

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ILLUMINA, INC.,
Petitioner,

v.

RAVGEN, INC.,
Patent Owner.

IPR2021-01271
Patent 7,727,720 B2

Before ZHENYU YANG, TIMOTHY G. MAJORS, and DAVID COTTA,
Administrative Patent Judges.

COTTA, Administrative Patent Judge.

DECISION

Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

Illumina, Inc. (“Petitioner” or “Illumina”)¹ filed a Petition to institute *inter partes* review of claims 1, 3–9, 21, 22, and 24–30 of U.S. Patent No. 7,727,720 B2 (Ex. 1001, “the ’720 patent”). Paper 1 (“Pet.” or “Petition”). Ravgen, Inc. (“Patent Owner”)² filed a Preliminary Response. Paper 6 (“Prelim. Resp.”). With our authorization, Petitioner and Patent Owner filed a Preliminary Reply and Preliminary Sur-Reply addressing certain matters raised in the Preliminary Response. Paper 7 (“Prelim. Reply”); Paper 8 (“Prelim. Sur-Reply”).

Under 35 U.S.C. § 314(a), *inter partes* review may not be instituted unless the Petition “shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” Petitioner has established a reasonable likelihood of prevailing on its assertion that the challenged claims are unpatentable based on the grounds advanced here. We decline to deny the Petition on a discretionary basis as requested by Patent Owner. Thus, for reasons explained below, we institute *inter partes* review of claims 1, 3–9, 21, 22, and 24–30 of the ’720 patent.

A. Related Patents & Proceedings

The ’720 patent issued June 1, 2010, from U.S. Patent Application No. 11/212,812 (“the ’812 Application”), filed August 26, 2005. Ex. 1001, codes (21), (22), (45). The ’812 Application is a continuation of Application

¹ Petitioner identifies itself, Illumina Cambridge, Ltd., and Verinata Health, Inc. as the real parties-in-interest. Pet. 2.

² Patent Owner identifies itself as the real party-in-interest. Paper 4, 1.

No. PCT/US2004/006337, filed March 1, 2004, which itself claims priority through a chain of several continuation and continuation-in-part applications with filing dates in 2003, and a provisional application filed May 8, 2002. *Id.* at codes (60), (63). Related U.S. Patent No. 7,332,277 (“the ’277 patent”) issued on February 19, 2008, and claims priority to common applications. *Id.* at code (56); IPR2021-00788, Exhibit 1001 at codes (60), (63).

The parties identify multiple lawsuits involving the ’277 and ’720 patents. Pet. 1–2; Paper 4, 1; Paper 9, 1. With relevance to the pre-institution arguments raised here, those lawsuits include: *Ravgen, Inc. v. Illumina, Inc. et al.*, No. 1:20-cv-01644-RGA (D. Del) (“the Illumina lawsuit”), *Ravgen, Inc. v. Laboratory Corp. of America Holdings*, No. 6:20-cv-00969-ADA (W.D. Tex.) (“the Labcorp lawsuit”), *Ravgen, Inc. v. Natera, Inc. and NSTX, Inc.*, No. 1:20-cv-00692-ADA (W.D. Tex.) (“the Natera lawsuit”), and *Ravgen Inc. v. Quest Diagnostics Inc.*, No. 6:20-cv-00972-ADA (W.D. Tex. Oct. 16, 2020) (“the Quest lawsuit”).³ *Id.* According to the parties, Patent Owner has also asserted the ’720 patent against other defendants such as PerkinElmer, Inc., Myriad Genetics, Inc.,

³ This case has been transferred to the Central District of California. *See, Ravgen v. Quest Diagnostics*, No. 2:21-cv-09011-RGK-GJS (C.D. Cal); *see also, In re Quest Diagnostics Inc.*, No. 2021-193, 2021 WL 5230757 (Fed. Cir. Nov. 10, 2021) (directing, on petition for writ of mandamus, transfer of the matter to the District Court for the Central District of California). Herein, we use “the Quest lawsuit” to refer collectively to both proceedings.

