

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

10X GENOMICS, INC.,
Petitioner,

v.

PRESIDENT AND FELLOWS OF HARVARD COLLEGE,
Patent Owner

Case IPR2023-01299
U.S. Patent No. 11,098,303

PATENT OWNER'S PRELIMINARY RESPONSE

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I. INTRODUCTION

Petitioner 10x Genomics (“Petitioner” or “10x”) challenges Patent Owner President and Fellows of Harvard College’s (“Patent Owner” or “Harvard”) groundbreaking U.S. Patent No. 11,098,303 (“the ’303 patent”), deploying a series of Grounds based principally around U.S. Patent No. 10,829,814 (“Fan”). The Petition, however, suffers from multiple fatal flaws. At this preliminary stage, Patent Owner raises three, each of which is an independent basis to deny institution.

First, in a parallel district court action involving Petitioner, Patent Owner, and exclusive licensee and real party-in-interest Vizgen, Inc. (“Vizgen”), Petitioner has asserted that the “error detection or correction system” recited in independent claim 1 *is* governed by 35 U.S.C. § 112(f). It therefore has taken the position that the opposing construction in the district court—that the limitation *is not* governed by 35 U.S.C. § 112(f)—is incorrect. Yet, in this proceeding, Petitioner entirely ignores its proposed district court construction, purportedly relying instead on “Co-Plaintiffs’ interpretations” of the claims in the district court, *i.e.*, that the limitation *is not* governed by Section 112(f). Paper 2 at 12. Those positions are in direct conflict with one another. Petitioner should not be permitted to have its cake in this manner and eat it too, alleging in one proceeding that Section 112(f) applies, but adopting the exact opposite position in the other proceeding. That alone is a basis to deny institution.

Second, the Petition fails to establish a reasonable likelihood that it will prevail in establishing anticipation or obviousness of at least limitations (d) and (g) of claim 1, the sole independent claim of the '303 patent. Those claim elements refer to, *inter alia*, “removing the fluorescent signaling entity” from the “plurality of readout probe-hybridized complexes.” Ignoring the plain language of the claim, Petitioner instead seeks merely to establish that the art taught “removal” by washing unhybridized probes away from the sample as a whole. That is not what the claims say. As such, none of Petitioner’s Grounds can establish unpatentability of any of the '303 patent claims.

Third, the Board should decline to institute trial under 35 U.S.C. § 314(a) and the decision in *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 15 (PTAB Mar. 20, 2020) (precedential). Petitioner waited a year after being served with a counterclaim for infringement before filing the Petition, and the Grounds in the Petition rely on references and anticipation/obviousness theories that are simultaneously being asserted by Petitioner in the district court. Moreover, the district court case is poised to be tried in October 2024, long before any final written decision in this proceeding would be expected to issue. When taken together with the other *Fintiv* factors—as well as the Petition’s failure to make out a reasonable case of unpatentability, let alone a compelling one—that posture strongly favors denying institution.

Accordingly, Patent Owner respectfully requests that the Board decline to institute trial.

II. BACKGROUND

A. The '303 Patent

The '303 patent relates to detecting mRNAs or other nucleic acids within a cell, tissue, or other sample to determine “the expression state, spatial distribution within cells and intact tissues, and variation among cells of individual mRNAs.” EX1001, 1:39-41. The prior-art technique for performing such detection was single-molecule fluorescent *in situ* hybridization (smFISH), which involves using FISH probes (*e.g.*, primary nucleic acid probes) that hybridize directly to *a single RNA species* and that contain multiple copies of a fluorescent label. *Id.*, 1:35-48. The general strategy for smFISH utilizes multiple smFISH probes to the same RNA species with the same fluorescent label to visualize individual RNA transcripts by hybridizing (*i.e.*, binding) a unique fluorescent probe to each target, capturing images of the cell or sample, and analyzing the images to determine the identities and locations of the targets. *Id.*, 1:35-49, 43:20-43.

The smFISH technique was limited, however, by its low throughput, and typically, “only a few genes” could be studied at a time. EX1001, 1:43-49. Even “state-of-the-art efforts” at improving smFISH through “combinatorial labeling”—*i.e.*, color-based barcodes or sequential hybridization—could only “enable[]

simultaneous measurements of 10-30 different RNA species in individual cells.” *Id.*, 43:40-59. This limited multiplexing method using smFISH probes is known in the art as “seqFISH.” These art methods, *e.g.*, smFISH and seqFISH, however, are inadequate for “measurement of hundreds to thousands of RNAs within a single cell.” *Id.*, 43:43-49. Multiplexing requires an error-robust encoding scheme to accurately image the spatial organization of the “hundreds to thousands” of RNA transcripts within a cell (*in situ*). *Id.*, 44:9-36 (“[S]caling up the throughput of smFISH to the systems scale faces a significant challenge because not only does the number of addressable RNA species increases exponentially with N”—“each RNA species [is identified] by multiple (N) distinct signals”—“but the detection error rates also grow exponentially with N... . [And] as N increases, the fraction of RNAs properly detected (the calling rate) would rapidly decrease and, more troublingly, the fraction of RNAs that are identified as incorrect species (the misidentification rate) would rapidly increase,” wherein “the majority of RNA molecules would be misidentified after 16 rounds of hybridizations!”).

The invention of the ’303 patent—described as “multiplexed error-robust fluorescence in situ hybridization”—addresses these problems. EX1001, 42:65-43:19, 43:60-44:8, 44:37-45:25. The invention employs a unique “two-step labeling scheme ... to encode and readout cellular RNAs,” as well as “error-robust encoding

schemes” that enable the detection of certain errors and/or the correction of others. *Id.*, 44:37-45:25.

The invention involves two different sets of probes, which allow detecting a large number of nucleic acid sequences using error-robust *in situ* hybridization nucleic acid probes (“encoding probes”) that reduce misidentification of nucleic acid targets in a sample wherein probe pools for distinct targets encode distinct codewords. EX1001, 5:48-62. Those encoding probes, also called “primary probes,” each contains a “target sequence” enabling the primary probe to hybridize to a specific nucleic acid target and “one or more read sequences,” wherein each read sequence corresponds to a position within the codeword. *Id.*, 44:67-45:5, claim 1(a). These primary probes bind to nucleic acid targets in a sample, thereby creating “a plurality of first hybridized complexes.” *Id.*, 2:14-15, 4:33-35, 8:1-6, 8:62-64, claim 1(a). The second set of probes, known as “readout nucleic acid probe[s]” or “secondary probe[s],” is used to read the first probes’ target sequences in a series of sequential steps, like reading one position at a time of an N-bit code. *Id.*, 2:25-36, 8:1-6, 35:58-36:11, claim 1(b).

To accomplish this, first, “the plurality of first hybridized complexes within the sample” is exposed to “a first readout nucleic acid probe,” which includes “a sequence that specifically hybridizes to one of the read sequences” in the hybridized complexes and “a fluorescent signaling entity capable of producing a fluorescent

signal.” EX1001, 9:26-51, 18:12-20, claim 1(b). The binding of the secondary probes to certain read sequences in the primary probes thus creates “a plurality of readout probe-hybridized complexes.” *Id.*, claim 1(b). The sample is then ready for a measurement: “a fluorescent signal from each of the plurality of readout probe-hybridized complexes” is “detect[ed],” and images are taken of the sample. *Id.*, 35:58-36:11, claim 1(c).

The process is then repeated to read the next position(s) in the codeword by hybridizing a different set of “readout nucleic acid probes” to read sequence(s) corresponding to the next position(s) in the code to form a “different plurality of readout probe-hybridized complexes.” EX1001, claim 1(e). The “fluorescent signal” from the first readout probe is “remov[ed] ... from each of the plurality of readout probe-hybridized complexes,” either “by inactivating the fluorescent signaling entity,” or “removing the fluorescent signaling entity from each of the plurality of readout probe-hybridized complexes.” *Id.*, 12:4-6, 23:57-24:6, 24:38-43, 25:12-17, 25:43-50, 36:1-6, 37:39-41, claim 1(d). “[A]fter [the] step” of “removing the fluorescent signal,” the sample is exposed “to a different readout nucleic acid probe,” again including “a sequence that specifically hybridizes to one of the read sequences” and a “fluorescent signaling entity,” thereby creating “a different plurality of readout probe-hybridized complexes.” *Id.*, 36:1-8, claim 1(d)-(e). The sample is again imaged to “detect[] a fluorescent signal from each of the

different plurality of readout probe hybridized complexes.” *Id.*, 36:1-8, claim 1(f). Then, once more, “the fluorescent signal” is “remov[ed] ... from each of the different plurality of readout probe hybridized complexes” through either “inactivati[on]” of the entity or “remov[al]” of the entity from the readout probe or the readout probe from the complex. *Id.*, claim 1(g). Those steps—binding, detecting, and removing—are then “repeat[ed] ... one or more times using a different readout nucleic acid probe.” *Id.*, claim 1(h)

These sequential hybridization rounds “produc[e] codewords representing the plurality of different nucleic acid targets at locations within the sample.” EX1001, claim 1(i). Each primary probe reads out “one or more” positions in the valid codeword assigned to the specific nucleic acid target, wherein a pool of those primary probes, *see id.*, claim 1(a) (“the plurality of first hybridized complexes comprises multiple encoding nucleic acid probes of the different encoding nucleic acid probes”), encodes the assigned unique valid codeword, so matching the produced codewords to the “valid codewords” in the “codebook” enables identification of each target. *Id.*, 4:23-47, 10:41-58, 20:4-17, 21:17-34, 36:12-62, claim 1(j), Figs. 1A, 1B.

