.* (citing JA10 at 7:43-44). And contrary to Illumina's arguments, the prosecution history further supports Plaintiffs' construction. Plaintiffs' opening brief explains that during prosecution neither the applicants nor the Examiner found it necessary or appropriate to define amplification systems in the claims according to a specific set of components. D.I. 67 at 8-9.

[2] *See, e.g.*, *Power-One, Inc. v. Artesyn Techs., Inc.*, 599 F.3d 1343, 1349 (Fed. Cir. 2010) ("The fact that the claim is not defined using a precise numerical measurement does not render it incapable of providing meaningful guidance to the jury because the claim language, when taken in context of the entire patent, provides a sufficiently reasonable meaning to one skilled in the art of distributed power systems.").

[3] To the extent that enzymes are required by the claims, such a requirement is encompassed by the use of the separate words "enzymatic" or "enzymes," not "amplification system" itself. Plaintiffs do not dispute that polymerase enzyme systems would include nucleic acid amplification enzymes, and that such were part of the prior art to the patents.

The statements cited by Illumina do not contradict this; they support it. For example, the applicants' statement in the December 23, 1994 amendment that "all systems" contain certain components was not a narrowing statement intended to limit the claims, but rather an explanation that one of ordinary skill in the art would understand which components are needed for particular amplification systems without being instructed by the patent. *See* JA575. The other cited statement also emphasizes that a specific set of components is ***not*** important to the invention, but rather depends on whatever amplification system is used: "***Whatever exponential enzymatic nucleic acid amplification is selected for use in applicants' method***, the necessary components for that amplification system must be provided so that templates for that system will be amplified, just as would be required were the amplification system used without applicants' method." JA574. Similarly, Illumina's citation to the table describing components for particular amplification systems is nothing more than a summary of "***some*** [not all] combinations of components" from the examples described in the specification. JA616 ("The following table lists some combinations of components which Applicant teaches can be used in the claimed methods."); *see also* JA615 (statement in the same amendment explaining that "a wide variety [of amplification systems] are disclosed and that there is no teaching that the invention is limited to a particular system or systems"). A construction of the claim terms in dispute thus need not specify those components.

2. "Aqueous liquid phase that includes a cell-free, enzymatic, exponential nucleic acid amplification system" ('478 patent, claims 1, 2, 6, 7, 11, 12; '698 patent, claims 17, 18, 20, 21, 23)

"Aqueous liquid phase that includes a cell-free nucleic acid polymerase enzyme system" ('568 patent, claims 1, 2, 4, 10)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"aqueous liquid phase that includes a cell-free, enzymatic, exponential nucleic acid amplification system" "aqueous liquid phase that includes a cell-free nucleic acid polymerase enzyme system"	*No construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* aqueous liquid portion that includes a set of components that together can perform cell-free, enzymatic, exponential amplification of a nucleic acid aqueous liquid portion that includes a cell-free nucleic acid polymerase enzyme system	a solution dissolved in water containing a buffer, a nucleic acid amplification enzyme, nucleotide substrates, and, where required, oligonucleotide primers

Once "amplification system" is construed, these terms require no further construction; their meanings are plain on their face. Illumina, however, seeks to construe these terms narrowly in order to engineer a noninfringement argument that these terms are not met if any component of an amplification system—despite being in the liquid phase—is not ***dissolved in the liquid phase***. For example, Illumina argues that this claim term is not met if a component in the amplification system is attached to a solid matrix, even if that component is still physically in or exposed to the liquid and able to participate in an amplification reaction. To that end, Illumina argues that "aqueous liquid phase" "simply means that the components of the amplification system are free in a water-based solution." D.I. 65 at 11-12. This is contradicted by the intrinsic evidence as shown in Plaintiffs' opening brief and further discussed below. D.I. 67 at 9-12.

The ordinary meaning of "aqueous" is simply "water-based," not "dissolved in or mixed with water" as Illumina suggests.[4] D.I. 65 at 12. The intrinsic evidence is consistent with this ordinary meaning. The claim language states that the claimed aqueous liquid phase merely "includes" an amplification system, which does not require any dissolution but instead generically allows for individual components of the amplification system to be either dissolved or suspended in solution or attached to the solid matrix.[5] As discussed in Plaintiffs' opening brief, but not discussed in Illumina's brief: (i) the applicants explained during prosecution of the '478 patent that claim 1 requires that certain components "be in the aqueous phase ***but does not require that [they] be totally free in solution*** in the aqueous phase" (D.I. 67 at 12), and (ii) '568 patent claim 8 expressly requires that enzymes be linked to the matrix, showing that the aqueous liquid phase in claim 1, from which claim 8 depends, covers amplification systems with individual components (*e.g.*, enzymes) that are linked to the solid matrix (*id.*).

Indeed, Illumina cites to passages from the patent that actually ***support*** Plaintiffs' construction; those cites are explicit that the amplification system can be "included" in the aqueous liquid phase ***either*** by having its components free in liquid ***or*** attached to the solid matrix while immersed in liquid (and thus still in liquid). D.I. 65 at 12, n.34 (citing JA8 at 4:54-56 ("The enzyme(s) included in the amplification system can be either present in the liquid phase

[4] Illumina relies on several dictionaries, but none support its argument. Conspicuously, Illumina omits the first definition from its first cited dictionary that ***supports*** Plaintiffs' position: "of, having the characteristics of, or relating to water"—*i.e.*, water-based, ***not*** water-based ***solution***. *Compare* D.I. 65 at 12, n.33 *with* Pendleton Decl., Exh. A. Illumina's other dictionary definitions are irrelevant as they are about definitions of "aqueous solution" instead of just "aqueous," which by itself does not mean "in solution." *See* Pendleton Decl., Exhs. B, C.

[5] If the Court determines that "aqueous" needs to be clarified for the jury, Plaintiffs would agree to define that word as "water-based" such that "aqueous liquid phase" would be construed as "liquid water-based portion." JA9 at 6:54-55.

or immobilized on the solid matrix."); JA10 at 7:46-69[6] ("Enzymes included in the enzyme systems can be either dissolved in the liquid phase, or be immobilized on the solid matrix.")).[7] Finally, compounding the problems with Illumina's proposed construction is the fact that it disregards various words in the claim terms at issue, such as "cell-free," "exponential" and even "amplification system" and "polymerase enzyme system" as Illumina construes those terms, thereby providing a separate basis for rejecting it.

3. "Forming a liquid mixture of the sample and said amplification system" ('698 patent, claims 1-3, 6, 12, 15, 16)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"forming a liquid mixture of the sample and said amplification system"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* combining the sample and the amplification system together in a liquid	mixing the sample and every component of the amplification system into solution (i.e., not linked to the water-insoluble matrix)

Similar to "aqueous liquid phase," Illumina seeks to concoct a noninfringement argument by proposing a construction that would require that all components of the amplification system and the sample be dissolved in solution. This proposal to construe the claims to require

[6] Illumina's citation to JA11 at 10:46-69 appears to be a typo that should be JA10 at 7:46-49.

[7] Illumina's other cites to the intrinsic record do not support its proposed requirement that every component of an amplification system be "free in a water-based solution." Illumina's citation to JA7 at 1:23-27 is not even relevant to this term, as it merely gives examples of prior art methods for amplification and does not purport to limit the invention. Additionally, Illumina's citation from JA1011 does not indicate that the matrix containing a polymerase enzyme and the liquid phase containing a polymerase enzyme are mutually exclusive as Illumina suggests. D.I. 65 at 12, n.35. That cite only highlights that the patent claims a matrix that immobilizes a liquid phase containing an amplification system. In other words, because the matrix immobilizes the liquid phase that contains the polymerase enzyme, the matrix in turn also contains the polymerase enzyme. Thus, the matrix containing a polymerase enzyme is not necessarily distinct from the liquid phase containing a polymerase enzyme. Its remaining cites just state what is apparent from the face of the claim term: the aqueous liquid phase is not the solid matrix, and the aqueous liquid phase includes a set of components that together can amplify a nucleic acid.

dissolution should be rejected for the same reasons discussed above. Furthermore, the claim language itself opposes Illumina's re-write of "liquid mixture" to "liquid solution." A mixture is not a solution, but a combination of different elements.[8]

None of Illumina's citations to the intrinsic record suggest otherwise.[9] For example, Illumina cites to Example 3 from the specification, which describes an amplification system and sample that are "mixed with" a bisacrylamide solution. *See* JA35 at 18:55-61. But there, the specification distinguishes between a mixture and a solution, underscoring their difference. Illumina also cites to JA32 at 11:18-22, which describes the use of monolayer media with amplification components that are mixed together. However, that citation says nothing about dissolving the components into a liquid. Illumina's additional citations to other terms in the same claims are just not relevant. D.I. 65 at 14. First, as discussed above, Plaintiffs do not dispute that a liquid is not a solid. Second, the phrase "migrate by diffusion" refers to synthesized nucleic acids and has nothing to do with the sample or the amplification system that is mixed together as claimed.[10] Illumina's swimming pool analogy does not change the analysis because it is nonsensical—one of ordinary skill in the art would never use the phrase "liquid

[8] This is confirmed by the definition of "mixture" in common dictionaries. *See* The Academic Press Dictionary of Science and Technology at 1395 (1992) ("*Science*. The mass that results from the thorough blending of two or more substances."); The Am. Heritage Dictionary of the English Language at 1159 (1992) ("5. *Chemistry*. A composition of two or more substances that are not chemically combined with each other and are capable of being separated."). Exhs. A and B. Notably, despite Illumina's heavy reliance on numerous dictionaries for other claim terms, Illumina does not cite dictionary definitions of "mixture." No wonder—the dictionaries contradict Illumina's interpretation of "liquid mixture" as a "liquid solution."