Progenity, Inc., and Ariosa Diagnostics, Inc. in other lawsuits pending in district courts in the Western District of Texas and the District of Delaware. *Id.*

The parties also identify other matters involving the '720 patent pending before the Patent Office. Pet. 1–2; Paper 4, 1. The '720 patent is challenged in IPR2021-00791 (filed by Quest Diagnostics), and IPR2021-01026 (filed by Laboratory Corporation of America Holdings). Pet. 3; Paper 4, 1; Paper 9, 1. In addition to the above, the parties identify Ex Parte Reexamination Control Nos. 90/014,703 and 90/014,869, addressing, respectively, claims of the '720 patent. *Id.*

B. Asserted Grounds of Unpatentability

Petitioner asserts five grounds of unpatentability in this Petition (Pet. 4–5), which are provided in the table below:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1, 3–8, 21, and 24	102 ⁴	Landes ⁵
22	103(a)	Landes, Marx ⁶
1, 3–6, 24	103(a)	Yen-Lieberman ⁷

⁴ The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”), amended 35 U.S.C. §§ 102 and 103. Based on the filing date of the '720 patent, we apply the pre-AIA versions of §§ 102 and 103.

⁵ Landes et al., International Publication No. WO 03/062441, published July 31, 2003 (Ex. 1003, “Landes”).

⁶ Marx et al., *Reducing White Blood Cells in Platelet Units*, 31(8) Transfusion 743–747 (1991) (Ex. 1029, “Marx”).

⁷ Yen-Leiberman, *Diagnosis of Human Cytomegalovirus Disease*, 22(14) Clinical Microbiology Newsletter 105–109 (2000) (Ex. 1033, “Yan-

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
7–9, 21, 25–30	103(a)	Yen-Lieberman, Gocke ⁸
22	103(a)	Yen-Lieberman, Gocke, Marx

Petitioner relies on the declaration of Dr. Brynn Levy, among other evidence. Ex. 1043. Patent Owner responds with a declaration from Dr. Glenn D. Prestwich, along with other evidence. Ex. 2001.

C. Technology Overview & the '720 Patent

The '720 patent discloses a “rapid, non-invasive method for determining the sequence of DNA from a fetus” that can be used “for detection of chromosomal abnormalities.” Ex. 1001, 1:23–35. The '720 patent explains that a variety of invasive and non-invasive techniques are available for prenatal diagnosis, including amniocentesis, fetal blood cells in maternal blood, and maternal serum alpha-fetoprotein. *Id.* at 2:42–46. According to the patent, however, “techniques that are non-invasive are less specific, and the techniques with high specificity and high sensitivity are highly invasive.” *Id.* at 2:46–49; *see also id.* at 3:24–27 (citing an increased fetal mortality risk of about 0.5% with amniocentesis).

The '720 patent acknowledges the prior non-invasive use of fetal cells and cell-free fetal DNA (“cffDNA”), both isolated from maternal blood, for prenatal diagnosis. *Id.* at 4:59–5:44. With regard to fetal cells, the patent notes that the “presence of fetal nucleated cells in maternal blood makes it

Leiberman”).

⁸ Gocke et al., U.S. Patent No. 6,156,504, issued Dec. 5, 2000 (Ex. 1034, “Gocke”).

possible to use these cells for noninvasive prenatal diagnosis,” and that such “cells can be sorted and analyzed by a variety of techniques to look for particular DNA sequences.” *Id.* at 4:60–65. Yet the patent states that “it is still difficult” to get many fetal cells from maternal blood and “[t]here may not be enough to reliably determine anomalies of the fetal karyotype or assay for other abnormalities.” *Id.* at 5:15–21. The ’720 patent states that fetal DNA “has been detected and quantitated in maternal plasma and serum” and that “fetal DNA present in the maternal serum and plasma is comparable to the concentration of DNA obtained from fetal cell isolation protocols.” *Id.* at 5:24–34. “However,” according to the patent, “the diagnostic and clinical applications of circulating fetal DNA is limited to genes that are present in the fetus but not the mother” and that “a need still exists for a non-invasive method that can determine the sequence of fetal DNA and provide definitive diagnosis of chromosomal abnormalities in a fetus.” *Id.* at 5:38–44.

The ’720 patent describes a method that is said to increase the proportion or percentage of the cffDNA component in a sample from a pregnant female for subsequent analysis. According to the ’720 patent, the ability to detect chromosomal abnormalities has been “hindered by the low percentage of free fetal DNA” in maternal samples. Ex. 1001, 89:26–30. “Increasing the percentage of free fetal DNA would enhance the detection” of mutations, trisomy, and other genetic abnormalities. *Id.* at 89:30–35.