The ’303 patent issued on August 24, 2021, from Application No. 15/329,683, the national stage entry of PCT/US2015/042556, which was filed on July 29, 2015. EX1001, cover sheet. The patent claims priority to Provisional Application Nos.

62/142,653 (filed April 3, 2015), 62/050,636 (filed September 15, 2014), and 62/031,062 (filed July 30, 2014). *Id.*

B. District Court Litigation

In May 2022, Petitioner¹ sued Vizgen in the District of Delaware, alleging multiple counts of infringement of other patents. EX2001. The case was assigned to Judge Matthew Kennelly, serving as a visiting judge from the Northern District of Illinois. EX2008, 1, 13. The district court case is being litigated on a coordinated case management schedule with two other cases involving Petitioner; neither case involves the '303 patent. EX2008, 25 (Docket No. 147).

On August 30, 2022, Vizgen answered Petitioner's complaint and counterclaimed against Petitioner for infringement of the '303 patent. EX2008, 15 (Docket Nos. 29-30); EX2002. Patent Owner later joined as a counterclaim-plaintiff. *E.g.*, EX1059. Three months after the counterclaim was asserted, initial infringement contentions were served on Petitioner. EX2008, 19 (Docket No. 74). Nine months after that, and exactly one year after being served with the infringement counterclaim, Petitioner filed its Petition. *See* Paper 2.

¹ Patent Owner was also named as a plaintiff in that proceeding because it has licensed to Petitioner patents being asserted against Vizgen.

C. The Challenged Claims

The Petition challenges all twelve claims of the '303 patent. Paper 2 at 3.

Claim 1 is independent and recites:

1. A method for detecting a plurality of different nucleic acid targets within a sample by in situ hybridization, comprising:

(a) producing a plurality of first hybridized complexes within a sample containing a plurality of different nucleic acid targets by exposing the sample to a plurality of different encoding nucleic acid probes,

wherein each of the plurality of encoding nucleic acid probes comprises (i) a target sequence that specifically hybridizes to a different nucleic acid target or a different location of an identical nucleic acid target of the plurality of different nucleic acid targets and (ii) one or more read sequences such that each of the plurality of first hybridized complexes comprises multiple encoding nucleic acid probes of the different encoding nucleic acid probes located in its different locations;

(b) producing a plurality of readout probe-hybridized complexes by exposing each of the plurality of first hybridized complexes within the sample to a first readout nucleic acid probe, wherein the first readout nucleic acid probe comprises a first portion and a second portion, the first portion comprising a sequence that specifically hybridizes to one of the read sequences, and the second

portion comprising a fluorescent signaling entity capable of producing a fluorescent signal;

(c) detecting a fluorescent signal from each of the plurality of readout probe-hybridized complexes;

(d) removing the fluorescent signal from each of the plurality of readout probe-hybridized complexes by inactivating the fluorescent signaling entity or removing the fluorescent signaling entity from each of the plurality of readout probe-hybridized complexes;

(e) after step (d), producing a different plurality of readout probe-hybridized complexes by exposing the sample to a different readout nucleic acid probe, wherein the different readout nucleic acid probe comprise a first portion and a second portion, the first portion comprising a sequence that specifically hybridizes to one of the read sequences, and the second portion comprising a fluorescent signaling entity capable of producing a fluorescent signal;

(f) detecting a fluorescent signal from each of the different plurality of readout probe hybridized complexes;

(g) removing the fluorescent signal from each of the different plurality of readout probe hybridized complexes by inactivating the fluorescent signaling entity or removing the fluorescent signaling entity from each of the different plurality of readout probe hybridized complexes;

(h) repeating steps (e) to (g) for one or more times using a different readout nucleic acid probe, wherein the different readout nucleic acid probe comprises a first portion and a

second portion, the first portion comprising a sequence that specifically hybridizes to one of the read sequences, and the second portion comprising a fluorescent signaling entity capable of producing a fluorescent signal;

(i) producing codewords representing the plurality of different nucleic acid targets at locations within the sample, wherein each of the codeword represents one of the plurality of different nucleic acid targets and comprises multiple binary values 1 and 0, wherein a value of 1 is obtained when the fluorescent signal is detected from one of the plurality of readout probe hybridized complexes or one of the different plurality of readout probe-hybridized complexes at a respective location within the sample while a value of 0 is obtained when the fluorescent signal is not detected from one of the plurality of readout probe-hybridized complexes or one of the different plurality of readout probe-hybridized complexes at the respective location within the sample;

(j) matching the codewords with valid codewords in a codebook by comparing the codewords to the valid codewords in the codebook, and if one of the codewords is not matched with one of the valid codewords in the codebook, applying an error detection or correction system, matching the one of the codewords with another of the valid codewords in the codebook, or discarding the one of the codewords, wherein the codebook comprises

the valid codewords of the plurality of nucleic acid targets;
and

(k) determining the plurality of nucleic acid targets in the
sample based on results from the matching step.

EX1001, claim 1. For purposes of this Preliminary Response, Patent Owner refers to limitations (d) and (g) as the “Removing Limitations.”

The remaining claims are dependent and will be addressed separately only if the Board institutes trial.

III. LEVEL OF ORDINARY SKILL IN THE ART

Solely for purposes of this Preliminary Response, Patent Owner does not contest the definition of the person of ordinary skill in the art (“POSA”) set forth in the Petition. *See* Paper 2 at 11-12.

IV. CLAIM CONSTRUCTION

A. Petitioner’s Claim Construction Arguments Warrant Denial

Petitioner purports to “appl[y] Co-Plaintiffs’ interpretations of the 303 patent claims from the concurrent litigation,” relying on the infringement allegations from the parallel district court proceedings. Paper 2 at 12. In doing so, the Petition fails to specify exactly how those “interpretations” connect to any particular claim construction. The Petition thus fails to actually identify whether any express construction is needed, let alone for each such claim term that Petitioner believes

requires an express construction “[h]ow the challenged claim is to be construed,” as Petitioner was obligated to do. 37 C.F.R. § 42.104(b)(3).

That deficiency in the Petition is compounded by Petitioner’s contradictory approaches to claim construction in this proceeding and in the district court with respect to whether a particular limitation is a means-plus-function limitation. The proposed claim constructions from the district court litigation are as follows:

Claim Term	Vizgen's Proposed Construction	10x's Proposed Construction
“matching the codewords with valid codewords in a codebook by comparing the codewords to the valid codewords in the codebook”	Plain and ordinary meaning	“determining that each bit of a produced codeword is the same as each bit in the corresponding position of a valid codeword in the codebook”
“if one of the codewords is not matched with one of the valid codewords in the codebook, applying an error detection or correction system, matching the one of the codewords with another of the valid codewords in the codebook, or discarding the one of the codewords”	Plain and ordinary meaning	The embodying system must be capable of performing the following conditional steps: “if each bit in a produced codeword does not correspond with the bit in the same location of a valid codeword, applying an error detection or correction system [as construed] and either assigning the corrected codeword to another valid codeword or discarding the codeword.”
“an error detection or correction system”	This claim limitation is not governed by 35 U.S.C. § 112(f). No construction necessary.	This limitation is governed by 35 U.S.C. § 112(f). • Function: detecting or correcting unmatched bits in a produced codeword. • Structure: “A Hamming system, a Golay code, or an extended Hamming system (or a SECDED system, i.e., single error correction, double error detection)” as disclosed in Col. 11:12-28, Col. 20:51-21:34, Col. 38:4-17, Col. 65:36-68:63.

