

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

COMPLETE GENOMICS, INC.,)
Plaintiff,)
v.) C.A. No. 19-970 (MN)
ILLUMINA, INC.,)
Defendant.)
ILLUMINA, INC. and ILLUMINA)
CAMBRIDGE LTD.,)
Counterclaim-Plaintiffs,)
v.)
COMPLETE GENOMICS, INC., BGI)
AMERICAS CORP. and MGI AMERICAS)
INC.,)
Counterclaim-Defendants.)

MEMORANDUM ORDER

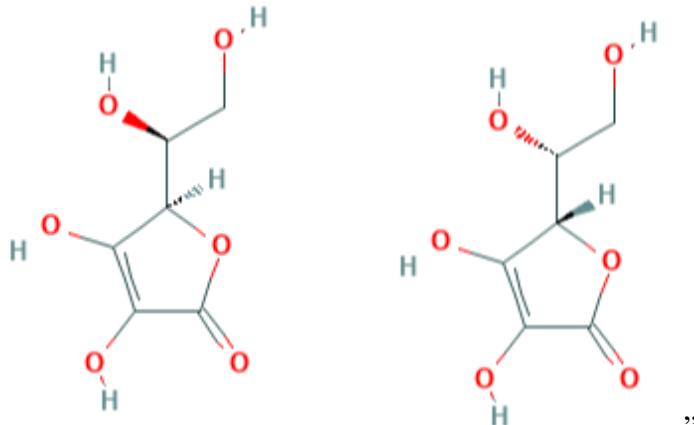
At Wilmington this 16th day of February 2021:

IT IS HEREBY ORDERED that the claim terms of U.S. Patent Nos. 9,222,132 (“the ’132 Patent”), 10,662,473 (“the ’473 Patent”), 9,217,178 (“the ’178 Patent”), 9,303,290 (“the ’290 Patent”) and 9,970,055 (“the ’055 Patent”)¹ with agreed-upon constructions are construed as follows (*see* D.I. 115 at 14; D.I. 105 at 4-5; *see also* D.I. 171 & 200):

1. “sequencing-by-extension” means “sequencing by synthesis” (’132 Patent, claim 1; ’473 Patent, claim 1)

¹ The ’132 and ’473 Patents are asserted by Complete Genomics, Inc., whereas the ’178, ’290 and ’055 Patents are asserted by Illumina, Inc. and Illumina Cambridge Ltd.

2. “detection position” means “a position in a target sequence for which sequence information is desired” (’132 Patent, claims 1 & 5)
3. “ascorbic acid” means “an organic compound with the chemical formula C₆H₈O₆ and one of the following structures



(’178 Patent, claims 1 & 6; ’290 Patent, claims 1, 2 & 7; ’055 Patent, claims 1 & 2)

4. “inhibiting light-induced degradation of nucleic acids during a detection step of a nucleic acid sequencing reaction,” which only appears in the preamble, is a limitation (’178 Patent, claim 1; ’290 Patent, claim 2)²
5. “a salt thereof / the salt of” does not require construction (’178 Patent, claims 1 & 6; ’290 Patent, claims 1, 2 & 7; ’055 Patent, claims 1 & 2)
6. “a [first / second] fluorescent label” means “at least one fluorescent element, isotope, or chemical compound attached to enable the detection of the compound”³ (’132 Patent, claims 5-8)

Further, as announced at the continued hearing on January 29, 2021, IT IS HEREBY ORDERED that the disputed claim terms of the ’132, ’473, ’178, ’290 and ’055 Patents are construed as follows:

² The parties reached agreement on this construction in the time between the original hearing and the continued hearing. (See D.I. 200; *see also* D.I. 214 at 57:11-20).

³ The parties reached agreement on this construction at the hearing. (See D.I. 214 at 52:24-53:9; *see also* D.I. 200).