With the aim of increasing the percentage of cffDNA relative to circulating maternal DNA in a maternal sample, the ’720 patent describes adding an agent that inhibits cell lysis. *Id.* at 210:19–24 (Example 15)

(“[T]he use of cell lysis inhibitors, cell membrane stabilizers, or cross-linking reagents can be used to increase the percentage of fetal DNA in the maternal blood.”); *id.* at 89:35–37 (“The percent of fetal DNA in plasma obtained from a pregnant female was determined both in the absence and presence of inhibitors of cell lysis”). The ’720 patent explains that, “[w]hile lysis of both maternal and fetal cells is inhibited, the vast majority of cells [in a maternal blood sample] are maternal, and thus by reducing the lysis of maternal cells, there is a relative increase in the percentage of free fetal DNA.” *Id.* at 33:42–45. The patent identifies numerous agents as cell lysis inhibitors, cell membrane stabilizers, or cross-linking reagents. *See, e.g., id.* at 32:65–33:28 (listing, for example, formaldehyde, formalin, cleavable crosslinkers, cholesterol, vitamin E and its derivatives, and glucose); *see also id.* at 6:49–65; 11:43–12:5; 216:14–218:55 (Table XXIII (“A representative list of cross-linkers that can be used to impede maternal cell lysis”)).

The ’720 patent provides results on the use of formalin (i.e., formaldehyde in aqueous solution) as the lysis-inhibiting agent. *Id.* at 89:25–92:26 (Example 4), 210:16–218:55 (Example 15). In Example 4, the patent describes collecting a 5 ml blood sample from a pregnant subject, separating the sample into two tubes (each containing EDTA⁹), and adding formaldehyde (25µl/ml) to one of the tubes. *Id.* at 89:40–46. The samples were centrifuged and 800 µl of each maternal plasma sample was then used for DNA purification and further processing to determine the relative

⁹ The ’720 patent states that EDTA is a “magnesium chelator.” Ex. 1001, 32:61–64.

amount of cffDNA in the samples. *Id.* at 89:47–92:26. According to the ’720 patent, “the percentage of fetal DNA present in the sample that was treated with only EDTA was 1.56%” and the “percentage of fetal DNA present in the sample treated with formalin and EDTA was 25%.” *Id.* at 91:34–41. The patent reports that the percent of total cffDNA in eighteen blood samples with and without formalin was then calculated, with the results (mean percentage cffDNA) provided in Table V. *Id.* at 91:45–92:10 (reporting, *inter alia*, a mean percentage fetal DNA of 19.47% with formalin versus 7.71% without formalin); *see also id.* at 210:16–215:65 (Example 15 (reporting further results on formalin use in Table XXI)).

D. Challenged Claims

The ’720 patent includes thirty claims. Of those, claims 1, 3–9, 21, 22, and 24–30 are challenged here. Pet. 4. Claim 1, the only independent claim, is illustrative of the claims challenged in this Petition and reads as follows:

1. A method for detecting a free nucleic acid, wherein said method comprises: (a) isolating free nucleic acid from a non-cellular fraction of a sample, wherein said sample comprises an agent that inhibits lysis of cells, if cells are present, and wherein said agent is selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor; and (b) detecting the presence or absence of the free nucleic acid.

Ex. 1001, 535:15–21.

E. Prosecution History

The application that issued as the ’720 patent was filed on August 26, 2005. Ex. 1001, codes (21), (22). The Examiner initially rejected pending

claim 1 as anticipated by Kiessling. Ex. 1012, 1145. The Examiner also rejected claim 1 as obvious over the combination of Kiessling and Anker. *Id.* at 1149–50. With respect to what the Examiner described as the “key limitation i.e., wherein an agent that impedes cell lysis is added to the sample,” the Examiner found that Kiessling disclosed adding formaldehyde, paraformaldehyde, or glutaraldehyde to the sample to impede cell lysis. *Id.* at 1145. The Examiner further found that Kiessling taught that “the addition [of] one of these fixatives fixes (i.e. impedes the cell lysis of) the leukocytes present in the sample (i.e. human blood) and disinfects the sample.” *Id.*