EX2006, 55, 61, 64; *see also* EX2004, 2; EX2005, 5-8.

The above table reflects a direct conflict in Petitioner’s claim construction arguments that warrants denial. Specifically, because Petitioner relies on “Co-Plaintiffs’ interpretations” in the district court proceeding for purposes of the Petition, Petitioner’s position in this proceeding is that the claim phrase “an error detection or correction system” “*is not* governed by 35 U.S.C. § 112(f).” However, Petitioner has asserted before the district court that the same limitation “*is* governed by 35 U.S.C. § 112(f),” and that the opposing proposed construction is incorrect. EX2006, 64-72 (emphasis added); *see also* EX2004, 2; EX2005, 7-8. Those two positions are diametrically opposed to one another—Petitioner cannot simultaneously take the position that a claim term is both governed by Section 112(f) and not governed by Section 112(f). Unsurprisingly, such an inconsistency has been a basis to deny institution. *See Orthopediatrics Corp. v. K2M, Inc.*, IPR2018-01546, Paper 10 at 12 (PTAB Feb. 14, 2019) (“By failing to reconcile its proffered claim construction here with its very different [means-plus-function] construction proffered in District Court ... Petitioner fails to satisfy [its] burden.”); *see also Ebates Performance Mktg., Inc. v. IBM Corp.*, IPR2022-00439, Paper 11 at 12 (PTAB Oct. 3, 2022) (“Petitioner has proposed constructions that it alleges are incorrect. Having proposed constructions it alleges are incorrect, Petitioner is unlikely to prove in a trial that those constructions are correct.”).

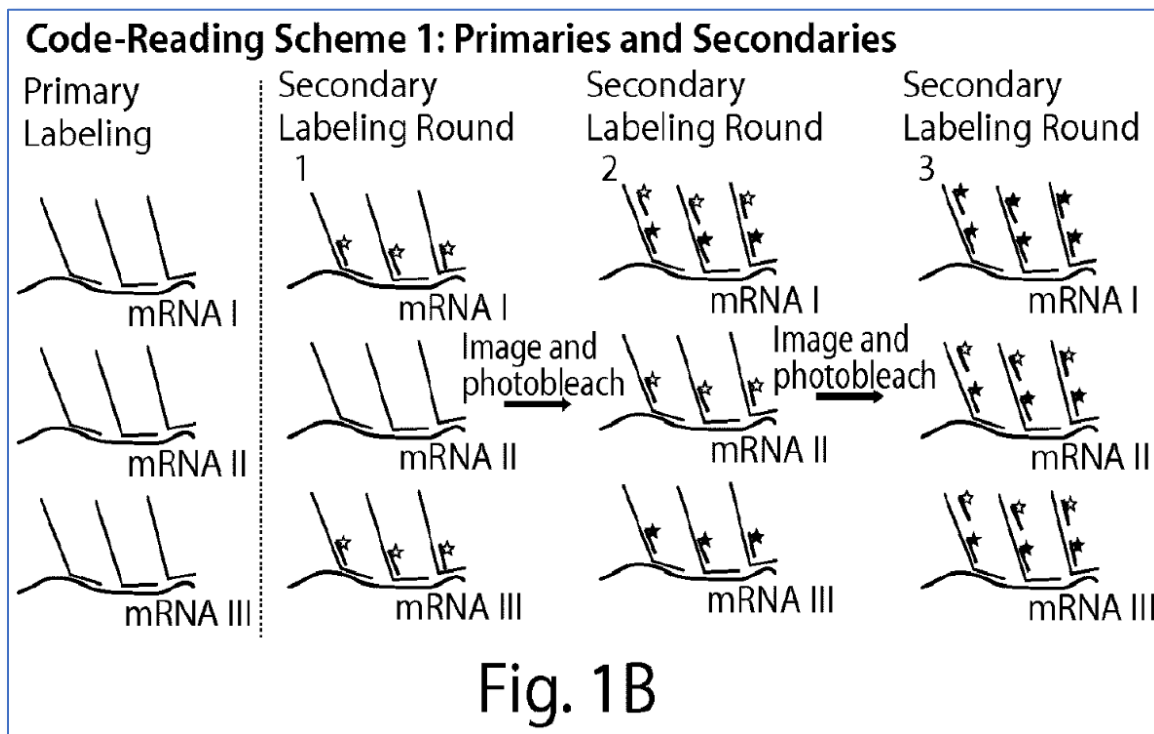
Petitioner's approach to claim construction is rendered even more problematic because Petitioner's proposed construction in the district court is a mean-plus-function construction. Yet, in this proceeding, Petitioner has failed to fulfill the most basic requirements with regard to its district court construction, let alone established unpatentability under that construction. Section 42.104(b)(3) of Title 37 requires that, where a construction under Section 112(f) is implicated, the Petition "must identify the specific portions of the specification that describe the structure, material, or acts corresponding to each claimed function." The Trial Practice Guide is in accord: "Where claim language *may* be construed according to 35 U.S.C. § 112(f), a petitioner *must* provide a construction that includes both the claimed function and the specific portions of the specification that describe the structure, material, or acts corresponding to each claimed function." Patent Trial and Appeal Board, Consolidated Trial Practice Guide at 45 (Nov. 2019) (emphasis added). Petitioner also has not even attempted to argue that the prior art it cites renders the claims anticipated or obvious under the construction it advanced in district court. Petitioner's failure to meet these requirements, despite insisting in district court that the claims must be construed under Section 112(f), warrants denying institution. *See Orthopediatrics*, IPR2018-01546, Paper 10 at 11.

B. The Removing Limitations

This Preliminary Response identifies a fundamental flaw in the Petition regarding the Removing Limitations. Although Patent Owner submits that no express construction of those terms is necessary at this preliminary stage and that they can be understood according to their plain and ordinary meaning, *see Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (“[C]laim terms need only be construed ‘to the extent necessary to resolve the controversy.’”) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)), a few words are in order regarding what the plain language of the Removing Limitations requires.

The '303 patent claims recite multiple rounds of creating readout probe-hybridized complexes. In the first round, there is a “primary labeling” phase that involves producing a plurality of “first hybridized complexes”—that is, “encoding nucleic acid probes” (primary probes) hybridize with, and thus bind to, “nucleic acid targets.” Subsequently, there is a series of “secondary labeling rounds” that form a series of “readout probe-hybridized complexes.” Specifically, “readout nucleic acid probes” (fluorescently labeled secondary probes) hybridize with, and thus bind to, the “first hybridized complexes” via the “read sequences” of the primary probes. Additional rounds of secondary readout probe binding involve hybridization with different fluorescently labeled secondary probes. Imaging of the fluorescent signals

takes place following each of those secondary labeling rounds. An illustrative example of this hybridization scheme is shown in Figure 1B.



EX1001, Fig. 1B.

In the '303 patent, the fluorescent signals must be removed (as set forth in detail below) between each secondary labeling round, such that the fluorescent labels from previous secondary labeling rounds are not imaged in subsequent rounds. The specifics of such removal are recited in the Removing Limitations of claim 1, reproduced below:

- (d) removing the fluorescent signal from each of the plurality of readout probe-hybridized complexes by inactivating the fluorescent signaling entity or removing

the fluorescent signaling entity from each of the plurality of readout probe-hybridized complexes;

(g) removing the fluorescent signal from each of the different plurality of readout probe hybridized complexes by inactivating the fluorescent signaling entity or removing the fluorescent signaling entity from each of the different plurality of readout probe hybridized complexes;

The plain language of the Removing Limitations thus provides two options for “removing the fluorescent signal” from the “readout probe-hybridized complexes” in which the fluorescently labeled secondary probes are bound. One is to inactivate the fluorescent signaling entity such that it no longer produces its fluorescent signal. Another is to remove the fluorescent signaling entity from the “readout probe-hybridized complexes.”