1. “nucleic acid templates” means “nucleic acid molecules derived from target nucleic acid(s) that may include one or more adaptors” (’132 Patent, claims 1-8)
2. “for each of a plurality of said single-stranded nucleic acid templates, determining the identity of nucleotides at detection positions in the nucleic acid template in multiple cycles of a sequencing-by-extension reaction” means “for each of a plurality of said single-stranded nucleic acid templates, determining the identity of a nucleotide at a detection position in the nucleic acid template in each of multiple cycles of a sequencing by extension reaction” (’132 Patent, claims 1-4)
3. “a [first / second] fluorescent signal” means “light emitted by a fluorescent molecule or molecules that is detected within a defined wavelength range” (’132 Patent, claims 1-4)
4. “polynucleotide template[s]” means “nucleic acids derived from target nucleic acid(s) that may include one or more adaptors” (’473 Patent, claims 1-3 & 5)
5. “the first/second nucleotide and the first/second type of third nucleotide have different fluorescent intensities” shall be given its plain and ordinary meaning (’473 Patent, claim 1)
6. “amplicons” means “products of one or more polynucleotide amplification reactions” (’473 Patent, claim 3)
7. “irradiating” does not require construction (’178 Patent, claim 1; ’290 Patent, claim 2)

The parties briefed the issues (*see* D.I. 104, 105 & 115) and submitted an appendix containing intrinsic and extrinsic evidence, including expert declarations (*see* D.I. 106), and Illumina Cambridge Ltd. and Illumina, Inc. (together, “Illumina”) also provided a tutorial describing the relevant technology (*see* D.I. 107). The Court carefully reviewed all submissions in connection with the parties’ contentions regarding the disputed claim terms, heard oral argument (*see* D.I. 180 & 214) and applied the following legal standards in reaching its decision:

I. LEGAL STANDARDS

“[T]he ultimate question of the proper construction of the patent [is] a question of law,” although subsidiary fact-finding is sometimes necessary. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*,

135 S. Ct. 831, 837-38 (2015). “[T]he words of a claim are generally given their ordinary and customary meaning [which 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.” *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (internal citations and quotation marks omitted). Although “the claims themselves provide substantial guidance as to the meaning of particular claim terms,” the context of the surrounding words of the claim also must be considered. *Id.* at 1314. “[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent.” *Id.* at 1321 (internal quotation marks omitted).

The patent specification “is always highly relevant to the claim construction analysis . . . [as] it is the single best guide to the meaning of a disputed term.” *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). It is also possible that “the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor’s lexicography governs.” *Phillips*, 415 F.3d at 1316. “Even when the specification describes only a single embodiment, [however,] the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction.” *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)).

In addition to the specification, a court “should also consider the patent’s prosecution history, if it is in evidence.” *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc), *aff’d*, 517 U.S. 370 (1996). The prosecution history, which is “intrinsic evidence, . . . consists of the complete record of the proceedings before the PTO [Patent and Trademark

Office] and includes the prior art cited during the examination of the patent.” *Phillips*, 415 F.3d at 1317. “[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be.” *Id.*

In some cases, courts “will need to look beyond the patent’s intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period.” *Teva*, 135 S. Ct. at 841. Extrinsic evidence “consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises.” *Markman*, 52 F.3d at 980. Expert testimony can be useful “to ensure that the court’s understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field.” *Phillips*, 415 F.3d at 1318. Nonetheless, courts must not lose sight of the fact that “expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence.” *Id.* Overall, although extrinsic evidence “may be useful to the court,” it is “less reliable” than intrinsic evidence, and its consideration “is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence.” *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

I. THE COURT’S RULING

The Court’s ruling regarding the disputed claim terms of the ’132, ’473, ’178, ’290 and ’055 Patents was announced from the bench at the conclusion of the hearing as follows:

... At issue are two patents asserted by Complete Genomics against Illumina with seven disputed terms and three patents asserted by Illumina against Complete Genomics. There is just one disputed term in the Illumina patents.

I am prepared to rule on all of the disputes. I will not be issuing a written opinion, but I will issue an order stating my rulings. I want to emphasize before I announce my decisions that although I am not issuing a written opinion, we have followed a full and thorough process before making the decisions I am about to state. I have reviewed the patents in dispute and all of the evidence submitted in the extensive Joint Appendix. There was briefing on each of the disputed terms, and Illumina submitted a technology tutorial. We had an argument on December 22nd of last year and another here today. All of that has been carefully considered.