[9] Where Illumina applies citations for its proposed construction of "aqueous liquid phase" to its proposed construction of "liquid mixture," D.I. 65 n.38 & n.39, Plaintiffs apply their discussion of those citations from the section on "aqueous liquid phase" in this section. *See supra* 4-6.

[10] This phrase also has nothing to do with whether synthesized nucleic acids are in solution, just whether they are capable of movement to other zones.

mixture" to describe swimmers in a swimming pool under either party's construction (or anybody's construction). A more relevant analogy might be soup, which is a liquid mixture of its ingredients, such as vegetables and noodles, but not a solution of those things. Thus, if the Court deems construction of this term necessary, the term means combining the sample and amplification system components in liquid to allow the elements of the mixture to interact.

4. "Entrapping" (all claims)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"entrapping"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* keeping within limited zones	continuously holding substantially motionless and preventing any convection and intermixing

Contrary to Illumina's arguments, this term requires no construction because it is readily understandable based on the claim language and the specification, which Plaintiffs demonstrated in their opening brief. D.I. 67 at 13-14. As the parties agree, the specification uses "entrapping" to describe the invention, which involves an "immobilized medium for amplification of nucleic acids [that] comprises a liquid phase entrapped within a solid matrix that … is capable of preventing convection and intermixing of different zones of the liquid phase." *See* D.I. 65 at 3; D.I. 67 at 15 (both quoting JA8 at 4:46-52). The specification repeatedly explains that entrapping refers to preventing different nucleic acid templates from intermingling such that colonies of a single nucleic acid can be formed without cross-contamination, thereby embodying and furthering the goals expressed in the specification. *See* JA10 at 7:50-52 ("During amplification in an immobilized medium, nucleic acids grow as colonies rather than spread throughout the reaction volume."); JA9 at 5:36-42 ("Entrapment of nucleic acids in an immobilized medium according to the invention substantially prevents competition between

different templates, since their progeny is not allowed to spread all over the reaction volume."). This meaning of "entrapping" as preventing intermingling of amplification reactions that would otherwise interfere with the formation of discrete colonies of a single nucleic acid is readily understandable from the patent. Accordingly, no further construction is needed.

If the Court deems construction necessary, however, Plaintiffs' proposed construction, "keeping within limited zones," should be adopted because it is derived from the specification and is consistent with the overall purpose of the invention—the formation of distinct colonies of a single nucleic acid. The specification repeatedly explains that the amplification reaction is entrapped in limited "zones": "[a]ccording to [the] invention, exponential amplification of nucleic acids … is carried out in an immobilized medium rather than in solution as it is done in the prior art, in order to ***keep the templates and the reaction products within limited zones*** at fixed locations of the reaction volume." JA9 at 6:47-52. *See also* JA1 at Abstract ("[T]he progeny of each molecule (clone) and the expression products ***remain in the same zone***"); JA8 at 4:61-64 ("The nucleic acid molecules become entrapped somewhere in the medium, and their exponential amplification results in a 'colony' ***within a limited zone*** surrounding the progenitor template."); JA9 at 5:1-5 ("Provided that the nucleic acid sample has been properly diluted, ***different colonies occupy separate zones*** within the immobilized medium …."); *id*. at 6:16-19 ("Expressing nucleic acids in an immobilized medium results in the expression products being accumulated ***within the zones where the nucleic acid templates are entrapped***."); JA11 at 9:14-20 ("Carrying out the reaction in an immobilized medium allows the contaminating nucleic acids to be amplified at, and their competition to the growth of the desired nucleic acids be restricted to, ***limited zones*** of an immobilized medium ***where the contaminating templates were originally entrapped***."); *id.* at 9:24-26 ("[S]ubstrates are present in ***separate zones*** …."); JA13 at 14:3-6

("Expressing nucleic acids in an immobilized medium results in the expression products being accumulated ***within the zones where the nucleic acid templates are entrapped***.").

While Illumina cites to some of those very same portions of the specification for support of its construction, it inexplicably overlooks the critical language focusing on the requirement of keeping the reaction within limited "zones." For example, although Illumina claims that its proposed construction mirrors the cited passage below, it disregards the core of the description—keeping the liquid phase within "different zones" so that discrete colonies will be formed:

> term in the specification, that definition ordinarily controls."[4] Here, the Chetverins repeatedly defined the term "entrapping" by describing the characteristics of the matrix in "our invention":
>
> > According to our invention, the immobilized medium . . . comprises a liquid phase entrapped within a solid matrix that possesses a highly expanded surface with the average pore size ranging from 100 μm to 5 nm, and therefore is capable of preventing convection **and** intermixing of different zones of the liquid phase."[5]

D.I. 65 at 3. In its brief, Illumina ignores the highlighted language that ties convection and intermixing to the more fundamental goal of entrapping to prevent convection and intermixing across ***different zones of the liquid phase*** (*i.e.*, to prevent cross-contamination). Another passage cited by Illumina also emphasizes the importance of preventing convection and intermixing "of ***different zones*** of the liquid phase," but again Illumina ignores the discussion of zones in its brief. JA9 6:57-58 (D.I. 65 at 3-4, n.5). Instead, Illumina asserts that "entrapping" means "continuously holding substantially motionless and preventing any convection and intermixing." But this proposal does nothing more than cherry-pick select words from the specification and impermissibly disregards the context, purpose, and discussion of the entrapping feature expressed in the numerous passages from the patent cited above.[11]

[11] *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) ("[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in

In fact, contrary to Illumina's claim construction (and noninfringement) arguments, the specification expressly contemplates the movement of liquid provided that amplification reactions are kept within limited zones. For example, one embodiment practices the invention by "continuously washing" the immobilized medium with a substrate solution. *See* JA11 10:13-14. This disclosure in the specification trumps Illumina's efforts to arbitrarily exclude any flow of liquid based on a dictionary definition of "convection."[12] Illumina also improperly seeks to inject the words "continuously" and "any" into their construction of "entrapping" in a manner not used in the passage from the patent that it purports to "mirror," much less in the claims.

Finally, Illumina's assertion that "zones" is an ambiguous term should be rejected; the specification is clear what "zones" are for purposes of entrapment—areas in which the reaction products are contained to prevent cross-contamination, as discussed above. For example, the specification describes zones as "fixed locations of the reaction volume" which "different colonies occupy." *See* JA9 at 6:47-52; JA9 at 5:2-5; *see also* JA8 at 4:46-51; JA11 at 9:14-20. Indeed, Illumina ***itself*** relies on portions of the specification that explicitly discuss entrapping to limit motion across zones. *See* D.I. 65 at 3 (citing to JA8 4:46-52, which discusses "preventing convection and intermixing of different zones of the liquid phase"); *id.* at 3-4, n.5 (citing JA9 6:53-60, which discusses a matrix penetrating a liquid phase so that there is a lack of convection and intermixing of different zones).

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which the disputed term appears, but in the context of the entire patent, including the specification.").

[12] *See id.* at 1318-21 (explaining in detail why dictionary definitions are a less reliable source for understanding claim terms than the claim language or specification of the patent); *see also id.* at 1321 ("[H]eavy reliance on the dictionary divorced from the intrinsic evidence risks transforming the meaning of the claim term to the artisan into the meaning of the term in the abstract, out of its particular context, which is the specification.").