Where the second removal option is employed (*i.e.*, removing the fluorescent signaling entity from the readout probe-hybridized complexes), the plain language of the '303 patent claims provides that the removal does *not* remove the primary probe that is bound to the target nucleic acid sequence. Step (e) recites: “*after step (d), producing a different plurality of readout probe-hybridized complexes by exposing the sample to a different readout nucleic acid probe,*” *i.e.*, a different fluorescently labeled secondary probe. EX1001, claim 1(e) (emphasis added). In other words, the claim contemplates, and step (e) requires, the formation of new

readout probe-hybridized complexes by exposing the sample to a different fluorescently labeled secondary probe. However, in order for that to occur, the primary probe must still be available to form such a readout probe-hybridized complex, *i.e.*, it must still be hybridized with the nucleic acid target. That understanding dovetails with other language in step (e), where the different readout nucleic acid probe “specifically hybridizes to one of *the* read sequences.” *Id.* The antecedent basis for “*the* read sequence[]” is from the “first hybridized complexes” produced in step (a) by hybridization of the target sequence and the primary probe—as such, that primary probe must remain in place following the Removing Limitations. *Id.*, claim 1(a); *see Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1343 (Fed. Cir. 2008) (noting that “a definite article” like “‘said’ or ‘the’” “refer[s] to the initial antecedent phrase”).

Petitioner asserts that “[t]he Co-Plaintiffs interpret th[ese] limitation[s] as broad enough to encompass a method in which the fluorescently labeled probe is removed.” Paper 2 at 26; *see id.* at 30-31, 62. As discussed in greater detail below, Petitioner appears to take the position that the ’303 patent claim phrase “removing the fluorescent signaling entity from each of the ... readout probe-hybridized complexes” encompasses removing unhybridized probes “from the sample” by “washing,” which is what the Petition asserts is the approach taken in Fan. Specifically, the Petition states: “The 303 patent confirms that ‘removal of the

signaling entity’ includes removing it ‘*from the sample*, or from the nucleic acid probe, *etc.*’ and includes using ‘*washing*,’ just like Fan.” *Id.* at 27 (italics in original, underlining added) (citations omitted). The Petition likewise asserts that “Fan also explains that its ‘methods and compositions make use of hybridization, amplification, *washing* and detection within individual cells.’” *Id.* at 44 (emphasis modified) (citations omitted); *see id.* at 46, 71. Fan, however, describes “washing” as an approach that is used with *unhybridized* probes. For example, claim 1 of Fan refers to “probe that is not hybridized” is “removed by washing.” EX1005, claim 1(c), 1(f).

Unlike the Petition’s description of the method in Fan, the Removing Limitations are not directed to washing unhybridized probes from a sample. As explained above, the plain language of the claim recites removing the fluorescent signaling entity *from the readout probe-hybridized complexes*. Those complexes comprise a secondary probe bound to a primary probe, which is in turn bound to the nucleic acid target. Moreover, the very language from the ’303 patent on which Petitioner relies to suggest that the term “removing” is broad—a reference to “removal of the signaling entity (e.g., from the sample, or from the nucleic acid probe, etc.),” EX1001, 23:57-59 (cited in Paper 2 at 27)—*differentiates between* removal “from the sample” and “from the nucleic acid probe.” The claim language is express about what the fluorescent signaling entity must be removed from: it

recites removal “from ... the ... hybridized complexes.” EX1001, claim 1(d), (g). Removing the signaling entity from the complexes therefore cannot merely be a matter of removing unhybridized probes by washing them from the sample as the Petition suggests, as unhybridized probes are not part of the recited hybridized complexes to begin with.

The above understanding of the Removing Limitations is further supported by the plain language of ’303 patent claim 7. That claim recites, “The method of claim 1, further comprising removing the readout nucleic acid probes *unhybridized* to each of the plurality of first hybridized complex *prior to step (c)*.” EX1001, claim 7 (emphasis added). Such a removal of unhybridized probes prior to claim 1 step (c) (and therefore prior to step (d)) would not make sense if the “removing” limitation of step (d) encompassed washing of such probes from the sample generally. *See Actelion Pharms. Ltd. v. Mylan Pharms. Inc.*, 85 F.4th 1167, 1171 (Fed. Cir. 2023) (noting that a “canon of construction” is that “different terms have different meanings”) (citation omitted). Indeed, the Petition relies on claim element 1(c) of Fan and its reference to removing probes that are “not hybridized” by “washing” to support its analysis for claim 7 of the ’303 patent. *See* Paper 2 at 46-47.

Petitioner also cites to the initial infringement contentions in the district court litigation to support the Petition’s implicit position concerning the meaning of the Removing Limitations. *E.g.*, Paper 2 at 26-27, 62 (citing EX1047). Petitioner

misreads those contentions. Petitioner asserts that “[t]he Co-Plaintiffs interpret this limitation as broad enough to encompass a method in which the fluorescently labeled probe is removed.” Paper 2 at 26; *see id.* at 62. However, the contentions do not provide that the Removing Limitations encompass *any* form of removal of a fluorescently labeled probe, as Petitioner suggests. Rather, the infringement contentions expressly recognize that the Removing Limitations require “removing the fluorescent signal *from each of the plurality of readout probe-hybridized complexes.*” EX1047, 0072-0077 (emphasis added). The contentions further analyze the cited material in light of that limitation, as well as in light of the plain language of the Removing Limitations that such removal be performed either “by inactivating the fluorescent signaling entity or removing the fluorescent signaling entity from each of the plurality of readout probe-hybridized complexes.” *Id.* Nowhere do the infringement contentions assert that the Removing Limitations may be satisfied simply by washing the sample to remove unhybridized probes, as suggested by Petitioner’s invalidity analysis. *E.g.*, Paper 2 at 26-27, 62. To the contrary, the infringement contentions refer to washing in connection with the analysis for ’303 patent claim 7, which as discussed above is directed to removal of *unhybridized* probes. *See* EX1047, 0140-0141.

V. PETITIONER FAILS TO SHOW A REASONABLE LIKELIHOOD OF UNPATENTABILITY

The Petition fails to show a reasonable likelihood of unpatentability, at a minimum because the Petition fails to explain how the prior art relied upon in the Grounds anticipates or renders obvious the Removing Limitations. Each of the Petition’s four Grounds relies, in whole or in part, on Fan.² However, Petitioner’s analysis of Fan fails to demonstrate that the prior art discloses or renders obvious the Removing Limitations. That immediately undermines Ground 1—anticipation by Fan—and because the Petition also fails to explain how any of its secondary references fills the resulting gap, it renders Grounds 2-4 deficient as well.

A. The Petition Fails to Show That Fan Discloses or Renders Obvious the Removing Limitations

At the outset, the purported focus of the Petition is on removing the fluorescent signaling entity rather than inactivating it. That is, one way for a method to satisfy the Removing Limitations is to “inactivat[e] the fluorescent signaling entity.” *See supra* § IV.B. However, the Petition does not assert that any of Fan, Gunderson, Larsson, or Curry discloses or renders obvious this limitation. Instead, the analysis of those references is directed toward the limitation “removing the

² Patent Owner reserves the right to challenge the Petition on additional bases in the event that trial is instituted.

fluorescent signaling entity from each of the plurality of readout probe-hybridized complexes.” *See* Paper 2 at 26-27, 30-31 (discussing Fan); *id.* at 54, 62-63 (discussing Curry). That analysis fails.

To carry its burden, and as discussed above, *supra* § IV.B, Petitioner alleges that discussions in Fan relating to “removing” by “washing” unhybridized decoder probes from a sample meet the Removing Limitations. Paper 2 at 27. That is, Petitioner argues expressly that “[t]he 303 patent confirms that ‘removal of the signaling entity’ includes removing it ‘*from the sample*, or from the nucleic acid probe, etc.’ and includes using ‘*washing*,’ just like Fan.” Paper 2 at 27 (emphasis in original) (citations omitted). But as explained above, the Removing Limitations by their plain language require “removing the fluorescent signaling entity from ... *readout probe-hybridized complexes*.” *See supra* § IV.B. Moreover, the portion of the ’303 patent cited by Petitioner distinguishes between “removal of the signaling entity ... from the nucleic acid probe,” *e.g.*, “the signaling entity [is] chemically cleaved from the nucleic acid probe,” and removal “from the sample,” *e.g.*, a cleaved signaling entity is “washed away via fluid flow.” EX1001, 23:57-24:3 (cited in Paper 2 at 27). Having proposed no construction of the Removing Limitations in its Petition, Petitioner should not be allowed to engage in claim construction *sub silentio*, let alone in a manner that is inconsistent with the plain language of the claim. *Straight Path IP Grp., Inc. v. Sipnet EU S.R.O.*, 806 F.3d 1356, 1361 (Fed.

Cir. 2015) (“[R]edefinition or disavowal is required where claim language is plain”).