Now as to my rulings. As an initial matter, I am not going to read into the record my understanding of claim construction law generally. I have a legal standard section that I have included in earlier opinions, including somewhat recently in *Best Medical International v. Varian Medical Systems, Inc.*, C.A. No. 18-1599. I incorporate that law and adopt it into my ruling today and will also set it out in the order that I issue.^[4]

I'll start with the disputed terms of the Complete Genomics patents and address the first and fifth terms together as they involve essentially the same dispute.

The first term is "nucleic acid template[s]" in claims 1 through 8 of the '132 Patent. Complete Genomics proposes the construction "nucleic acid molecules derived from target nucleic acid(s) that may include one or more adaptors." Illumina proposes the construction "a nucleic acid with one or more interspersed adaptors" and adds that "[a]n interspersed adaptor is an oligonucleotide that is inserted at spaced locations within the interior region of a target nucleic acid."

The fifth term is "polynucleotide template[s]" in claims 1, 2, 3 and 5 of the '473 Patent.

Complete Genomics proposes the construction "nucleic acids derived from target nucleic acid(s) that may include one or more adaptors." Illumina proposes "a nucleic acid with one or more

⁴ The parties did not raise any disputes as to the person of ordinary skill in the art that are relevant to the issues raised in connection with claim construction.

interspersed adaptors” and once again adds its definition of an interspersed adaptor.

For these terms, the main dispute is whether the templates at issue may include adaptors or must include adaptors, or more particularly interspersed adaptors, as Illumina argues.

Here, I will construe the first and fifth terms to mean “nucleic acid molecules derived from target nucleic acid(s) that may include one or more adaptors” and “nucleic acids derived from target nucleic acid(s) that may include one or more adaptors,” respectively.

These constructions are supported by the intrinsic evidence. First, allowing the templates to include adaptors but not requiring them to include adaptors is consistent with the claim language. For example, claims 2 and 7 of the '132 Patent are dependent claims that add the further limitation that the nucleic acid template comprises adaptors. If I were to construe the first and fifth disputed terms to require not only adaptors but interspersed adaptors, the dependent claims would be broader than the independent claims – or the additional limitation would be meaningless.

Similarly, the specification supports my construction. Although the specification in places references “the present invention” in discussing embodiments including adaptors, I do not think that the “present invention” language is so clear as to override the claim language and read into the term “template” a requirement that it include adaptors.

Instead, as I read the “present invention” language, it refers to embodiments of the present invention. Indeed, not all statements of “the present invention” include adaptors. For example, the Abstract states: “The present invention is directed to methods and compositions for acquiring nucleotide sequence information of target sequences. In particular, the present invention provides methods and compositions for improving the efficacy of sequencing reactions by using fewer labels to distinguish between nucleotides and by detecting nucleotides at multiple detection positions in a target sequence.”

Similarly, the summary of the invention states that “the present invention provides methods and compositions for base calling in sequencing reaction” without reference to adaptors.

In looking at the patents as a whole and at all the uses of the “present invention” language, I understand the references to the “present invention” that Illumina cites to be discussions of embodiments. That is consistent with how the patentee used the term “present invention” in most instances.

And my construction is also consistent with statements the patentee made to clarify that the invention was broader than use of DNBs [DNA nanoballs] with concatemers and adaptors. For example, at column 18, lines 51 through 58, the '132 Patent states that “[t]he present invention provides methods and compositions for identifying multiple bases in a target nucleic acid by utilizing sets of probes that can distinguish between four possible bases at one or more positions in a target sequence using fewer than four labels in a set of sequencing probes. The methods of the present invention allow for multiple base calls per sequencing cycle, thus reducing the time and cost of sequencing and detection of sequences of target nucleic acids.” Again, this language does not refer to use of adaptors. It also goes further, stating at lines 59 through 63: “Although the following description of sequencing applications of the present invention is provided in terms of DNBs, it will be appreciated that these methods can be applied to any nucleic acid targets and are not necessarily limited to concatemers comprising target sequence and adaptors.”