In response, Patent Owner amended claim 1 to recite that the nucleic acid detected and isolated was “free” nucleic acid and to specify that the agent that impedes cell lysis was “selected from the group consisting of membrane stabilizer, cross-linker, and cell lysis inhibitor.” *Id.* at 1180. Patent Owner then argued that amended claim 1 was distinguishable over Kiessling because Kiessling analyzed DNA from within leukocytes while the amended claims focus on free nucleic acid. *Id.* at 1189–90 (“The methodology disclosed in Kiessling ‘fixes’ leukocytes, and subsequently DNA is isolated from the fixed leukocytes. Conversely, the methods of [the pending claims] are directed to isolating free nucleic acid. Nowhere does Kiessling teach or suggest a method for detecting free nucleic acid comprising *inter alia* isolating free nucleic acid from a sample.”) (internal citation omitted). Patent Owner also argued that the claimed method solved long-felt needs and achieved unexpected results. *Id.* at 1191–1192.

Initially the Examiner found Patent Owner’s amendment and arguments persuasive, withdrawing the rejections based on Kiessling and

Anker and explaining that “[t]he most persuasive argument(s) related to the applicant[’s] assertion that there was a long felt need and the evidence of an unexpected result.” *Id.* at 2100. Shortly thereafter, however, the Examiner reinstated the anticipation rejection over Kiessling. *Id.* at 2124. In the same office action, the Examiner also made several obviousness rejections of certain of the dependent claims over Kiessling alone and in combination with various other prior art references. *Id.* at 2128–2132. In doing so, the Examiner explained that “absent an unexpected result [the claimed method] would have been *prima facie* obvious.” *Id.* at 2128, 2130, 2131.

In response, Patent Owner argued that the Examiner misunderstood Kiessling, again arguing that the claimed method was distinguishable over Kiessling because “[t]he Kiessling methods do not involve the isolation of free nucleic acid from samples, and therefore, do not teach methods for detection of free nucleic acid.” *Id.* at 2148–49. Patent Owner also repeated its argument that the claimed method solved a long felt need and demonstrated unexpected results. *Id.* at 2150.

The Examiner responded by maintaining the anticipation argument over Kiessling and adding obviousness rejections over several different combinations of art. *Id.* at 2167–74. The Examiner added an obviousness rejection over the combination of Amicucci or Saito in view of Kiessling, finding that “both Amicucci et al. and Saito et al. teach a method of detecting free nucleic acid which comprises all of the limitations of Claim 1, except these authors do not teach that their maternal samples comprise[] an agent that impedes cell lysis.” *Id.* at 2168. The Examiner nonetheless found claim 1 obvious because Kiessling taught the use of a cell lysis inhibitor. *Id.*

Patent Owner responded by amending claim 1 to recite that the free nucleic acid is isolated from “a non-cellular fraction” of the sample. *Id.* at 2238. Appellant also argued that the claimed method was distinguishable over Kiessling because “Kiessling ‘fixes’ leukocytes, and subsequently DNA is isolated from the fixed leukocytes,” i.e., “isolation of DNA from a cellular fraction.” *Id.* at 2245. Thus, according to Patent Owner, Kiessling did not teach or suggest detecting free nucleic acid from a non-cellular fraction of a sample. *Id.* Patent Owner also repeated its argument that the claimed method solved a long felt need and demonstrated unexpected results. *Id.* at 2247–48.

The Examiner subsequently stated that the pending claims were “deemed to be allowable over the prior art of record in light of the applicant’s amendment filed 02 JUN 09 and the persuasive argument(s) therein.” *Id.* at 2271. After the filing of a terminal disclaimer to address a non-statutory obviousness-type double patenting rejection (*id.* at 2280), the Examiner issued a notice of allowance (*id.* at 2286–88).

II. DISCRETION UNDER 35 U.S.C. § 314(a)

A. *Standard for Exercising Discretion under Section 314(a)*

Under Section 314(a), the Director has discretion to deny institution. *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2140 (2016) (“[T]he agency’s decision to deny a petition is a matter committed to the Patent Office’s discretion.”). Indeed, “the PTO is permitted, but never compelled, to institute an IPR proceeding.” *Harmonic Inc. v. Avid Tech, Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016).

The Director, and the Board under the Director's delegated authority, may deny institution based on a number of considerations and in a variety of circumstances. For example, it is within the Board's discretion to deny serial petitions or to deny one or more concurrently-filed (i.e., parallel) petitions that challenge the same patent. Such discretion is explained in *General Plastic Indus. Co. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19 (PTAB Sep. 6, 2017) (precedential as to Section II.B.4.i) ("*General Plastic*") as well as in the Board's Consolidated Trial Practice Guide ("CTPG"). *General Plastic* at 16–19 (discussing factors the Board considers); CTPG 56–61 (discussing the *General Plastic* factors and considerations that inform discretion based on parallel-petitioning activity).