The portions of Fan cited in the Petition with respect to the Removing Limitations reinforce that Fan does not disclose or suggest those limitations. While the Petition repeatedly cites 2:56-58 of Fan, as well as the parallel citation of 3:14-15 in the Fan Provisional, that excerpt merely states that “[i]n some aspects of the above embodiments, the first labeled decoder probe is removed prior to hybridizing the second labeled decoder probe.” *See* Paper 2 at 27, 30, 32, 62. Such generic language nowhere discloses that such removal is *from a readout probe-hybridized complex* as required by the Removing Limitations. Indeed, the cited portion of Fan says nothing at all about *hybridized* decoder probes as opposed to *unhybridized* probes. *See* EX1005, 2:56-58; EX1006, 3:14-15.

On the contrary, claim 1 of Fan demonstrates that the language in column 2 on which Petitioner relies does *not* meet the Removing Limitations of the ’303 patent. Claim element 1(e) of Fan *separately recites* “de-hybridizing” and “removing,” thereby reinforcing that “de-hybridizing” a hybridized probe and “removing” an unhybridized probe are different operations in the context of Fan’s disclosures. *See* EX1005, claim 1(e); *see Actelion*, 85 F.4th at 1171. Importantly, as will be elaborated below, *infra* § V.B, claim element 1(e) of Fan is not prior art to the ’303 patent under Section 102(d); it appears nowhere in the provisional, and

the filing date for the Fan patent itself (*i.e.*, the non-provisional application) post-dates the '303 patent's priority date. However, it does confirm that when Fan talks about “removing” a probe in column 2, this does not mean, and fails to disclose or suggest, removing it from a readout probe-hybridized complex.

The Petition also references 9:25-27 of Fan in connection with the Removing Limitations, as well as the corresponding portion of the Fan Provisional 13:28-30, *see* Paper 2 at 27, 30, 32, 62, but those citations fail as well. The cited excerpts provide: “For example, one advantage is the simplicity and robustness of the decoding process, which involves hybridization and washing of oligo pools at room temperature.” EX1005, 9:25-27; EX1006, 13:28-30. However, that excerpt reflects that “washing” as used in Fan is to remove probes that are *unhybridized*. That understanding is supported by other portions of Fan—cited repeatedly in the Petition—which distinguish between the steps of washing and hybridization. *See* EX1005, 10:62-64 (“The methods and compositions make use of *hybridization*, amplification, *washing* and detection within individual cells.”) (emphasis added); Paper 2 at 44, 46, 71. Indeed, Petitioner admits that washing as used in Fan refers to unhybridized probes by relying on the *same disclosures* in Fan with respect to '303 patent claim 7, which recites “removing the readout nucleic acid probes *unhybridized* to each of the plurality of first hybridized complex prior to step (c).” *See* Paper 2 at 46-47 (citing EX1005, 9:25-27, 10:62-64) (emphasis added). The

understanding that Fan uses washing to refer to unhybridized probes is further reinforced by steps (c) and (f) of Fan claim 1, which describes “remov[al] by washing” as the approach used with a “probe that is not hybridized.” EX1005, claim 1(c), 1(f).

In sum, the relied-upon portions of Fan do not disclose removing fluorescent signaling entities from hybridized complexes. Because Fan fails to disclose the Removing Limitations, it cannot anticipate the claims of the ’303 patent. *See Verdegaaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987). Moreover, the Petition nowhere asserts that the POSA would have been motivated with a reasonable expectation of success to modify Fan to remove fluorescent signaling entities from hybridized complexes. Instead, the Petition relies upon Fan as disclosing the Removing Limitations without the need for any modifications. *See* Paper 2 at 26-27. Obviousness arguments from Fan therefore cannot save Petitioner.

B. The Reference to “De-hybridizing” in Fan Claim 1(e) Is Not in the Prior Art

Implicitly recognizing that the Fan Provisional nowhere discloses the Removing Limitations, both the Petition and the accompanying Spellman Declaration also cite to claim element 1(e) of the issued Fan patent and its reference to “de-hybridizing and removing ... the first fluorescently labeled decoder probe.” Paper 2 at 27, 30, 32, 62 (citing EX1005, claim 1); EX1002 ¶¶ 71, 128, 144, 149

(same). However, because that subject matter lacks written-description support in the Fan Provisional, it cannot be relied upon as prior art under 35 U.S.C. § 102(d).

The Petition asserts that Fan is prior art as of the filing date of the Fan Provisional, which is June 19, 2014. Paper 2 at 4. The Petition needs to rely on that date, because (1) it accords the '303 patent the filing date of its first provisional, which is July 30, 2014, and (2) the filing date of the non-provisional application that issued as the Fan patent is June 17, 2015, *i.e.*, later in time. *Id.* at 4, 10, 58; EX1005, cover. For subject matter in the Fan patent to obtain the benefit of the June 19, 2014 filing date of the Fan Provisional, Fan must satisfy the requirements of Section 102(d). That statutory provision sets forth the requirement that, “with respect to any subject matter described in [a] patent or application,” in order for that patent to be relied upon as prior art as of the filing date of an earlier application, that earlier application must “describe[] the subject matter.” 35 U.S.C. § 102(d). The Board has held that, under Section 102(d), Petitioner has the burden of showing that “the provisional or other earlier application(s) to which the reference patent document claims a right of priority ... ‘describe[s] the subject matter’ relied upon in the reference patent document as prior art.” *Penumbra, Inc. v. RapidPulse, Inc.*, IPR2021-01466, Paper 34 at 32 (PTAB Mar. 10, 2023) (precedential as to § II.E.3) (quoting 35 U.S.C. § 102(d)(2)); *see Forescout Techs., Inc. v. Fortinet, Inc.*, IPR2021-01328, Paper 12 at 9-10 (PTAB Jan. 27, 2022).

Petitioner fails meet its burden under Section 102(d) to establish that claim limitation 1(e) of Fan, reciting “de-hybridizing and removing the first fluorescently labeled decoder probe,” is described by the Fan Provisional. To show that element 1(e) has support in the Fan Provisional, the Petition relies on testimony from Dr. Spellman. Paper 2 at 14 (“As Dr. Spellman explains and demonstrates in Appendix C, all the elements of Fan’s claim 1 are described in Fan-Provisional.”). Dr. Spellman, in turn, refers to a portion of the Fan Provisional that states: “In some aspects of the above embodiments, the first labeled decoder probe is *removed* prior to *hybridizing* the second labeled decoder probe.” EX1002 at 255 (Spellman App’x C) (emphasis added) (citing EX1006, 2:56-58) ; *see id.*, ¶ 87. While that portion of the Fan Provisional may describe “removing” a “fluorescently labeled decoder probe” in general, there is no support for, or even mention of, “*de-hybridizing*” such a probe from a probe-hybridized complex. To the contrary, as discussed above, *supra* § V.A, claim 1(e) itself treats “de-hybridizing” and “removing” as two distinct steps, reflecting that a disclosure of “removing” in Fan is not a disclosure of “de-hybridizing.” That understanding is reinforced further by the Petition’s interpretation of “removing” in Fan as “washing” *unhybridized* probes “from the sample,” as discussed above. *Supra* § V.A; *see* Paper 2 at 27 (“The 303 patent confirms that “removal of the signaling entity” includes removing it “*from the sample*, or from the nucleic acid probe, etc.” and includes using “*washing*,” just like

Fan.”) (italics in original; underlining added) (citations omitted). Moreover, while the Petition cites to Fan Provisional claims 1-3 in connection with the Removing Limitations, *see* Paper 2 at 27, 30, 32, 62, Petitioner makes no argument that they disclose or suggest de-hybridization. That is not surprising, as—like Petitioner’s other citations to the Fan Provisional, but unlike claim element 1(e) of Fan itself—the provisional claims say nothing about de-hybridization.

C. The Petition Fails to Show That Any of Gunderson, Larsson, or Curry Discloses or Renders Obvious the Removing Limitations

In Grounds 2-4, the Petition relies on Gunderson, Larsson, and Curry in combination with Fan. However, the Petition fails to show that any of those references discloses or renders obvious “removing the fluorescent signaling entity from ... hybridized complexes” as set forth in the Removing Limitations.

1. Gunderson and Larsson (Grounds 2 and 3)

The Petition identifies no disclosures in Gunderson or Larsson that could be linked to the Removing Limitations. Paper 2 at 50-53. The Petition does not rely on Larsson at all with respect to those limitations. Indeed, the Petition only identifies Larsson as relevant to claims 2, 4, and 5, rather than claim 1, which is the claim that recites the Removing Limitations.