5. "Completely entrapping" ('478 patent, all claims; '698 patent, claims 17, 18, 20, 21, 23; '568 patent, all claims)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"completely entrapping"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* completely keeping within limited zones	entrapping all (*i.e.*, the entirety or whole) of [the thing listed after the term]

Illumina has failed to show why this term requires construction; as shown in Plaintiffs' opening brief, the meaning of this term is plain and unambiguous from the patent. *See* D.I. 67 at 16. If construction is warranted, it is properly construed to mean "completely keeping within limited zones," for the reasons discussed above. Illumina's proposed construction, "entrapping all (*i.e.*, the entirety or whole) of [the thing listed after the term]," does little more than proffer an alternate definition for the word "completely," which itself needs no construction. To the extent the parties disagree over what "all (*i.e.*, the entirety or whole) of [the thing listed after the term]" encompasses, that dispute focuses on the term listed after "completely entrapping"—*i.e.*, "aqueous liquid phase that includes a cell-free enzymatic, exponential nucleic acid amplification system" ('478 patent, claim 1 (JA18); '698 patent, claim 17 (JA38)), "aqueous liquid phase that includes a cell-free nucleic acid polymerase enzyme system" ('568 patent, claim 1 (JA57)), "amplification system" ('478 patent, claim 14 (JA18)), and "nucleotide substrates" ('568 patent, claim 16 (JA57)), all of which are the subject of separate claim construction arguments.

Illumina's brief explains exactly why Illumina is going to such lengths to re-write this term: it wants to devise a noninfringement position based on the asserted flow of liquid outside the areas of entrapment. But such a claim construction is unsupported by the intrinsic evidence; there is no requirement that <u>all liquid</u> must be entrapped within a solid matrix. The specification

explicitly notes that the avoidance of mobile liquid outside of the immobilized medium is merely "preferabl[e]"—as opposed to mandatory—and establishes that the invention permits mobile liquid outside of the immobilized medium, contradicting Illumina's argument otherwise. JA10 at 8:36-41. Indeed, the claims do not require that the solid matrix entrap ***all*** liquid, but just the aqueous liquid phase ***that includes an amplification system*** (*i.e.*, a set of components that are together capable of amplifying a nucleic acid, *see supra*). *See, e.g.*, '478 patent claim 1 (JA18). To the extent there is additional liquid that includes something <u>less</u> than such a set of components (*i.e.*, does not include all of the components that are together capable of amplifying a nucleic acid), that is irrelevant for purposes of meeting the limitations of the claims, which are open-ended "comprising" claims.[13] This is consistent with the goal of the invention to keep the amplification reaction, and not necessarily all liquid, in limited zones.

Illumina also tries to muster up a prosecution history estoppel in an effort to exclude systems with free-flowing liquid outside the zone of entrapment. The legal requirement for establishing such estoppel is a "clear and unmistakable disavowal" of claim scope,[14] which is not present here. Illumina first selectively quotes the following passage from the prosecution history of the '478 patent without acknowledging the highlighted portions:

[13] Claims using transitional terms, such as "comprising" and "including," are construed as open-ended, generally allowing for extra elements or steps that are not explicitly recited in the claims. *See CIAS, Inc. v. Alliance Gaming Corp.*, 504 F.3d 1356, 1360 (Fed. Cir. 2007) ("In the patent claim context the term 'comprising' is well understood to mean 'including but not limited to.'").

[14] *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1326 (Fed. Cir. 2003) ("To balance the importance of public notice and the right of patentees to seek broad patent coverage, we have thus consistently rejected prosecution statements too vague or ambiguous to qualify as a disavowal of claim scope. … Consequently, for prosecution disclaimer to attach, our precedent requires that the alleged disavowing actions or statements made during prosecution be both ***clear and unmistakable***.").

> There is no disclosure in Stapleton of forming nucleic acid colonies. Nor is there any disclosure of a liquid phase completely entrapped within solid media: Stapleton allows migration of nucleic acids to different zones (e.g. Stapleton discloses a liquid film between the carrier and the matrix (p. 7, line 64-67; and also teaches using agarose during PCR amplification p. 12, which, as one skilled in the art would know, means that the agarose will liquify and nucleic acids in different pores will not be separated during amplification).

Compare JA546 *with* D.I. 65 at 8. The highlighted portions that Illumina omits from its brief only further support Plaintiffs' construction that focuses on maintaining an amplification reaction within different limited zones. Specifically, in that paper, the applicants distinguished the invention from a reference ("Stapleton") disclosing "a device for processing biological samples" with a "liquid film between the carrier and the matrix," and made no disavowal (let alone one that is clear and unmistakable) of covering mobile liquid outside of the claimed immobilized medium. Rather, the applicants again confirmed the importance of avoiding migration of nucleic acids between zones by distinguishing Stapleton on the basis that it does not disclose a liquid phase completely entrapped within a solid matrix because it allowed for nucleic acids to migrate between zones. This evidence thus ***confirms*** Plaintiffs' construction of "completely entrapping" as completely keeping within limited zones. There is no prosecution history estoppel here.[15]

Illumina also tries to manufacture an estoppel based on the applicants' discussion in the prosecution history of the '568 patent of the O'Driscoll and Chang prior art references. But as with Stapleton, these statements distinguish O'Driscoll and Chang on the basis that neither

[15] Because of the important policy considerations at issue, the Federal Circuit has required that the "clear and unmistakable disclaimer" cannot be present when "a prosecution argument is subject to more than one reasonable interpretation, one of which is consistent with a proffered meaning of the disputed term." *SanDisk Corp. v. Memorex Prods., Inc.*, 415 F.3d 1278, 1287 (Fed. Cir. 2005); *see also Phillips*, 415 F.3d at 1317.

discloses entrapment of an aqueous liquid phase that includes an amplification system. The applicants stated that, unlike in those references, "continuous layers are to be avoided" in their invention, tying their statement to the specification's explanation that "mobile liquid outside of the immobilized medium should preferably be eliminated, so that nucleic acid or protein molecules cannot be transferred to another location during the reaction." *See id*. (citing to JA10 8:36-49). Hence, the applicants were not disclaiming continuous layers per se, but the inability to prevent migration of amplification reactions across zones to form nucleic acid colonies.

Finally, Illumina's remaining citation from the prosecution history of the '568 patent does not constitute a clear and unmistakable disavowal of anything. *See* D.I. 65 at 9, n.22. The focus of the applicants' statement was just to explain whether polymerase enzymes and nucleic acid molecules interact in a manner such that resulting amplification products cannot diffuse to other colonies. *See* JA1010. This again is consistent with Plaintiffs' construction of "completely entrapping" (and "entrapping").

The nail in the coffin of Illumina's prosecution history estoppel argument comes from the same page of the prosecution history of the '478 patent that Illumina relies on in its brief, but again selectively cites. JA587 (cited in D.I. 65 at 9, n. 21). There, the applicants explained that, although the aqueous liquid phase (and thereby the full amplification system) is completely entrapped by the solid matrix, "individual components, e.g., nucleotides, need not be completely entrapped in the matrix." JA587. This establishes beyond doubt that the invention encompasses a system in which individual components of an amplification system can be transported in and out of the matrix, *e.g.* by a mobile liquid, so long as the ***set*** of components that ***together*** can amplify a nucleic acid remains entrapped.

6. "Thin Layer" ('698 patent, claims 1-3, 6, 12, 15, 16, 18; '568 patent, claims 1, 2, 4, 10)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"thin layer"	*No construction necessary.*	A layer having a thickness of at least 1 millionth of a meter

Illumina improperly reads a lower limit of one millionth of a meter (called a "micron") into the claimed "thin layer."[16] Illumina's proposal is contradicted by the intrinsic evidence, which its brief does not address, such as (i) the express teaching in the patent that the thickness of the thin layer is not tied to a specific number but is instead based on other considerations, such as the mechanical strength of the solid matrix (JA11-12 at 10:64-11:1), (ii) the dependent claims that recite a lower limit of one micron (or no limit at all) such that the related independent claims are not so limited (*see, e.g.*, '698 patent, claims 1 and 6 (JA18)),[17] and (iii) the '568 patent, claim 16, which expressly covers embodiments where the matrix layer is less than a micron. *See* D.I. 67 at 17-19. Hence, the patent does not disclaim layers thinner than a micron.

With the intrinsic evidence squarely against it, Illumina again resorts to manufacturing a purported disavowal of claim scope, relying heavily on the use of the phrase "down to 1 µm" to describe ***examples*** of layer thicknesses that "***can*** also be used" in the invention. D.I. 65 at 17-18 (citing JA12 at 11:1-4). But Illumina not only improperly converts "can" to "must," Illumina also ignores the context of this statement as it was used during prosecution, which involved the question of whether the term "thin layer" was sufficiently definite (*i.e.*, supported by the written description in the patent). *See* JA496. The applicants explained that the term "thin layer" was

[16] *See SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1340 (Fed. Cir. 2001) (describing "reading a limitation from the written description into the claims" as "one of the cardinal sins of patent law").

[17] *See Phillips*, 415 F.3d at 1315 ("[T]he presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim.").

definite based on the ***examples*** in the specification of layers ranging from one micron to 10 millimeters. *See id.* That is not a "clear and unmistakable disavowal," and Illumina's estoppel argument should be rejected.[18] Indeed, the allowed claims demonstrate that there was no such disavowal of claim scope given that claim 16 of the '698 patent expressly recites a limit lower than one micron. Illumina's efforts to limit this term should be rejected.