When deciding whether discretionary denial based on serial-petitioning activity is appropriate, we consider the factors set forth in *General Plastic*, which include:

1. whether the same petitioner previously filed a petition directed to the same claims of the same patent;
2. whether at the time of filing of the first petition the petitioner knew of the prior art asserted in the second petition or should have known of it;
3. whether at the time of filing of the second petition the petitioner already received the patent owner's preliminary response to the first petition or received the Board's decision on whether to institute review in the first petition;
4. the length of time that elapsed between the time the petitioner learned of the prior art asserted in the second petition and the filing of the second petition;

5. whether the petitioner provides adequate explanation for the time elapsed between the filing of the multiple petitions directed to the same claims of the same patent;
6. the finite resources of the Board; and
7. the requirement under 35 U.S.C. § 316(a)(11) to issue a final determination not later than 1 year after the date on which the Director notices institution of review.

General Plastic at 16–19. The above seven factors are non-exclusive and, thus, not limiting. *Id.*

The Board may also deny institution of a petition based on parallel proceedings before the courts where the validity of the subject patent is already at issue. In *NHK*, the Board denied institution relying, in part, on § 314(a) because the parallel district court proceeding was scheduled to finish before the Board reached a final decision. *NHK Spring Co. v. Intriplex Techs., Inc.*, IPR2018-00752, Paper 8 (PTAB Sept. 12, 2018) (precedential) (Decision on Institution). “*NHK* applies to the situation where the district court has set a trial date to occur earlier than the Board’s deadline to issue a final written decision in an instituted proceeding.” *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 at 3 (PTAB Mar. 20, 2020) (precedential) (“*Fintiv*”). When determining whether to exercise discretion to deny institution under *NHK* due to an earlier trial date, we consider the following factors (“*Fintiv* 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
6. other circumstances that impact the Board's exercise of discretion, including the merits.

Id. at 6. “These factors relate to whether efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in the parallel proceeding.” *Id.* In evaluating these factors, we take “a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review.” *Id.*

Patent Owner argues, applying the factors set forth in *General Plastic* or *Fintiv* to the circumstances here, that we should deny the Petition on a discretionary basis under § 314(a). We decline to do so for the reasons explained below.

B. Analysis of the General Plastic Factors

1. Factor 1: Whether the same petitioner previously filed a petition directed to the same claims of the same patent

This Petition is Illumina's first and only petition challenging the claims of the '720 patent. Pet. 53. Under such circumstances, standing alone, the Board ordinarily weighs *General Plastic* Factor 1 against discretionary denial. *See Unified Patents, Inc. v. Certified Measurement, LLC*, IPR2018-00548, Paper 7 at 7–8 (PTAB Sept. 5, 2018).

Nevertheless, “our application of the *General Plastic* factors is not limited solely to instances when multiple petitions are filed by the same petitioner.” *Valve Corp. v. Elec. Scripting Prods., Inc.*, IPR2019-00062, Paper 11 at 2 (PTAB April 2, 2019) (precedential) (“*Valve*”). Where “different petitioners challenge the same patent, we consider any relationship between those petitioners when weighing the *General Plastic* factors.” *Id.* And, in some case, it may be appropriate to deny a follow-on petition on a discretionary basis even if the follow-on petition is filed by a different party. *Id.* at 10. This is explained in the Board’s *Valve* decision, where the Board weighed “[t]he complete overlap in the challenged claims and the significant relationship between Valve [(follow-on petitioner)] and HTC [(first petitioner)] [to] favor denying institution.” *Id.*

Petitioner contends that it “is not a party, real party-in-interest, or privy to the other Patent Office proceedings” challenging the ’720 patent. Pet. 53. Petitioner also notes that its challenge relies on different prior art than presented in any earlier filings with the Board challenging the ’720 patent. Prelim. Reply 1–2 (noting reliance on Landes and Yen-Lieberman as anticipating prior art).