My reading of the specification is also consistent with other discussions of embodiments that suggest that use of adaptors is not mandatory. For example, at column 9, lines 20 to 22, the '132 Patent states: “These fragmented nucleic acids are used to produce target nucleic acid templates that generally include one or more adaptors.” The use of the word “generally” in that passage connotes that the use of adaptors may be the common approach, but it does not convey that adaptors are required.^[5]

And finally, I note that my construction is also consistent with how Illumina and its expert understood a claim term including a template in the IPR. Specifically, when addressing the limitation that recites “providing an array comprising single-stranded nucleic acid templates disposed at positions on a surface,” Illumina stated:

⁵ (See also '132 Patent at 8:33-39 (“Although the embodiments of the invention described herein are generally described in terms of circular nucleic acid template constructs, it will be appreciated that nucleic acid template constructs may also be linear. Furthermore, nucleic acid template constructs of the invention may be single- or double-stranded, with the latter being preferred in some embodiments.”)).

“Limitation 1(a) recites the routine aspect of sequencing by synthesis using an array of single-stranded templates.”^[6]

Of course, that is not dispositive, but it suggests that it is not so clear and apparent from the specification that templates had to include adaptors, let alone interspersed adaptors. And it reflects how a person of skill in the art, Illumina’s expert, would read the patents.

The second term is “for each of a plurality of said single-stranded nucleic acid templates, determining the identity of nucleotides at detection positions in the nucleic acid template in multiple cycles of a sequencing-by-extension reaction” in claims 1 through 4 of the ’132 Patent. Complete Genomics proposes the construction “for each of a plurality of said single-stranded nucleic acid templates, determining the identity of a nucleotide at a detection position in the nucleic acid template in each of multiple cycles of a sequencing-by-extension reaction.” Illumina proposes “for each of a plurality of said single-stranded nucleic acid templates, determining the identity of nucleotides at multiple detection positions in the nucleic acid template in each of multiple cycles of a sequencing-by-extension reaction.”

The crux of the dispute is whether the claim term requires a sequencing-by-synthesis (or “SBS”) method in which one nucleotide is detected per template per SBS cycle or one in which multiple nucleotides must be detected in a single template in a single SBS cycle.

Here, I will construe the term to mean “for each of a plurality of said single-stranded nucleic acid templates, determining the identity of a nucleotide at a detection position in the nucleic acid template in each of multiple cycles of a sequencing by extension reaction.”

This construction is consistent with the plain meaning as supported by the prosecution history and the specification.

During prosecution of the application that became the ’132 Patent, the patentee added language to claim 37 that the sequencing reactions involve “extending individual anchor probes by one nucleotide per cycle” in one or more SBS cycles and that each of those SBS cycles involved “determining the identities of nucleotides

⁶ (D.I. 106-1, Ex. 7 at 18).

at the detection positions . . .”^[7] In describing that amendment, the patentee stated that “[e]xtension by one nucleotide per cycle was added at the suggestion of the Examiner and is a property of sequencing by synthesis.”^[8] Thus, the language about “determining the identities” plural of “nucleotides” also plural at “detection positions” is referring to the addition of one nucleotide per cycle. And this language, consistent with the specification,^[9] makes clear that the patent included sequencing by extension, which involves extension by one nucleotide at a time.

The third term is “a [first / second] fluorescent signal” in claims 1 through 4 of the ’132 Patent. Complete Genomics proposes the construction “light emitted by a fluorescent molecule or molecules that is detected within a defined wavelength range.” Illumina proposes “the wavelength and intensity of the fluorescent light arising from the first/second label.”

Here, not only do the parties dispute what the term means, they dispute what the dispute is. Illumina says that the dispute is the number of labels that are used. Complete Genomics says that the dispute is two-fold: (1) whether signal means the same thing as label and (2) does the signal need to be defined with respect to two components, both the wavelength, the color, and the intensity at which it is fluorescent.