7. "Incubating said immobilized medium" ('478 patent, claims 1, 3, 6, 7, 11, 12; '698 patent, claims 17, 18, 20, 21, 23); and

8. "Incubating said trapped mixture" ('698 patent, claims 1-3, 6, 12, 15)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"incubating said immobilized medium"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* maintaining the immobilized medium under conditions that promote the claimed reaction	maintaining all of the immobilized medium provided in step (a) under conditions that promote exponential amplification
"incubating said trapped mixture"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* maintaining the trapped mixture under conditions that promote the claimed reaction	maintaining all of the trapped medium provided in step (b) under conditions that promote exponential amplification

The parties disagree on whether these terms require construction. Plaintiffs' opening brief shows that the plain and ordinary meaning of these terms is apparent and that no further construction is warranted. Illumina fails to show that deviation from such plain and ordinary meaning is warranted. But should the Court find construction necessary, these terms should be

[18] *See, e.g., Arbitron, Inc. v. Int'l Demographics, Inc*., Civil Action No. 2:06-CV-434, 2009 WL 68875, *17 (E.D. Tex. Jan. 8, 2009) (finding that "inventors' statements [during prosecution] merely identified the relevant written description support and had no limiting effect") (attached as Exh. C). *See also ACTV Inc. v. Walt Disney Co.*, 346 F.3d 1082, 1092 (Fed. Cir. 2003) ("Because the written descriptions of the patents lack an indication of the patentee's clear intent to limit the term URL to absolute URLs, and because the written descriptions further support a broader interpretation, we decline to impose such a limit.").

construed as discussed in Plaintiffs' brief. The claimed act of incubating does not require that the object of incubating remain completely static as proposed by Illumina. First, Illumina points to no support for injecting the word "all" into the claims through its constructions where the word doesn't even exist in the claims. Second, Illumina also relies on a strained reading of "said" to mean there can be no change in the antecedent object. This is inapposite to the customary meaning of the word "said."[19] Indeed, the intrinsic record expressly contemplates changes to the object that is being incubated. For example, during prosecution of the '478 patent, the applicants explained that "individual components, e.g., nucleotides, need not be completely entrapped in the matrix," indicating that individual components can be removed or added during incubation. JA587. Illumina's construction is unduly restrictive (not to mention illogical) in prohibiting any change to the immobilized medium or trapped mixture.

9. "Wherein the average distance between the nearest solid surfaces is smaller than the distance which the synthesized nucleic acid product can migrate by diffusion during the reaction" ('698 patent, claims 1-3, 6, 12, 15)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"wherein the average distance between the nearest solid surfaces is smaller than the distance which the synthesized nucleic acid product can migrate by diffusion during the reaction"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* wherein the average distance between the nearest solid surfaces is sufficiently small to prevent synthesized nucleic acid products from migrating between zones during the reaction	wherein the average distance between the nearest solid surfaces is less than the distance that any nucleic acid product synthesized during the accused reaction can move (*i.e.*, from one location in the matrix to another) during that reaction

The parties dispute whether this claim term requires construction. Plaintiffs submit that the meaning of this term is clear on its face, and Illumina has not shown otherwise. If the Court

[19] By its logic, Illumina would construe the term "eating said steak" to forbid adding steak sauce.

concludes that construction is necessary, the parties dispute whether the term should be construed in a manner that is divorced from the context of the claims (as Illumina does) or in a manner that is in line with the claim language and specification as a whole (as Plaintiffs do). Illumina's reductionist approach should be rejected as it results in an interpretation contrary to how one of ordinary skill in the art would read the claims. This is apparent from the fact that Illumina's arguments in support of its construction go far beyond what its construction actually says. In particular, although Illumina appears to construe "can migrate by diffusion" as "can move (*i.e.*, from one location in the matrix to another)," it then argues that "can move" means "does move."[20] D.I. 65 at 21 ("'migrate by diffusion' requires that the product actually move between locations in the matrix."). This backdoor effort at claim-rewriting should be rejected.

Contrary to Illumina's assertions, there is nothing ambiguous about Plaintiffs' proposed construction. Unlike Illumina's proposal, Plaintiffs' proposal is based in the intrinsic evidence, which shows that this claim term is directed to maintaining physical barriers to migration of synthesized nucleic acid products between zones so that discrete nucleic acid colonies may be formed. As explained in the prosecution history of the '568 patent, the specification "teach[es] that pore size is chosen to prevent migration of copies of the target from one colony to another." JA1011 (citing to JA9-10 at 6:60-7:6). Thus, if the Court deems construction necessary, Plaintiffs' construction should be adopted.

[20] Illumina's arguments appear to preclude the possibility of proving infringement by circumstantial evidence. *See Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1326 (Fed. Cir. 2009) (accepting evidence that establishes that accused products "can necessarily infringe under certain circumstances").

10. "Distributing in said aqueous liquid phase" ('478 patent, claims 1, 2, 6, 7, 11, 12; '698 patent, claims 17, 18, 20, 21, 23)

"Distributing in said amplification system" ('478 patent, claims 14, 15, 16)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"distributing in said aqueous liquid phase" "distributing in said amplification system"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* separating nucleic acid molecules in the aqueous liquid phase separating nucleic acid molecules in the amplification system	entirely dissolving in [the aqueous liquid phase/amplification system] (*i.e.*, not linking to the water-insoluble matrix)

Again, the parties disagree over whether this claim term requires construction. The only unique issue here is "distributing" because "aqueous liquid phase" and "amplification system" are addressed elsewhere. "Distributing" has a plain and ordinary meaning; no construction is needed. But again, Illumina seeks to contort an ordinary term to read a dissolution requirement into the claims, arguing that "distributing" means "entirely dissolving in." That is contrary to the common understanding of "distributing," which is how the patent uses it.

Illumina's disregard for the plain meaning of "distributing" is shown by its cherry-picked dictionary definition. Instead of relying on any of the eight other dictionaries that it cited for other terms, Illumina turns to a web dictionary that is not even contemporaneous with the filing of the patent and in the context of the wrong field of chemistry to support its definition of "distributing." One need only look at those other dictionaries to understand why: "distributing" is defined as "dispersing," "spreading," or "scattering," consistent with Plaintiffs' proposed construction.[21] There is no ordinary definition of "distributing" that equates it with "dissolving,"

[21] *See, e.g.*, Webster's Third International Dictionary 660 (1981) ("2a: to spread out or scatter so as to cover a surface or a space") (attached as Exh. D); Roget's 21st Century Thesaurus in

which makes sense because the two concepts are distinct.[22] Indeed, consistent with its plain meaning and with Plaintiffs' proposed construction, the patent explains that the "step of distributing ***separates*** individual templates, resulting in nucleic acid amplification to form at least one separate, detectable colony of said nucleic acid product in said medium." *See, e.g.*, '478 patent, claim 1 (JA18). Illumina fails to identify any intrinsic evidence that suggests that the patent uses "distributing" in any way other than its ordinary meaning.[23] Nothing in the patent or prosecution history equates the concept of distributing with dissolution. D.I. 67 at 23-24.

11. "A preformed immobilized medium" ('568 patent, claims 1, 2, 4, 10)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"a preformed immobilized medium"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* an immobilized medium that is formed prior to amplification	an immobilized medium that is formed prior to addition of a template for amplification

The dispute here is whether this term requires construction, and, if so, whether the immobilized medium must be formed prior to the addition of a template for amplification or more generally prior to amplification. As explained, this term is explicitly defined by the claims, and no further construction is warranted. *See* D.I. 67 at 24. If the Court deems construction necessary, however, Illumina's position that templates can only be added to the immobilized medium after its formation should be rejected because it contradicts the intrinsic evidence. *See* D.I. 67 at 24-25. Notably, Illumina disregards the statement in the specification that "[n]ucleic

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Dictionary Form 269 (1992) (including "spread," "scatter," and "disperse" as potential synonyms for "distribute," but not including "dissolve") (attached as Exh. E).

[22] Nor does "distributing" mean "introduced," as Illumina urges without basis. *See* D.I. 65 at 16.