As for Gunderson, while the Petition cites to page 875 in its discussion of the Removing Limitations for Ground 4 (Fan and Curry)—although not for Grounds 2 or 3, where Petitioner actually relies on Gunderson—the Petition nowhere specifies

what language it is relying upon from that page for the Removing Limitations. Paper 2 at 62. That alone undermines any ability of Petitioner to rely on Gunderson to invalidate the Removing Limitations. Petitioner has not even attempted to show how anything on that page (or anywhere else in Gunderson) would have led the POSA to practice the Removing Limitations. Thus, Gunderson cannot cure the deficiency in Petitioner's case based on Fan.³

2. Curry (Ground 4)

Petitioner's arguments in Ground 4, combining Fan with Curry, fare no better. *See* Paper 2 at 62-63. In particular, the only citations to Curry in the Petition in connection with the Removing Limitations relate to Curry's disclosure that its "libraries [of probes] are hybridized successively, measured, then *washed* away to allow the sample to be hybridized to the next library." *Id.* at 62 (citing EX1009,

³ To purportedly show the obviousness of claim 7 of the '303 patent, the Petition cites the following language of Gunderson: "[f]ollowing hybridization, three 1-min washes ... were used to *remove unbound oligonucleotides*." Paper 2 at 47 (alterations in original) (citing EX1007, 875). However—and just like the Petitioner's description of Fan—that disclosure in Gunderson involves washing away *unbound* nucleotides; it has no bearing on the Removing Limitations and also does nothing to establish obviousness of independent claim 1.

9:33-35) (alterations in original). However, Curry makes clear that it uses “washing” to refer to unhybridized probes, stating: “[a]fter *unbound probe* is removed, e.g., by *washing*” EX1009, 1:8-9 (emphasis added). Curry thus fails to disclose the Removing Limitations.

Implicitly acknowledging that neither Fan nor Curry discloses or renders obvious the Removing Limitations, Petitioner attempts to fill that void with the POSA’s general knowledge, stating: “To the extent it is argued that the washing and removal in Fan (and Fan+Curry) do not disclose these ‘removing’ steps, these steps were well known based on a POSA’s general knowledge in the art.” Paper 2 at 62. The Petition then contends that “a variety of routine methods for removing or inactivating the fluorescent signal” were known. *Id.* However, merely listing a variety of steps the POSA could have taken falls well short of demonstrating that the art in fact provided the POSA with a reason to perform any of those steps with a reasonable expectation of success. In that regard, the Federal Circuit has held the “common sense and common knowledge” of a POSA “cannot be used as a wholesale substitute for reasoned analysis and evidentiary support, especially when dealing with a limitation missing from the prior art references specified.” *Arendi S.A.R.L. v. Apple Inc.*, 832 F.3d 1355, 1361-62 (Fed. Cir. 2016).

Put differently, the Removing Limitations are a significant aspect of the claimed invention that the ’303 patent addresses at length. EX1001, 8:49-57, 9:44-

51, 9:66-10:11, 12:4-6, 23:46-24:6, 25:44-50, 37:39-49, 48:45-47. The examiner specifically included the Removing Limitations in deciding to allow the '303 patent to issue. EX1004, 2388-2392. As such, they are simply not the sort of “unusually simple” limitations that, when absent from Grounds’ references, can be supplied simply by expert testimony about the POSA’s knowledge. *DSS Tech. Mgmt., Inc. v. Apple Inc.*, 885 F.3d 1367, 1375 (Fed. Cir. 2018) (quoting *Arendi*, 832 F.3d at 1362).

Even if expert testimony could somehow cure the deficiency in Petitioner’s prior-art case—which it cannot—Dr. Spellman’s testimony here comes nowhere close to the required showing that the POSA would have had reason to practice the Removing Limitations. Like the Petition, Dr. Spellman’s declaration merely lists a variety of ways in which the fluorescent signaling entity can be inactivated or removed. EX1002, ¶¶ 240-43. Nowhere does he spell out what the POSA would have been motivated to do or how this matches the Removing Limitations. The closest Dr. Spellman (or the Petition) comes is to assert generally that “[r]emoving or inactivating fluorescent signals is especially suitable for Fan’s probe design because” probes “*need not be* physically removed.” Paper 2 at 63; *see* EX1002, ¶ 242. However, that is at most an observation that the POSA *could*—not *would*—have inactivated the fluorescent signaling entities, which is insufficient for purposes of motivation. Moreover, the approach in Dr. Spellman’s testimony is an about-face from the Petition’s arguments about each of the references in the Grounds; as

discussed above, those arguments are directed to “removing” the fluorescent signaling entities from a hybridized complex. *See* § V.A; *see Juniper Networks, Inc. v. Core Optical Techs., LLC*, IPR2020-01664, Paper 9 at 11 (PTAB Apr. 16, 2021) (denying institution when “Petitioner [did] not identify clearly and adequately a single proposed combination of teachings ... that purportedly would result in the claimed subject matter as a whole. Rather, Petitioner addresse[d] each limitation separately and, for some, argue[d] that there [were] multiple alternatives as to how that one limitation, when considered in isolation, would have been obvious.”). Petitioner has thus failed to meet its burden to identify a particular solution or a motivation to modify Fan to employ a particular identified method among the “variety” known to the POSA and reach the particular claimed method. *See InTouch Techs., Inc. v. VGO Commc’ns, Inc.*, 751 F.3d 1327, 1347 (Fed. Cir. 2014); *Innogenetics, N.V. v. Abbott Lab’ys*, 512 F.3d 1363, 1373 (Fed. Cir. 2008).

VI. INSTITUTION SHOULD BE DENIED UNDER 35 U.S.C. § 314(a)

Even if Petitioner could meet the standard for institution on the merits, which it cannot, the Board should deny institution under 35 U.S.C. § 314(a) and *Fintiv*. The Petition (at 74) appears to recognize that it has a *Fintiv* problem—a problem created by (1) Petitioner’s decision to file the Petition a year after being sued for infringement, and (2) the anticipated trial date, just yesterday rescheduled to October 7, 2024, EX2008, 37 (Docket No. 291), which will be months before any final

written decision would be expected in this proceeding.⁴ Indeed, the Petition’s threadbare discussion of *Fintiv* relies primarily on whether the Petition has demonstrated “compelling unpatentability bases.” Paper 2 at 74. That is not the case—as discussed above, the Petition has not even demonstrated a reasonable likelihood of unpatentability. When taken in combination with the fact that an analysis of *Fintiv* factors 1-5 strongly favors denying institution, Patent Owner respectfully requests that denial should follow.

A. The *Fintiv* Factors

Under *Fintiv*, the Board evaluates the following nonexclusive factors:

1. whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted;
2. proximity of the court’s trial date to the Board’s projected statutory deadline for a final written decision;
3. investment in the parallel proceeding by the court and the parties;
4. overlap between issues raised in the petition and in the parallel proceeding;
5. whether the petitioner and the defendant in the parallel proceeding are the same party; and

⁴ In connection with the new trial date, the district court asked the parties to submit any proposed changes to other deadlines by December 18, 2023. The parties have not finalized their schedule proposals, but any changes are expected to be minor.

6. other circumstances that impact the Board’s exercise of discretion, including the merits.

Fintiv, IPR2020-00019, Paper 15 at 7-8 (citing *NHK Spring Co. v. Intrix-Plex Techs., Inc.*, IPR2018-00752, Paper 8 at 20 (PTAB Sept. 12, 2018) (precedential)). “In evaluating the factors, the Board takes a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review.” *Id.* at 8; see Katherine K. Vidal, *Interim Procedure for Discretionary Denials in AIA Post-Grant Proceedings with Parallel District Court Litigation* (June 21, 2022).

Here, discretionary denial is warranted under Section 314(a) and *Fintiv* because: (1) there is essentially no likelihood of a stay being granted; (2) there is every reason to believe that trial in the District of Delaware will occur about five months before the Board’s projected statutory deadline for any final written decision; (3) the parties and district court will have substantially invested in claim construction, fact discovery, and expert discovery by the time of the Board’s institution decision; (4) the same prior art and invalidity theories in the Grounds are being relied upon by Petitioner in the district court proceeding; and (5) the parties to this proceeding are also parties to the district court proceeding. Thus, the first five factors favor denying institution. Moreover, based on the shortcomings in the Petition identified above, Petitioner has failed to “present[] a compelling unpatentability challenge” under the sixth factor. *Commscope Techs. LLC v. Dali Wireless, Inc.*, IPR2022-01242, Paper 24 at 50-51 (PTAB Mar. 17, 2023)

(precedential). Accordingly, the Board should exercise its discretion to deny institution.