Patent Owner cites the petitions from Quest and Labcorp (filed in April and May of 2021) and the reexamination request from Natera (filed in March of 2021), all of which predate Illumina’s Petition filed on July 20, 2021. Prelim. Resp. 45. According to Patent Owner, “because a significant relationship exists between Petitioner and the prior challengers, and there is significant overlap between the challenged claims and invalidity theories,” Factor 1 favors denial. *Id.* at 45–46. In support of the alleged “significant

relationship,” Patent Owner contends that Illumina, Quest, Labcorp, and Natera have each been charged with infringement in various lawsuits based on “similar noninvasive genetic tests” that “include[] the same key component—blood collection tubes sourced from Streck, Inc.” *Id.* at 46 (citing Exs. 2086, 2087, 2088, and 2089 (complaints in each lawsuit)). Patent Owner argues that Streck “appears to be assisting the defendants” because Streck allegedly helped Natera run experiments in support of a noninfringement defense in the Natera lawsuit. *Id.* Moreover, Patent Owner argues that, Natera, Quest, and Labcorp “have entered into supply agreements with Illumina for sequencing technology used in genetic testing, including accused genetic tests.” *Id.* (citing Exs. 2091–2093 (press releases)); Prelim. Sur-Reply 1 (asserting that the “earlier challengers source gene-sequencing technology from Petitioner”).

Petitioner responds that Patent Owner’s argument about the alleged “significant relationship” is unsupported. Prelim. Reply. 1. Petitioner states that it “has not received any assistance from Streck . . . and is not involved in any of the ongoing litigations or proceedings that relate to Natera, Quest, and LabCorp.” *Id.* And, Petitioner explains, the number and staggered nature of the challenges to the ’720 patent “is a result of [Patent Owner’s] own making—[Patent Owner] sued Petitioner well after it sued the other third parties.” *Id.*

We do not agree with Patent Owner that Factor 1 weighs in favor of discretionary denial here. To the extent there is any relationship between Illumina and the earlier challengers, we find that such relationship is not a “significant” one, such as contemplated by *Valve*. First, although Illumina,

Natera, Quest, and Labcorp are each defendants accused of infringing the '720 patent, unlike *Valve*, they are not co-defendants in the same case. *Valve* at 9–10. Nor were Illumina and the other parties sued at the same time—Patent Owner instead sued those parties in seriatim district court complaints filed over approximately six months starting in mid-2020. Exs. 2086, 2087, 2088, and 2089. Thus, the staggered nature of the alleged follow-on challenges by those parties can be reasonably explained by Patent Owner's elected timetable for suing the defendants.

Second, the “significant relationship” in *Valve* turned in large part on the fact that co-defendants and serial petitioners in that case, HTC and Valve, were each accused of infringement based on the same device—HTC's VIVE device. *Valve* at 9–10. Indeed, there was evidence that Valve not only licensed its technology to HTC but also that Valve helped HTC design the accused VIVE device. *Id.* at 10. Here, by contrast, Illumina and, for example, Natera were sued based on *their own* alleged infringing prenatal tests. *See, e.g.*, Ex. 2086 ¶¶ 40–41 (identifying Illumina's “Verifi® Plus Prenatal Test”), Ex. 2087 ¶ 5 (identifying Natera's “Panorama” prenatal test and various other tests for non-prenatal uses, such as in transplant rejection and cancer detection). And there is no persuasive evidence to show that Illumina co-developed Natera's (or the other parties') accused tests, or vice-versa.

Patent Owner contends that Illumina and others use Streck's tubes as a “key component” of the alleged infringing tests because those tubes include an agent that inhibits cell lysis as claimed. Prelim. Resp. 46. But Illumina is not Streck and there is no evidence of a “significant relationship”

between Illumina and other users of Streck's tubes. Illumina also represents, with only Patent Owner's conjecture in opposition, that "Petitioner has not received any assistance from Streck with respect to the '720 patent." Prelim. Reply 1. Even accepting Patent Owner's contention that Streck has helped Natera, we see no basis to impute that alleged relationship to Illumina. Also, that Illumina and Natera (or others) may have executed supply agreements under which Illumina agreed to supply sequencing kits/consumables is not clearly connected to the infringement asserted by Patent Owner or, at most, only at an attenuated level.¹⁰ *See, e.g.*, Ex. 2087 (complaint against Natera mentioning Illumina only once ("Illumina HiSeq 2500 Rapid Run" used to sequence amplicons), in paragraph 29, in a long string cite about Natera's Prospera test for transplant rejection); Exs. 2091–2093 (press releases).