[23] Illumina's citations to the intrinsic record are not about distributing nucleic acids, but focus instead on preventing the migration of nucleic acids. *See* D.I. 65 at 15-16, n.44-47.

acids intended for amplification … should be introduced into the liquid phase of a layer … prior to its immobilization." JA12 at 12:63-66. Illumina's request to read a preferred embodiment out of the claims should be rejected.[24]

12. "Nucleotide substrate" ('568 patent, claim 16)

Term(s)	Plaintiffs' Construction	Illumina's Construction
"nucleotide substrate"	*No further construction necessary. Should the Court determine that construction is required, Plaintiffs propose:* a substance comprising a nucleotide on which an enzyme acts	nucleotides, nucleotide analogs, or similar structures used as the building blocks of a new nucleic acid strand. Nucleic acids, such as primers, are not nucleotide substrates

The dispute here is whether a nucleotide substrate is limited to a single nucleotide or can comprise more than one nucleotide. As shown in Plaintiffs' opening brief, the intrinsic evidence does not support such a narrow reading. Indeed, it is notable that Illumina equates "synthesized nucleic acids" with nucleic acid sample or the amplification system components, *see* D.I. 65 at 14 (citing to claim terms regarding the movement of synthesized nucleic acids in support of the separate claim term "forming a liquid mixture of the sample and amplification system"), yet seeks to distinguish between nucleotide substrates and primers and other nucleic acids for purposes of this term. Illumina cannot ask the Court to look one way when it is favorable to it and look the other way when it is not.

[24] *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576 (Fed. Cir. 1996) (a construction that excludes a preferred embodiment "is rarely, if ever, correct and would require highly persuasive evidentiary support").

II. ILLUMINA'S PATENTS: DISPUTED CLAIM TERMS

A. THE BRIDGHAM PATENTS (NOS. 6,831,994 AND 6,654,505)[25]

1. "Optical characteristic of each/said microparticle" ('994 patent, all claims; '505 patent, claims 2-5)

Term(s)	Life's Construction	Illumina's Construction
"optical characteristic of [each/said] microparticle"	an optical quality of the microparticle itself, not the attached analyte	an optical characteristic of the microparticle

The dispute on this term is whether the optical characteristic of the microparticle must be a feature of the microparticle itself or whether it could instead refer to a feature of an attached analyte. The claim language and specification require that the "optical characteristic" be "of each microparticle" and not the attached analyte. Also, the claims state that optical characteristics of microparticles are used to determine the centers of microparticles, and basing the center of the microparticle on an attachment to the microparticle would frustrate a the primary purposes of the invention—tracking positions of microparticles. *See* D.I. 67 at 27-29. Illumina's effort to construe this claim language so broadly as to undermine a fundamental feature of the invention should be rejected.[26]

[25] After the Court denied Plaintiffs' motion to stay the litigation on the four Illumina patents pending the reexamination of those patents in the PTO, Life learned that Illumina is seeking to use the pending reexamination proceedings to try to change the priority date of the '505 patent by relying on the filing dates of patent applications not previously part of the prosecution history. *See, e.g.*, Exh. F. If granted by the PTO, this would have profound effects on the litigation by, for example, expanding the prosecution history to include those new patents. If the prosecution history were expanded, claim construction may have to be repeated, since the prosecution history is taken into account when construing patent claims. *See, e.g., Phillips*, 415 F.3d at 1317.

[26] *See, e.g., Praxair, Inc. v. ATMI, Inc.*, 543 F.3d 1306, 1324 (Fed. Cir. 2008) ("The claims of the patent must be read in light of the specification's consistent emphasis on this fundamental feature of the invention."). Illumina also argues that the claim language "at least one optical characteristic" supports its construction that the characteristic need not be of the microparticle, apparently assuming that a microparticle can have only one optical characteristic. But the specification explains that a microparticle can have at least two types of optical characteristics (produced by "back-lighting" and "top-lighting," *see* JA1091-92 at 8:48-9:5), and both are

The '505 specification—including portions cited by Illumina—also supports Life's construction. The passage quoted at page 31 of Illumina's brief states that "detection means (114) periodically *records optical characteristics* of individual microparticles that ***provide a close approximation of microparticle centers***." D.I. 65 at 31 (first emphasis in original). Illumina ignores the fact that the optical characteristic is used to determine the center of the microparticle, and, by doing so, isolates "***of*** individual microparticles" from the claim language. Thus, when read in context, the passage supports Life's construction, not Illumina's.

Illumina's cites to the specification also highlight the distinction the patent makes between "optical characteristics" and "optical signals generated '***at***' or '***by***' the microparticle," a distinction that further supports Life's construction. *Id.* For example, Illumina points to column 9, lines 6-9 of the specification. But this passage says that "once microparticle centers are determined" ***then*** the optical ***"signals"*** are determined, referencing a period after the center of the microparticle is determined. This passage also emphasizes the difference between characteristics of signals generated by analytes at the microparticles and optical characteristics of the microparticles themselves. While Illumina states that the passage describes characteristics of the microparticles, a closer inspection shows that it does no such thing:

> In the preferred image processing approach, once microparticle centers (700) are determined, pixels (702) are assigned for determining characteristics, e.g. intensity, ***of an optical signal*** generated ***at*** each microparticle.

D.I. 65 at 32 (citing JA1092 at 9:6-9). This passage instead describes characteristics "of an ***optical signal***"—not an optical characteristic "of the ***microparticle***," and clarifies that the ***signal*** is generated "***at***" the microparticle, as contrasted with an ***optical characteristic*** "***of***" the microparticle. This is no isolated passage. The patent demonstrates that "characteristics of

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inherent to the microparticle, not the attached analytes. Thus, the "at least one" language refers to various characteristics of the microparticle itself, consistent with Life's construction.

microparticles" are entirely distinct from characteristics of the ***optical signals***. *See* D.I. 67 at 27-29.[27] *See, e.g.*, JA1092 at 10:28-39; JA1095 at 15:1-61. This distinction is important to practicing the invention because the patent calls for tracking the microparticles ***and*** analyzing the signals emitted from the analytes attached to the microparticles. Illumina's reliance on the language used to describe optical ***signals*** is thus misplaced, as it not only contradicts the rule of claim construction that different terms are presumed to have different meanings,[28] but vitiates a core purpose of the claimed invention.[29]

In sum, Illumina's arguments divorce "of each microparticle" from the claim term, and thereby actually highlight (presumably inadvertently) the distinction the intrinsic evidence makes between optical characteristics ***of*** the microparticle and optical signals generated ***at or by*** the microparticle. Similarly, Illumina's "plain claim language" argument actually reinforces Life's position. Illumina's proposed construction of "optical characteristic" should not be adopted.

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[27] For example the Abstract (to which Illumina cites (D.I. 65 at 32)) states that "an optical ***signal*** is generated at the surface of each microparticle which is characteristic of the interaction between the analyte carried by the microparticle." JA1051. The other portions of the specification cited by Illumina underscore this distinction. For example column 2, lines 5-8, of the specification emphasizes that "optical signals generated by, or as the result of, interactions of processing reagents and analytes on the surfaces of microparticles." JA1062.

[28] *See, e.g., Comaper Corp. v. Antec, Inc.*, 596 F.3d 1343, 1348 (Fed. Cir. 2010) ("There is an inference, however, that two different terms used in a patent have different meanings.").

[29] Illumina's "could-have-made" argument as to what Illumina now claims it could have argued during prosecution about the Resnick reference (D.I. 65 at 33) should carry no weight at all. Like its attempt to change the priority date of the '505 patent, *see supra* at note 25, Illumina is trying to rewrite history. But while the actual prosecution history is relevant as intrinsic evidence to the extent it expressly addresses a particular claim term, it is not relevant for a litigant to speculate about what the patent applicant could have argued and attach legal implications to such guesses. *See Schwarz Pharma, Inc. v. Paddock Labs., Inc.*, 504 F.3d 1371, 1377 (Fed. Cir. 2007) ("The fact that the inventors may have thought after the fact that they could have relied on other distinctions in order to defend their claims is irrelevant and speculative….").

2. "With sufficient resolution for individual microparticles to be distinguished" ('994 patent, all claims)

Term	Life's Construction	Illumina's Construction
"with sufficient resolution for individual microparticles to be distinguished"	the image resolution is sufficient to distinguish each individual microparticle from every other microparticle	the image resolution is sufficient to distinguish individual microparticles

The issue here is whether the imaging device must have sufficient resolution to distinguish each microparticle from every other. Illumina argues that the imaging device only needs a strong enough resolution to distinguish two microparticles from one another; under this interpretation, the remaining particles can clump together and appear as one. Illumina first rewrites the claim language to support its argument by deleting the "each" adjective from the specification's references to the microparticle and by effectively replacing "individual" with "plurality" to alter the meaning of the claim. But remarkably in the very next paragraph Illumina acknowledges that such rewriting of claims is improper. D.I. 65 at 34.

Illumina then ignores the '994 specification's mandate that the resolution of the imaging device must be sufficient to distinguish each microparticle from every other microparticle. As Life previously explained, the claimed invention provides a means for detecting a sequence of optical signals from ***each*** of the microparticles of the population. D.I. 67 at 30 (citing JA1088 at 2:20-26). This fundamental feature of ***the*** invention—expressed by both the claim language and the specification—would not be fulfilled if only two microparticles could be distinguished, because the optical signals from the remaining microparticles would appear as one signal, and there would be no way to detect the individual signals from ***each*** of the microparticles in the clump. When the specification uses language describing ***the*** invention, the invention as a whole (not merely a preferred embodiment) must meet the stated purpose. *See* D.I. 67 at 31, n.24.