I will try to address each of the purported disputes. First, I disagree that a signal and a label are the same. The patentee described two different words to describe these aspects of the claims and it is not clear from the intrinsic evidence that the patentee intended to use them interchangeably. Although a signal may arise from a label, that does not necessarily mean that the two are the same thing.

Second, I agree with Plaintiff that wavelength or color is used to define a signal, and that intensity may be used, but it is not required. For example, at column 32, lines 38 to 56, the ’132 Patent specification describes detecting the presence of incorporated nucleotides by taking images which show a binary event, either the presence or absence of fluorescent light of a particular color which

⁷ (D.I. 106-1, Ex. 10 at 346).

⁸ (*Id.* at 348).

⁹ (’132 Patent at 9:34-43).

indicates the presence or absence of the incorporated nucleotide.^[10] These examples do not refer to distinguishing signals based on intensity, only whether the image taken shows the presence or absence of a particular fluorophore based on color detection. The claim language is similar. The detecting step (element 1(b)(ii)) requires: “the presence or absence of fluorescent signals(s) associated with complementary nucleotides.” It does not refer to intensity. And, in fact, in the ’132 Patent IPR, Illumina and its expert similarly interpreted detection of the “signals” in claim 1 as being met by detecting the presence or absence of fluorescent emission of particular colors.^[11]

And finally, I agree with Complete Genomics that the first and second signals are defined and detected in a wavelength range. Fluorescent molecules fluoresce at wavelengths over a range, not at one single wavelength value. As Illumina’s expert explained in his IPR Declaration for the ’132 Patent, fluorescent dyes are excited by the absorption of light in a range. In response, they emit light across a different wavelength range, and their signal is detected across a range. That is evidence of how a person of skill in the art would understand the way fluorescent labels work. And there is nothing in the specification or claims that limits detecting the fluorescent signal to a single integer value rather than a range for a given color.

To sum all of that up, I will construe “a [first / second] fluorescent signal” to mean “light emitted by a fluorescent molecule or molecules that is detected within a defined wavelength range.”

The fourth term is “a [first / second] fluorescent label” in claims 5 through 8 of the ’132 Patent. In an effort to compromise, Complete Genomics now proposes “at least one fluorescent element, isotope, or chemical compound attached to enable the detection of the compound.” That construction uses the language describing a label in the ’132 Patent, but specifies that the label be fluorescent. Illumina agrees to that construction with the caveat that it may later need to argue about what that term means. I will address that if necessary at a later time, but for now will adopt the agreed-upon construction.

The sixth term is “the first / second nucleotide and the first / second type of the third nucleotide have different fluorescent

¹⁰ (’132 Patent at 35:38-56 (“An image is then taken. . . . [T]he first image would show a C1 + C3 signal. . . . When the next image is taken, only a C3 signal remains”); *see also id.* at 2:46-49, 26:60-67 (other examples using two colors on one of the nucleotides)).

¹¹ (*See, e.g.*, D.I. 106-2, Ex. 7 at 24-26 & Ex. 8 ¶¶ 76-80).

intensities” in claim 1 of the ’473 Patent. Complete Genomics asserts that no construction is necessary, but that if the term is construed it should mean “the first/second nucleotide molecule comprising a fluorescent dye emits light of a different intensity than the first/second type of the third molecule of the third nucleotide molecule comprising a fluorescent dye.” Illumina proposes the construction “the collection of molecules within the pool comprising the first/second nucleotide having a different fluorescent intensity than the collection of molecules within the pool comprising the first/second type of the third nucleotide.”

The dispute is whether the claim requires different intensities of emitted light from the individual nucleotides or from “collections” of those nucleotides.

I think that this term does not need to be construed and will give it its plain and ordinary meaning. This is consistent with the words of claim 1. The word “collection” does not appear anywhere in the claim. And the claim language uses the singular, referring to “a [] nucleotide” or “the [] nucleotide,” and to “a [] fluorescent dye” or “the [] fluorescent dye.” It does not necessarily require plural “nucleotides” or “dyes.”