On the question of overlap, we agree with Patent Owner that there is substantial overlap among the claims challenged by Illumina and prior petitioners. Illumina's Petition is, however, based on Landes and on Yen-Lieberman, neither of which was asserted, alone or in combination with other references, in the previous IPR proceedings. Prelim. Reply 1–2.

Patent Owner cites to Natera's reexamination request and draws parallels between theories advanced by in those proceedings and here. Prelim. Resp. 47. Natera's reexamination, however, does not weigh significantly in our analysis because, we do not find a significant relationship between Petitioner and Natera, and because, further to Patent

¹⁰ Streck, in contrast, features more prominently in Ravgen's infringement allegations against Natera. Ex. 2087 (referencing Streck tubes with the alleged lysis inhibiting agent over thirty-five times).

Owner's request, it has been stayed. IPR2021-00791, Paper 22 (Patent Owner's Motion to Stay the Natera Reexamination); IPR2021-00791 Paper 25 (Order Granting Patent Owner's Motion to Stay).

Patent Owner also identifies the Labcorp IPR as a source of overlap. Prelim. Resp. 47. However, none of the art relied upon in the Petition is identified as a basis for invalidity in the Labcorp IPR. *Compare* Pet. 5, with IPR2021-01206, Paper 1, 9–10. Patent Owner asserts that Illumina's Petition cites Lee,¹¹ a reference that Labcorp asserts is anticipatory in the Labcorp IPR. IPR2021-01206, Paper 1, 9. However, Petitioner's citations to Lee are string cites used to show the general knowledge of the POSA, not to support that Lee discloses the limitations recited in the challenged claims. *See, e.g.*, Pet., 6, 7, 16, 42, 45 (citing Ex. 1019).

Patent Owner argues that "Illumina's grounds present the same theory relying on ACD to meet claim limitations, including the claimed agent limitation." Prelim. Resp. 47. We agree that both the Labcorp IPR and the present Petition present the issue of whether the dextrose in ACD is "an agent that impedes cell lysis," as required by the challenged claims. Further, Patent Owner devoted considerable argument in its Preliminary Response to this issue in both this proceeding and in the Labcorp IPR. Given the prominence of the dextrose/ACD arguments in that case and here (*see infra* § III.E.2), we give weight to Patent Owner's argument that there will be

¹¹ Lee, *Quantitation of genomic DNA in plasma and serum samples: higher concentrations of genomic DNA found in serum than in plasma*, 41 Transfusion, 276-282 (2001) (Ex. 1019, "Lee").

overlap, at least with respect to the issue of whether the dextrose component of ACD meets the claim requirement for an “agent that impedes cell lysis.”

However, there are material differences between this case and the “substantial relationship” and circumstances in *Valve* that ultimately favored denial. For example, in *Valve*, both HTC and Valve had retained the same expert in support of their respective serial petitions, Valve had joined related instituted proceedings filed by HTC, and Valve had clearly used the Board’s denial of HTC’s earlier petition as a roadmap for Valve’s follow-on petition (we address the absence of road-mapping under Factor 3 below). *Valve* at 3, 12–13. None of those considerations are present with Illumina’s Petition. The facts here simply do not resemble, indeed they are far from, those in *Valve* that weighed in favor of discretionary denial.

For the reasons above, we find that Factor 1 weighs against denial of Illumina’s Petition.

2. Factors 2, 4, and 5

Factors 2, 4, and 5 relate, in general, to a petitioner’s knowledge of prior art asserted in a later petition when an earlier petition was filed, the time between a petitioner learning of the later-asserted art and the later-filed petition, and a petitioner’s explanation for any delay between filings.

General Plastic at 16–19. We agree with Petitioner, however, that where a later petitioner is not the same party as, or significantly related to, the earlier petitioner(s), Factors 2, 4, and 5 are less relevant in the overall *General Plastic* analysis. Prelim. Reply 2–3; cf. *Unified Patents, Inc. v. Certified Measurement, LLC*, IPR2018-00548, Paper 7 at 7-8 (PTAB Sept. 5, 2018).

Patent Owner argues that Petitioner could, with diligence, have located Landes and the other relied-upon references in April or May 2021, when Quest and Labcorp filed their petitions. Prelim. Resp. 49 (asserting that “Illumina had Natera’s reexamination request four months before the Petition” and had “Labcorp’s IPR petition two months before the Petition”). Patent Owner further contends that Illumina has not adequately explained the delay in filing Illumina’s own petition (in late July 2021). *Id.* at 50; Prelim. Sur-Reply 2–4 (arguing that Illumina knew or should have known of the asserted prior art earlier and noting date stamps on some of Petitioner’s exhibits to suggest Illumina gathered such evidence in March 2021).