3. "Signal tracking means effective to correlate the optical signals from each of the microparticles in each of the sequence of digital images with said center of said microparticle" ('994 patent, all claims)

Term	Life's Construction	Illumina's Construction
"signal tracking means effective to correlate the optical signals from each of the microparticles in each of the sequence of digital images with said center of said microparticle"	This "means plus function" limitation requires the same or equivalent structure disclosed in the patent for performing the claimed function, which is to correlate the optical signals from each of the microparticles in each of the sequence of digital images with said center of said microparticle. The disclosed structure is a microprocessor running software that performs the process shown in Fig. 8.	This is a "means plus function" limitation subject to an analysis under 35 U.S.C. § 112, ¶6. The claimed function is: correlating the optical signals from microparticles in a sequence of digital images with the centers of those microparticles. The disclosed structure is: data processor (818) running software that assigns pixels of the fluorescent images of the microparticles to the microparticle centers.

The parties agree that this term is in means-plus-function format subject to 35 U.S.C. § 112 ¶6, agree that the claimed function is correlating the optical signals from microparticles in a sequence of images with the centers of those microparticles, and agree that a computer running software performs the claimed function. The parties disagree on whether an algorithm must perform the claimed function. It is well established that "the corresponding structure for a § 112 ¶6 claim for a computer-implemented function is the ***algorithm*** disclosed in the specification."[30] Life's construction is based on the only possible algorithm disclosed in the specification and thus is the only legally tenable construction; Illumina, in contrast, ignores this legal requirement, identifies no algorithm, and, as a result, proposes an untenable construction.

Specifically, Illumina instead proposes a construction where the disclosed structure is "a data processor that runs software that assigns pixels of the fluorescent images of the microparticles to the microparticle centers." But "software that assigns pixels of the fluorescent images of the microparticles to the microparticle centers" is not a description of an algorithm, it

[30] *Harris Corp. v. Ericsson Inc.*, 417 F.3d 1241, 1249 (Fed. Cir. 2005).

is instead merely a repetition of the claimed function. Similar proposals have been repeatedly rejected by the Federal Circuit because they "simply describe[] the function to be performed, not the algorithm by which it is performed."[31] As Life explained in its opening brief, the only disclosure in the '994 specification that resembles an algorithm is the process shown in Figure 8 and described in the accompanying text. The fact that Figure 8 describes additional functions is irrelevant—this is the only algorithm-like disclosure in the specification, and the means-plus-function claim must be tied to an algorithm. If not, the claim will be invalid.[32] For these reasons, Life's construction should be adopted.

4. "Tracking positions of the microparticles" ('505 patent, claims 1-5)

Term	Life's Construction	Illumina's Construction
"tracking positions of the microparticles"	following the movement of microparticles during a sequence of processing steps	This preamble term is not a substantive limitation on claim 1, and thus does not require construction. One of ordinary skill would understand this term to relate only to the intended use of the claimed invention, and in that regard, to relate to the "correlating" term in the body of the claim.

The dispute here is whether this preamble term is a substantive limitation of the claim or not. Illumina goes to great lengths here to avoid having this term construed as a limitation, but as explained in Life's opening brief, Illumina has relied on this term as a claim limitation during the pending reexamination proceedings on this patent to try to distinguish the invention over the prior art.[33] Illumina's argument that the tracking term "was not relied on to overcome prior art

[31] *Aristocrat Techs. Austl. Pty Ltd. v. Int'l Game Tech.*, 521 F.3d 1328, 1333 (Fed. Cir. 2008); *see also* D.I. 67 at 33.

[32] *See, e.g., Finisar Corp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1340-41 (Fed. Cir. 2008); *Aristocrat*, 521 F.3d at 1337-38.

[33] *See* D.I. 67 at 35 and citations and Exhibits therein. Plaintiffs note that Illumina has taken fundamentally inconsistent positions in two forums (here and before the PTO). This dichotomy

during prosecution of the patent" (*see* D.I. 65 at 27) is therefore false. Illumina's effort to avoid this term as a claim limitation should be rejected on this basis alone, as several of the cases cited by Illumina hold.[34]

Illumina makes two additional arguments as to why this term is not a claim limitation, both of which should be rejected. Illumina first argues that "the 'tracking' term simply recites an intended use or purpose of the claimed software." D.I. 65 at 27. But Life's opening brief shows that the tracking function is repeatedly described throughout the patent as a core aspect of the invention. *See* D.I. 67 at 34-35. Even the cases cited by Illumina hold that a term in a preamble limits the invention if it recites essential structure or steps.[35]

Illumina next asserts that the "tracking" term is merely "duplicative" of the "'processing … including correlating' step in the body of the claim." D.I. 65 at 28. But Illumina's own

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cannot be based on or explained by differences in the forums' applicable claim construction rules or standards (*e.g.*, Illumina's argument before the PTO in favor of a ***narrow*** construction is ***contrary*** to the broadest reasonable construction standard in that forum, and Illumina's argument here is contrary to the established claim construction rules for issued patents). Illumina is on the wrong side in each forum and cannot have it both ways, or either way.

Plaintiffs also note that in the pending reexamination on the Illumina patents, the "broadest possible" construction is applied, which allows the patentee (Illumina) the opportunity to amend the claims to more clearly (and more narrowly) recite the claimed invention. This is not the standard for claim construction in the district court and, as a result, the correct constructions in the district court are often (but not always) more narrow than the interpretation of the claims by the PTO.

[34] *See Symantec Corp. v. Computer Assoc. Int'l, Inc.*, 522 F.3d 1279, 1288-89 (Fed. Cir. 2008) (holding that if a preamble term is added or used to overcome a rejection by the Patent Office, it will be treated as a substantive limitation); *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) (same); *Intirtool, Ltd. v. Texar Corp.*, 369 F.3d 1289, 1295 (Fed. Cir. 2004) (same).

[35] *See, e.g., Catalina*, 289 F.3d at 808. *See also Vizio, Inc. v. Int'l Trade Comm'n*, -- F.3d --, 2010 WL 2079769 at *9 (Fed. Cir. May 26, 2010) ("Here, we conclude that the 'for decoding' language in the preamble of claims 1 and 23 is properly construed as a claim limitation, and not merely a statement of purpose or intended use for the invention, because 'decoding' is the essence or a fundamental characteristic of the claimed invention.") (attached as Exh. M).

proposed construction of the "processing" step defeats this argument: not only does it fail to refer to tracking, but Illumina's explanation of its construction for this term also fails to refer to tracking. D.I. 65 at 28-30. The tracking step is plainly a claim limitation appropriate for construction. Illumina offers no proposed construction for this term; the only proposed construction is that proposed by Life—"following the movement of microparticles during a sequence of processing steps." This construction is consistent with the specification and with the statements that Illumina has made to the PTO and should be adopted by the Court here.

5. "Processing the plurality of digital images, wherein said processing includes correlating the optical signals generated at each microparticle with its corresponding image in each of the plurality of digital images" ('505 patent, claims 1-5)

Term	Life's Construction	Illumina's Construction
"processing the plurality of digital images, wherein said processing includes correlating the optical signals generated at each microparticle with its corresponding image in each of the plurality of digital images"	analyzing the digital images so as to match the light signal that comes from each microparticle during each process step with the images showing the different positions of the microparticle during the sequence of processing steps	processing the digital images so as to match the light that comes from each microparticle in one image with the light that comes from that microparticle in a second image

The parties agree that this claim limitation requires matching the optical (*i.e.*, light) signal that comes from each microparticle with something, but disagree about what that "something" is. Illumina argues that the optical signals in one image are to be matched with the optical signals in a second image. Although Illumina asserts that its proposed construction "simply translates the terse technical language into a more understandable form, requiring no more and no less than is actually recited in the term," the reality is that Illumina ignores the plain language and clear meaning and instead seeks to re-write the claim. The plain language of the claim states that optical signals generated at each microparticle are to be matched "with its corresponding image,"

not with other optical signals. Life's construction makes this requirement clear, and as Life explained in its opening brief, the specification supports this interpretation. *See* D.I. 67 at 36-38.

The portions of the specification cited by Illumina do not support its construction of matching light signals in one image with light signals in another image. The first passage cited is: "An important feature of detection means (114) of the invention is the ability to keep track of individual microparticles through multiple process steps and/or cycles."[36] But Illumina does not explain how, using its construction, matching optical signals from one image with optical signals from another image would accomplish this. Nor does the specification, which nowhere discusses signal-to-signal matching. In contrast, matching optical signals with images showing microparticle positions (Life's construction) does help enable this feature.