1. Factor One Favors Denial

The first factor favors denying institution, as there is no reasonable likelihood of a stay in the district court with respect to the '303 patent. The '303 patent is only one of six patents at issue in the parallel district court litigation, *see* EX1059, 81-107, and patent infringement is only one of the many causes of action in that litigation, including state-law claims, contract claims, and antitrust claims, *see id.*, 66-81, 107-20. In addition, the district court litigation is “being litigated on a case management schedule coordinated with at least two other related cases,” and thus it appears that it is highly unlikely that the court will stay litigation in all three cases. *See* EX2008, 25 (Docket No 147) (oral order denying earlier motion to stay).

Moreover, Patent Owner does not intend to request a stay if trial is instituted, and the Petition nowhere suggests that Petitioner intends to move for a stay if trial is instituted. That is not surprising, as the procedural history of the district court case suggests any such motion is unlikely to be successful. When Vizgen moved to stay the district court proceedings to pursue its unclean hands and license defenses, *see* EX2003, the court denied the motion, citing its “comprehensive case management schedule” and finding that Vizgen “ha[d] not offered a satisfactory explanation for why it cannot litigate the defenses within the existing case management schedule,”

EX2008, 25 (Docket No. 147). That schedule governs the litigation of the invalidity of the '303 patent at issue here. EX1051.

Finally, district courts routinely deny stays where, as here, the Petition for IPR is filed “on the last day permitted by statute.” *Greatbatch Ltd. v. AVX Corp.*, 2015 WL 8483986, at *1 (D. Del. Dec. 10, 2015); *see FastVDO LLC v. AT&T Mobility LLC*, 2017 WL 2323003, at *6 (S.D. Cal. Jan. 23, 2017) (collecting cases finding “that delay in seeking the PTO’s review of a patent within that year can adversely affect a district court’s view of a request for a stay pending review”).

2. Factor Two Favors Denial

The second *Fintiv* factor likewise strongly favors denial. Trial in the parallel litigation was just yesterday brought forward to October 7, 2024, EX2008, 37 (Docket No. 291), five months before the projected date for any final written decision, *see* 35 U.S.C. §§ 314(b)(1), 316(a)(11). The Board “generally take[s] courts’ trial schedules at face value absent some strong evidence to the contrary.” *Fintiv*, IPR2020-00019, Paper 15 at 13. The exact opposite is true: Petitioner *acknowledges* that trial was (at the time) most likely to occur in November 2024. *See* Paper 2 at 74. Petitioner’s assertion that “*much* of the substantive briefing and discovery in this IPR *may* be complete before the projected trial date”—the date by which *all* of the substantive briefing and discovery in the district court case *must* be completed—only further supports that institution would likely result in duplicative

discovery and briefing in parallel proceedings. *Id.* at 74 (emphasis added). That posture strongly favors denying institution. *See IBM Corp. v. Digital Doors, Inc.*, IPR2023-00967, Paper 7 at 9-10 (PTAB Dec. 1, 2023); *Zhuhai Cosmx Battery Co. v. Ningde Amperex Tech. Ltd.*, IPR2023-00585, Paper 12 at 13 (PTAB Oct. 24, 2023).

To the extent that consideration of median time-to-trial statistics is warranted despite the newly ordered trial date, they confirm that the parallel litigation will almost certainly reach trial before the Board issues its final written decision. The median time to trial in the District of Delaware is 34.7 months. EX2011, 1. Applying that statistic here results in a trial date projected for March 2025—the same month any Board final written decision would be expected to issue. Moreover, Judge Kennelly is a visiting judge with roughly 4% fewer cases than the average District of Delaware judge.⁵ Offsetting Delaware’s median time to trial to reflect

⁵ As of December 6, 2023, there were an estimated 1586 cases pending before Judges Andrews, Connolly, Noreika, and Williams but not before visiting judges, yielding an average of 396.5 cases per judge, EX2007, 1, whereas there were an estimated 381 cases before Judge Kennelly, *i.e.*, 3.9% fewer, EX2010, 1. Furthermore, Judge Kennelly, as of December 6, 2023, was presiding over only 14 patent cases, *see* EX2010, 1, while the average District of Delaware judge was presiding over 161.75,

Judge Kennelly’s reduced caseload results in a median of 33.3 months, which in turn yields a trial date projected for February 2025—a month before any Board final written decision would be expected to issue. As a result, regardless of whether the Board “consider[s] the scheduled trial date or the trial date expected based on time-to-trial statistics,” it is clear that the trial in the parallel litigation will almost certainly “commence several months before the expected date” of any Board final written decision. *Samsung Elecs. Co. v. Cal. Inst. of Tech.*, IPR2023-00130, Paper 10 at 16 (PTAB May 4, 2023); *see IBM Corp.*, IPR2023-00967, Paper 7 at 9-10.

3. Factor Three Favors Denial

There has been a substantial investment by the parties and district court in the parallel proceeding, so the third *Fintiv* factor strongly favors discretionary denial as well. The parties have exchanged their initial and supplemental infringement and invalidity contentions. EX2008, 19-20, 23, 25 (Docket Nos. 74-75, 91-92, 130, 142). Claim construction briefing was finished on October 20, 2023, *id.*, 33 (Docket No. 247), and the *Markman* hearing is scheduled for January 10, 2024, *id.*, 35-36 (Docket No. 275). Given the April 5, 2024, deadline for opening expert reports,

see EX2007, 2. That the 4% offset does not take this disparity into account provides all the more reason to believe that trial will not be pushed back beyond the statutory deadline for any Board final written decision.

EX1051, 3, it is quite likely that the district court will issue its claim construction order in the timeframe between the hearing and the projected date for the Board's institution decision. Document production, moreover, will be completed by December 22, 2023, EX2013, 2; EX2008, 34-35 (Docket Nos. 262-263), and the cut-off date for fact discovery is March 15, 2024, EX1051, 3, the day after the statutory deadline for the Board's institution decision. Opening expert reports are due on April 5, 2024, *i.e.*, just shortly after the deadline for the decision on institution. *Id.*, 3. This investment by the court and parties is clearly substantial and accordingly strongly favors discretionary denial. *See Duplo U.S.A. Corp. v. MGI Digital Tech. S.A.*, IPR2023-00936, Paper 8 at 18 (PTAB Dec. 5, 2023) ("We agree with Patent Owner that there has been substantial investment by the parties and the district court in the parallel proceeding, including the completion of preliminary disclosures and claim construction, and the near-completion of discovery."); *BOE Tech. Grp. Co. v. Element Capital Commercial Co.*, IPR2023-00808, Paper 9 at 23-24 (PTAB Nov. 15, 2023) (finding "significant progress" and that "the parties and the District Court have invested substantial resources" where, at the time of the institution decision, "[s]ignificant discovery has been completed, including the exchange of infringement and invalidity contentions, document requests and interrogatories, and proposed claim terms for construction"; the "date for the close of fact discovery is near"; and "the claim construction phase of the District Court

Litigation is now completed”); *Zhuhai Cosmox Battery*, IPR2023-00585, Paper 12 at 15-16 (the third factor favors discretionary denial where, “at the time of the institution decision, the undisputed evidence shows that parties have exchanged infringement and invalidity contentions, a claim construction hearing was scheduled, and fact discovery closes and initial expert reports will be completed”).

That the third factor strongly favors denial is likewise supported by Petitioner’s unreasonable delay in filing its Petition. *See Samsung Elecs.*, IPR2023-00130, Paper 10 at 18 (“As part of this [third] factor, we additionally consider whether Petitioner unreasonably delayed in filing the Petition in this case.”). Here, Petitioner waited exactly one year after it was served with a counterclaim for infringement of the ’303 patent to file its Petition. EX2002; EX2008, 15 (Docket Nos. 29-30); Paper 2 at 90; *see* 35 U.S.C. § 315(b). Petitioner, moreover, waited nine months after receiving the initial infringement claim chart, a fact which likewise favors denial. EX2008, 19 (Docket No. 74); *see Ericsson Inc. v. Godo Kaisha IP Bridge I*, IPR2022-00725, Paper 10 at 9 (PTAB Nov. 2, 2022) (rejecting promptness argument where infringement contentions were served more than six months before petition); *Ericsson Inc. v. Collision Commc’ns, Inc.*, IPR2022-01233, Paper 12 at 14-15 (PTAB Jan. 19, 2023) (similar; petitioner waited more than eight months “after receiving infringement contentions” and “almost a year from inception of the [infringement claim]”) (citation omitted); *cf. Next Caller Inc. v. TrustID, Inc.*,

IPR2019-00961, Paper 10 at 15-16 (PTAB Oct. 16, 2019) (delay from initial invalidity contentions to petition favored denial). As Petitioner recognizes, substantive briefing and discovery is unlikely to be completed in this IPR before the district court case goes to trial, *see* Paper 2 at 74, in no small part due to Petitioner's delay in filing its Petition.