My construction is also supported by the intrinsic evidence. The specification discloses ways of using “intensity difference[s] between the fluorophores” for sequencing.^[12] In the context of SBS, the specification teaches that “four bases in one position may be read with two colors using two different intensities of the two colors.”^[13] And it teaches that the differing intensities “could be achieved with dyes with the same emission wavelength but with different brightnesses.”^[14] This tracks what claim 1 recites regarding the different intensities.

The prosecution history similarly supports my conclusion that no additional construction of the claim words is needed. In a post-allowance amendment, the Applicant modified the language of claim 27 (issued as claim 1). Claim 27 originally recited a first and second “portion” of the third nucleotide, instead of a first and second

¹² (’473 Patent at 42:42-43:31).

¹³ (*Id.* at 43:15-24).

¹⁴ (*Id.* at 42:58-60:22).

“type.”^[15] The Applicant amended the claim to remove each reference to “portions” and to instead “recite there are two ‘types’ of third nucleotides.”^[16] By replacing “portion” with “type,” the Applicant sought to convey that the pool comprises two “differently labeled” types of the recited third nucleotide.^[17]

The seventh term is “amplicons” in claim 3 of the ’473 Patent. Complete Genomics proposes the construction “products of one or more polynucleotide amplification reactions.” Illumina proposes “a nucleic acid concatemer that is the product of a polynucleotide amplification reaction.”

Each side asserts that its proposal is based on a definition in the ’473 Patent. Here I agree with Complete Genomics. The ’473 Patent defines “amplicon,” stating that “[a]mplicon’ means the product of a polynucleotide amplification reaction.”^[18] It goes on to say “[t]hat is, it is a population of polynucleotides that are replicated from one or more starting sequences.” That is in the section of the patent offering definitions for many terms.

Although the ’473 Patent also states that concatemers are referred to as amplicons, I do not see that as a definition. Concatemers may be amplicons, but that does not mean that all amplicons are concatemers.

Those are my constructions for the Complete Genomics patents. Now for the one remaining term of the Illumina patents “irradiating.” Illumina proposes that no construction is necessary. Complete Genomics proposes that it means “repeatedly or prolongedely exposing to intense illumination.”

Here, I agree with Illumina that the term need not be construed. The parties don’t really dispute the standard meaning of irradiating. The issue is Complete Genomics’ attempts to add additional concepts from the specification and the prosecution history into the standard definition. The specification does not define “irradiating,” but states that “[m]ethods for detecting fluorescently labelled nucleotides generally require use of incident

¹⁵ (D.I. 106-1, Ex. 13 at CGI000049203 (Amendment After Allowance Under 37 C.F.R. § 1.312)).

¹⁶ (*Id.* at CGI000049208).

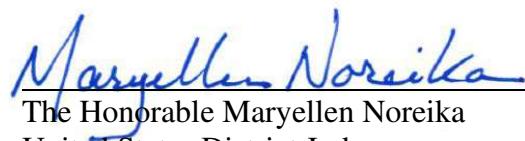
¹⁷ (*Id.*).

¹⁸ (’473 Patent at 9:1-4).

light (e.g. laser light) of a wavelength specific for the fluorescent label, or the use of other suitable sources of illumination, to excite the fluorophore. Fluorescent light emitted from the fluorophore may then be detected.”^[19]

As to the first part of Complete Genomics’ proposal, both claim 1 of the ’178 Patent and claim 2 of the ’290 Patent require that the claimed steps (a)-(d) be repeated at least ten times. The irradiating step is step (b) of the claimed method, and therefore the claim already requires repetition in irradiation by way of the last limitation.

Similarly, importing “intense” into the construction injects unnecessary ambiguity into this term’s meaning. Although the specification does explain that the claimed method “includes a detection step which requires repeated or prolonged exposure to intense illumination,”^[20] this is insufficient support for importing this concept into the construction of “irradiating.”



The Honorable Maryellen Noreika
United States District Judge

¹⁹ (’178 Patent at 4:19-23).

²⁰ (*Id.* at 2:20-22).