Illumina also asserts that the following passage shows how optical signals in one image are matched with optical signals in another image: "In the preferred image processing approach, once microparticle centers (700) are determined, pixels (702) are assigned for determining characteristics, e.g. intensity, of an optical signal generated at each microparticle (602)." JA1066 at 9:6-9. That is not correct; this passage describes how optical signals are matched to an image showing the microparticle centers (an image created by "top-lighting" or "back-lighting" the particles), as explained in the passage preceding the lines quoted by Illumina. "Top light" and "back light" are not the claimed optical ***signals***, but rather are the claimed optical ***characteristics*** of the microparticles. This passage thus supports Life's proposed construction.

None of Illumina's remaining arguments detract from the correctness of Life's construction. Life agrees with Illumina that each image in the plurality of images must be processed. As Life has explained, that processing includes correlating the light signals to images

[36] D.I. 65 at 29 (citing JA1065 at 8:48-50).

showing the positions of the microparticles. Illumina argues that the "correlating" step only requires "establishing a relationship between light generated at a microparticle in one image and light generated at that same microparticle in a second image." D.I. 65 at 30. But Illumina ignores the language of the claim, which is "correlating the optical signals generated at each microparticle ***with its corresponding image***." JA1075 at 27:54-56. The corresponding image is of the microparticle, not of another light signal. This construction is abundantly supported by the specification, *see, e.g.*, JA1061-1071 at 8:48-9:31; 10:3-20; 18:60-19:6; 19:38-20:15.

B. THE BALASUBRAMANIAN PATENT (NO. 7,232,656)

6. "Generating sequence reads" (all claims)

Term	Life's Construction	Illumina's Construction
"generating sequence reads"	determining the identity and order of at least two nucleotide bases	determining the identity of at least two nucleotide bases

The only dispute on this term is whether "generating sequence reads" requires that the ***order***, in addition to the identity, of at least two nucleotides be determined. Illumina and Life agree that the "plain and ordinary meaning" of a claim term governs absent the patentee defining the term to the contrary.[37] This principle drives claim construction here because the plain and ordinary meaning of "sequence" ***is*** order. The specification and the dictionaries relied on by Illumina confirm this definition. For example, the Oxford Dictionary of Biochemistry and Molecular Biology, on which Illumina relies,[38] provides three definitions for "sequence," all of which use the word "order" or some derivative thereof:

[37] *See* D.I. 65 at 15, 28, 34, 40, 45, 46 and 48.

[38] D.I. 65 at 12 n.33; Oxford Dictionary of Biochemistry and Molecular Biology (rev. ed.) (A.D. Smith, et al., eds., Oxford Univ. Press 2000) at 594 (attached as Exh. G).

sequence 1 the ordinal arrangement of the constituent parts of a biopolymer, e.g. the order of amino-acid residues in a polypeptide chain or of the nucleotide residues in a polynucleotide chain; the known arrangement of such units in any biopolymer or fragment. 2 any particular segment, occurring in or derived from a biopolymer, having a known order of its constituent parts; a synthetic polymer composed of parts equivalent to those occurring naturally and present in a particular known order. 3 to determine the order of residues in a biopolymer or fragment. —**sequential** *adj.*

This is no anomaly; indeed, all of the dictionaries cited by Illumina that address "sequence" confirm that sequence requires an ordering.[39] There can thus be no dispute that the ordinary meaning of "generating sequence reads" requires "determining the identity ***and order*** of at least two nucleotide bases." This is a term where the meaning is readily apparent, "and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words."[40]

The specification also supports Life's construction, even though Illumina seeks to omit the pertinent language. For example, Illumina quotes three lines of an example in the specification, but omits the text that immediately follows Illumina's excerpt explaining that order is required for ascertaining the sequence:

> For example, the method may be used to identify SNPs [(nucleotides)] that occur after cytosine [(C)]…. The addition of C is followed by monitoring the next base incorporation (using a labeled base). By repeating this process a sufficient

[39] *See, e.g.*, Webster's Third New International Dictionary at 2071 (Merriam-Webster, Inc., 1981) (3(a)(1) "a methodical arrangement or consecutive order") (attached as Exh. H); http://dictionary.reference.com (last visited June 25, 2010) ("9. *Genetics.* the linear order of monomers in a polymer, as nucleotides in DNA or amino acids in a protein;" "12. *Biochemistry*. to determine the order of (chemical units in a polymer chain), esp. nucleotides in DNA or RNA or amino acids in a protein") (attached as Exh. I); Academic Press Dictionary of Science and Technology at 1959 (Christopher Morris, ed., Harcourt Brace Jovanovich 1992) ("*Computer Programming.* a group of items in a specified order, according to identifiable keys") (Exh. J).

[40] *Phillips*, 415 F.3d at 1314.

> number of times, a partial sequence is generated where each base immediately following C is known.

JA1113 at 12:11-24. That is, when the method is practiced in this manner, the resulting sequence is CA, CC, CG, or CT, and the order and identity of at least two nucleotide bases is determined. Thus, this language further supports Life's construction. *See* D.I. 67 at 38.

7. "An array of polynucleotide molecules" (claim 3)[41]

Term	Life's Construction	Illumina's Construction
"an array of polynucleotide molecules"	an array of single DNA fragments, as opposed to clusters of many DNA fragments of the same type	an arrangement of different types of DNA fragments

Illumina focuses much of its argument trying to explain why "array" should be construed to mean "arrangement." Life does not dispute this aspect of Illumina's construction, and would agree with construing array to mean "arrangement." The dispute here centers on whether the required "array" of the claims must be of single molecules as opposed to clusters of the same molecule. The answer is yes—the patent specifically defines these terms: "The terms 'arrayed polynucleotides' and 'polynucleotide arrays' are used herein to define a plurality of single molecules that are characterized by comprising a polynucleotide." JA1109 at 4:51-54. In other words, arrays are made of DNA fragments, which are each single molecules. The patentee acted as its own lexicographer here, and this definition must govern.[42]

[41] In its opening brief, Life addressed the three terms "an array of polynucleotide molecules," "which molecules can be individually resolved by optical microscopy," and "arraying the fragments such that different fragments can be individually resolved by optical microscopy" together because all three terms relate to the "single molecule" aspect of the invention. Illumina addressed these terms separately in its opening brief, so Life does the same here to specifically address Illumina's arguments, while continuing to note that all three terms embody the same concept—resolution of single molecule arrays.

[42] *Phillips*, 415 F.3d at 1316.

Illumina argues that the patentee used the term "array" to describe both single molecule and cluster arrays (that is, arrays that comprise clusters of many molecules of the same type) and therefore the claims should not be limited to single molecule arrays. But when the patentee referred to cluster arrays it specifically labeled them as such, and distinguished cluster arrays from the arrays of single DNA fragments. This is shown by many of the passages relied on (but notably not quoted) by Illumina. For example, Illumina cites column 3, lines 20-24, to show that the claimed "array" can be a cluster array. But that cited passage explains the disadvantages of cluster arrays, and the paragraph above the passage makes clear that "***[t]he arrays of the present invention*** comprise what are effectively ***single molecules***." JA1109 at 3:13-14. In other words, Illumina's cited passage specifies that the invention does ***not*** include cluster arrays and distinguishes cluster arrays from the single molecule arrays of the present invention. This term requires that the array be of single molecules and Life's construction should be adopted.

8. "Which molecules can be individually resolved by optical microscopy" (claim 3)

Term	Life's Construction	Illumina's Construction
"which molecules can be individually resolved by optical microscopy"	each DNA molecule in the array can be distinguished from every other molecule by optical microscopy	wherein the polynucleotides having different sequences can be distinguished from each other using a microscope

As an initial matter, Life does not dispute Illumina's construction "by optical microscopy" as "using a microscope." Life would agree to a construction where "each DNA molecule in the array can be distinguished from every other molecule using a microscope." The sole issue here is similar to that presented by the "array" term above: must the DNA molecules be distinguishable from one another, or can molecules having the same sequence be clustered together and viewed as one? The specification provides the answer, defining the term "individually resolved" to "indicate that, when visualized, it is possible to distinguish ***one***

molecule on the array from its neighboring molecules." JA1109 at 4:37-39. Illumina ignores the express definition provided by the patentee and the phrase "individually resolved" in the claim.

Illumina again seeks to rewrite its claims, this time by replacing "molecules can be individually resolved" with "polynucleotides having different sequences can be distinguished from each other." D.I. 65 at 35. Illumina does this in a transparent attempt to create a claim which covers systems that do not resolve individual molecules but rather resolve clusters of DNA molecules with the same sequence from other clusters with different sequences. The definition of "individually resolved" provided by the patentee does not allow for this situation (nor does the prosecution history, because the patentee stated that the fragments are ***not*** amplified to form clusters),[43] and the claim should not be interpreted to allow for it either.