4. Factor Four Favors Denial

The fourth *Fintiv* factor likewise strongly favors denial because Petitioner is relying on the prior art references and invalidity theories from the Grounds in the district court proceeding. *Commscope Techs.*, IPR2022-01242, Paper 24 at 59. Petitioner asserts anticipation of claims 1-12 by Fan both here (Ground 1) and in the district court. *See* EX2012, 1 (“Claims 1-12 of the 303 Patent are anticipated or rendered obvious by Fan alone, or Fan in combination with other prior art, as outlined in the chart below.”). Petitioner likewise asserts obviousness based on the combination of Fan and Gunderson, and Fan, Gunderson, and Larsson, both here (Grounds 2-3) and in the district court. *Id.*, 21-23, 26, 28, 32, 39-43, 45-46, 49-50, 52 (citing Gunderson and Larsson). Petitioner also asserts obviousness based on the combination of Fan and Curry both here (Ground 4) and in the district court. *Id.*, 23-24, 26, 40, 43, 46-47, 50, 52 (citing Curry). Such overlap mandates denying institution. *See Fintiv*, IPR2020-00019, Paper 15 at 15 (“Thus, because the identical

claims are challenged based on the same prior art in both the Petition and in the District Court, this factor weighs in favor of discretionary denial in this case.”).

This case also presents an unusual risk of inconsistent results, weighing further in favor of discretionary denial. For example, the Board and district courts have recently articulated different approaches to *Dynamic Drinkware, LLC v. National Graphics, Inc.*, 800 F.3d 1375 (Fed. Cir. 2015), which may result in conflicting decisions as to whether Fan is prior art at all. *Dynamic Drinkware* held that one requirement for a U.S. patent to be able to obtain the benefit of a provisional application filing date is that at least one issued claim must have written-description support under 35 U.S.C. § 112 in the provisional. 800 F.3d at 1378. Applying that principle to Fan means that Fan is not prior art. The Petition relies on an analysis in Appendix C of the Spellman Declaration to purportedly show that claim 1 of Fan has support in the Fan Provisional. EX1002, ¶ 87. That analysis, however, relies on Fan’s incorporation by reference of Gunderson.⁶ By Federal Regulation, Gunderson cannot provide Section 112 written-description support for claim 1 of Fan because

⁶ EX1002, Appx. C at 251; *see* Paper 2 at 32-42 (relying solely on Fan’s incorporation by reference of Gunderson as disclosing steps 1(i), (j), and (k) of the ’303 patent); EX1002, ¶¶ 74-75, 153-54, 161-62, 170, 172-73 (same, for Dr. Spellman’s declaration).

it is a non-patent publication (non-essential material) rather than a U.S. patent or U.S. patent publication (essential material). *See* 37 C.F.R. § 1.57(d)-(e) (distinguishing between “essential” and “non-essential” material in the context of incorporation by reference, only the former of which can be used to provide written-description support under Section 112); *see* MPEP § 608.01(p) (“Nonessential subject matter is subject matter referred to for purposes of indicating the background of the invention or illustrating the state of the art.”). Fan thus cannot claim priority earlier than its filing date of June 17, 2015, which is after the July 30, 2014 priority date assumed in the Petition.

The Office recently designated as precedential the decision in *Penumbra*, IPR2021-01466, Paper 34 (PTAB March 20, 2023) (precedential as to § II.E.3), which held that *Dynamic Drinkware* does not apply to AIA patents like Fan. *Id.* at 32. Patent Owner respectfully submits, however, that the Board’s reasoning in *Penumbra* varies from the decision of the Federal Circuit in *Helsinn Healthcare S.A. v. Teva Pharmaceuticals USA, Inc.*, 855 F.3d 1356 (Fed. Cir. 2017), *aff’d*, 139 S. Ct. 628 (2019), concerning differences between the pre- and post-AIA versions of Section 102. And the one district court authority of which Patent Owner is aware disagrees with the Board on this point; it applied *Dynamic Drinkware* to a post-AIA patent. *Atlas Glob. Techs. LLC v. TP-Link Techs. Co.*, 2023 WL 5346490, at *4-5 & n.4 (E.D. Tex. Aug. 1, 2023). Patent Owner therefore expects to rely on *Dynamic*

Drinkware in the district court proceedings to show that Fan is not prior art, and there is at least a reasonable possibility that the district court will follow its sister court rather than the Board on this legal question. That would result in an inconsistent decision with the position of the Office, thus providing yet another reason that discretionary denial is appropriate. *See Kiosoft Techs., LLC v. Payrange, Inc.*, IPR2021-00086, Paper 12 at 15-16 (PTAB Mar. 22, 2021).

5. Factor Five Favors Denial

The fifth *Fintiv* factor strongly favors denial as well. Petitioner is a counterclaim-defendant in the parallel district court proceeding, while Patent Owner is a counterclaim-plaintiff. EX1059. Vizgen is also a counterclaim-plaintiff. *Id.* That the same parties are involved in both the district court litigation and the IPR—and that trial will almost certainly precede any final written decision—supports discretionary denial. *See IBM Corp.*, IPR2023-00967, Paper 7 at 12; *Zhuhai Cosmox Battery*, IPR2023-00585, Paper 12 at 17.

6. Factor Six Favors Denial

Finally, Petitioner has not presented compelling evidence of unpatentability. Indeed, the Petition has failed to demonstrate a reasonable likelihood that any of the '303 patent's claims is unpatentable, let alone a compelling unpatentability challenge, at a minimum because the Petition fails to show that any of the prior art in the Grounds discloses or renders obvious the Removing Limitations, as discussed

above. Even if the Board were to conclude (and it should not) that Petitioner has shown a reasonable likelihood of unpatentability, its case does not come close to establishing so compelling a case that it can overcome the significant reasons to deny institution under *Fintiv*.

* * *

Balancing the *Fintiv* factors strongly favors declining to institute trial. Accordingly, the Board should deny the Petition under Section 314(a).

VII. CONCLUSION

For the foregoing reasons, Patent Owner respectfully requests that trial not be instituted.

Date: December 14, 2023

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PATENT OWNER'S EXHIBIT LIST

Exhibit No.	Description
2001	Complaint, <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.), filed May 3, 2022, Dkt. No. 1
2002	Report to the Commissioner of Patents and Trademarks, <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.), filed August 30, 2022, Dkt. No. 30
2003	Vizgen's Motion to Stay, <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.), filed April 25, 2023, Dkt. No. 145
2004	Joint Claim Construction Statement, <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.), filed August 4, 2023, Dkt. No. 203
2005	Joint Claim Construction Statement, Exhibit B (595 Case), <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.), filed August 4, 2023, Dkt. No. 203-2
2006	Joint Claim Construction Brief, <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.), filed October 20, 2023, Dkt. No. 247
2007	Lex Machina, U.S District Court for the District of Delaware open federal district cases report
2008	Docket Report, <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.)
2009	RESERVED
2010	Lex Machina, District Judge Matthew F. Kennelly open federal district court cases report
2011	Table C-5, US District Courts-Median Time Intervals

2012	Attachment 2 to 10x Genomics, Inc.'s Initial Invalidity Contentions
2013	Stipulation to Extend Time, <i>10x Genomics, Inc. v. Vizgen, Inc.</i> , Case No. 1:22-cv-00595 (D. Del.), filed November 3, 2023, Dkt. No. 262

CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

In accordance with 37 C.F.R. § 42.24, as amended, the undersigned certifies that this Patent Owner Preliminary Response complies with the applicable type volume limitations of 37 C.F.R. §§ 42.24(a)(i) and 42.24(b)(1). Exclusive of the portions exempted by 37 C.F.R. § 42.24(a), this Patent Owner Preliminary Response contains 10,668 words as counted by the word processing program used for its preparation (Microsoft Word 2019).

/Dov P. Grossman/

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CERTIFICATE OF SERVICE
(37 C.F.R. § 42.6(e))

The undersigned hereby certifies that on December 14, 2023, I caused true and correct copies of the following materials:

- Patent Owner's Preliminary Response
- Patent Owner's Exhibit List
- Exhibits 2001-2008, 2010-2013

to be served via e-mail on the following:

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