9. "Arraying the fragments such that different fragments can be individually resolved by optical microscopy" (claim 7)

Term	Life's Construction	Illumina's Construction
"arraying the fragments such that different fragments can be individually resolved by optical microscopy"	separating single DNA fragments (as opposed to clusters of DNA fragments) on a support so that each fragment can be distinguished from every other fragment by optical microscopy	arranging the fragments so that the fragments having different sequences can be distinguished from each other using a microscope.

In its proposed construction of this term, Illumina again focuses on the construction of "arraying" and "by optical microscopy." But as explained above, Life would agree to a construction incorporating these terms: "arranging single DNA fragments (as opposed to clusters of DNA fragments) on a support so that each fragment can be distinguished from every other fragment using a microscope." Illumina attempts to obscure the only issue in dispute here: do the claims of the '656 patent allow for DNA fragments having the same sequence to be grouped together and viewed as one? The answer is no, for similar reasons to those discussed above. The

[43] *See* D.I. 67 at 43, n.43 (citing JA1720 (9/28/2006 Amendment at 10)).

patentee specifically defined "polynucleotide arrays" as arrays of single molecules and defined "individually resolved" to require that each molecule on the array be distinguishable from its neighboring molecules. *See* JA1109 at 4:37-39; 4:51-54. And the specification repeatedly disclaims what Illumina's construction is trying to encompass—arrays that comprise clusters of molecules of the same type. *See, e.g.*, JA1109 at 3:13-23; JA1109-10 at 4:66-5:02; JA1112 at 9:41-46. Life's construction remains true to the definitions and descriptions in the specification.

C. THE MACEVICZ PATENT (NO. 7,598,035)

10. "Population of polynucleotide fragments" (all claims)

Term	Life's Construction	Illumina's Construction
"population of polynucleotide fragments"	the collection of every fragment that is made when DNA is digested by a restriction enzyme	a collection of polynucleotide fragments

The two disputes on this term are whether the "population of nucleotide fragments" required by independent claims 1 and 3 must (i) include ***each and every*** fragment of DNA that results from (ii) the fragmentation of a polynucleotide by restriction enzyme digestion (and not another method). The intrinsic evidence mandates that the answer to both is "yes."[44]

On point (i), Illumina's recent filing with the PTO in the reexamination of this patent repeatedly asserts that the population must contain "***each*** of the polynucleotide fragments."[45]

[44] Illumina's claim that "the fragments play a nominal role in each method" is contradicted by the patent, which explains that the purpose of the claimed method is to obtain end segments of ***each fragment*** so that those segments can be sequenced and mapped. As explained in Life's opening brief, the fact that the fragments are ***restriction*** fragments is crucial to the mapping function—absent the known sequences resulting from restriction enzyme digestion, the mapping purpose would be compromised. D.I. 67 at 45-46.

[45] *See* D.I. 67, Exh. C at 9 ("The pending claims provide a method of forming pairs of segments derived from ***each*** polynucleotide fragment in the population."), 10 ("***Each*** *polynucleotide fragment* from the *population* is inserted into a vector…. For ***each*** *polynucleotide fragment* the result is a corresponding vector" (italics in original)), 24 ("Independent claims 1 and 3 are directed to methods of forming paired oligonucleotide segments derived from ***each***

This aligns with the claim language and the specification, which both emphasize that the population includes ***each*** fragment created. *See* D.I. 67 at 45; *see also, e.g.,* JA1127 at 2:30-34 ("In accordance with ***the invention***, a polynucleotide is separately digested with different combinations of ***restriction endonucleases*** and the ends of the restriction fragments are sequenced so that pairs of sequences from ***each fragment*** are produced."). While Life's proposal uses the term "every," there is no difference in meaning from the claim's use of the term "each." Dictionaries consistently use "every" to define "each,"[46] and Illumina certainly doesn't explain what difference it sees between the two terms.

On point (ii), Life's opening brief shows that the specification exclusively teaches creation of a population by restriction enzyme digestion; there is no disclosure of a population created by any other means, and even the title of the patent references "***Restriction*** Fragments." *See* D.I. 67 at 44-47. The Abstract of the patent is express that "[i]n accordance with ***the invention***, nucleotide sequences are determined at the ends of ***restriction*** fragments produced by a plurality of digestions with a plurality of combinations of ***restriction endonucleases***…."[47] JA1121. Because there is ***no*** disclosure in the patent of preparing the claimed population of DNA fragments with anything other than restriction enzyme digestion and the restriction enzyme digestion is referred to as part of "the invention," this is not a matter of importing claim

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polynucleotide fragment in a population of fragments." (emphasis from original removed)); *see also id.* at 14 (cited at D.I. 67 at 45).

[46] *See, e.g.,* Am. Heritage Dictionary 576 (Houghton-Mifflin Co. 3d ed. 1992) ("*pron.* Every one of a group considered individually; each one") (attached as Exh. K); The Merriam-Webster Dictionary 154 (2005) ("**each** *pron.*: every individual one") (attached as Exh. L).

[47] *See, e.g., Lydall Thermal/Acoustical, Inc. v. Federal-Mogul Corp.*, 344 Fed. App'x 607, 614 (Fed. Cir. 2009) ("[W]hen a patentee consistently describes one embodiment as 'the present invention,' '[t]he public is entitled to take the patentee at his word'") (citing *Honeywell Int'l, Inc. v. ITT Indus., Inc.*, 452 F.3d 1312, 1318 (Fed. Cir. 2006)).

limitations (as Illumina asserts), but defining the claims according to the way the term is exclusively used in the specification. A broader construction would indeed lack written description and enablement support in violation of Section 112 of the Patent Act. *See* 35 U.S.C. § 112 ¶1. Life's construction should therefore be adopted.

11. "Vector" (all claims)

Term	Life's Construction	Illumina's Construction
"vector"	a self-replicating nucleic acid molecule which may be employed to introduce a nucleic acid sequence or gene into a cell; such nucleic acid molecules are designated as vectors and may be in the form of a plasmid, hybrid plasmid, cosmid, viral vector, bacteriophage vector, etc.	a nucleic acid molecule which may be employed to introduce a nucleic acid sequence or gene into a cell.

The parties agree that a vector must be capable of introducing a nucleic acid sequence into a cell; the issue in dispute is whether the vector must also be self-replicating. As explained in Plaintiffs' opening brief, the patent and PTO itself teach that it must be. *See* D.I. 67 at 47-48. Indeed, self-replication is a core component of any cloning vector. *See, e.g.,* D.I. 67 at 48, n.51. Illumina disregards this authority, including the PTO's own definition requiring self-replication, as well as the vectors in the patent, which are capable of self-replication. Illumina has pointed to no vector that is ***not*** self-replicating (including those in Sambrook on Molecular Cloning, cited in the patent and by Illumina, D.I. 67 at 47) and instead relies entirely on attorney argument. Contrary to Illumina's assertion, Life is not seeking to limit the type of vector that can be employed but is merely making express what the patent and PTO require—that the vector be capable of self replication so that it can accomplish the goals of the invention. *See* D.I. 67 at 47-48.

12. "Ligating together the cleaved ends produced by said removing" (claims 1 and 2); "Ligating the pair of segments together" (claim 5)

Term	Life's Construction	Illumina's Construction
"ligating together the cleaved ends produced by said removing" "ligating the pair of segments together"	For a piece of DNA that was cut by a restriction enzyme, connecting one of the cut ends directly to the other cut end.	Connecting the cut ends

The parties agree that "ligating" means "joining together." The dispute is whether the term requires that the two ends to be ligated must be directly joined together or whether they can be connected via a piece of linking DNA. Plaintiffs' opening brief shows that the intrinsic evidence and the patentee's disclaimer of ligation via linking DNA in the prosecution and the reexamination of this patent require that the ends be ligated directly together, and Life's construction properly includes this requirement. *See* D.I. 67 at 48-50.

Illumina ignores this evidence and instead argues that Life's construction seeks to close claim 1 of the '035 patent to other steps. But this is not true—Life does not dispute that the claims are open-ended, and Life's proposal allows for the claimed process to be supplemented with other steps such as modification of the fragment ends prior to ligation. Life's construction does exclude, however, that which was disclaimed in the prosecution history—the ***indirect*** connection of two ends of a fragment via a piece of linking DNA. *See* D.I. 67 at 49, n.55.

CONCLUSION

For the above reasons and those in Plaintiffs' Opening Brief, Plaintiffs respectfully request that the Court adopt their positions as to each of the disputed claim terms.

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CERTIFICATE OF SERVICE

I hereby certify that on June 25, 2010 I electronically filed the foregoing with the Clerk of the Court using CM/ECF, which will send notification of such filing to:

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