As noted above, because we determine that Illumina is sufficiently unrelated to the prior petitioners, these factors carry less weight in the analysis. But even if Patent Owner’s characterizations of what Illumina knew (or should have known) and when it should have known it are accurate, we find that a few-months gap between the first petition and the Illumina Petition is not unreasonable under the circumstances. Prelim. Reply 2–3 (“While PO’s assertion is pure speculation, even if true, a two-to-three month timeframe to prepare a detailed request for *inter partes* review is entirely reasonable.”).

Patent Owner’s criticisms relevant to these factors hinge mostly on the notion that Illumina should have filed its petition at about the same time as the other petitioners, or not at all. Those criticisms are weak when the petitioners are unrelated parties and were not sued at the same time or in the same lawsuit. We do not overlook that, had all the petitions against the ’720 patent been filed at about the same time, we may have consolidated

proceedings before us for efficiency. Nevertheless, as Patent Owner did not or could not, coordinate the filing of its various lawsuits to approximately the same date, it cannot on this record fairly criticize unrelated petitioners for filing petitions on a schedule staggered by a few months. Patent Owner staggered the filing of its lawsuits over a period of about six months, with Illumina being sued last. This provides a reasonable explanation for the timing of Illumina's filing relative to the earlier filings.

Factors 2, 4, and 5 do not weigh in favor of discretionary denial for the reasons discussed above.

3. Factor 3: whether at the time of filing of the second petition the petitioner already received the patent owner's preliminary response to the first petition or received the Board's decision on whether to institute review in the first petition

As pointed out by Patent Owner, “[u]nder the third *General Plastic* factor, the Board considers the extent to which a later petitioner had the opportunity to ‘tailor its arguments to address issues identified by patent owner and/or the Board during a prior proceeding.’” Prelim. Resp. 49 (quoting *NetApp v. Realtime Data*, IPR2017-01354, Paper 16 at 11 (PTAB Nov. 14, 2017)). Patent Owner contends that “Illumina had access to the Patent Office’s grant of Natera’s reexamination, issued April 22, and first office action, issued July 6, before it filed the Petition” as well as “LabCorp’s IPR asserting Lee in anticipation grounds on May 28.” Prelim. Resp. 49. Patent Owner contends that “Petitioner’s delayed filing enabled it to tailor its arguments in response to issues addressed by Patent Owner, the Board, and/or the Patent Office Central Reexamination Unit during earlier

filed proceedings.” Prelim. Sur-Reply 3. We do not find this argument persuasive.

At the time Illumina filed its Petition, Patent Owner had not yet filed a response in Natera’s reexamination or in the Labcorp IPR. Manifestly, Petitioner could not have tailored its arguments to address issues identified by Patent Owner when Patent Owner had yet to file a response.

Although Petitioner did have access to the Examiner’s Office Action in the Reexamination proceeding, the Examiner in that proceeding rejected the pending claims based on different prior art than is relied upon by Petitioner. Ex. 2085, 5–7 (Office Action in reexamination proceeding). Patent Owner nonetheless argues that Petitioner’s challenge is “based on the same theories at issue in the prior proceedings” because it relies on the “same ACD and similar anticoagulant chelator compounds.” Prelim. Resp. 49. However, the Examiner in the Reexamination proceeding contends that ACD meets the “agent that impedes cell lysis” requirement in a different way than does the Petitioner. In particular, the Examiner relied on the anti-clotting properties of acid-citrate-dextrose (“ACD”) as evidence that ACD meets the requirement of the challenged claims for an “agent that impedes lysis” while Petitioner relies the presence of glucose in ACD as evidence that ACD meets that claim requirement. *Compare*, Ex. 2085, 6 (Office Action in the Reexamination, finding that “the anticoagulants used by Lee, acid-citrate-dextrose (ACD) and EDTA . . . are cell lysis inhibitors in the context of processing blood samples because they prevent lysis of WBCs caused by clotting”); *with* Pet. 28 (asserting that Landes meets the “agent that impedes cell lysis” requirement because “glucose is introduced to a

sample containing cell-free nucleic acid via the ACDA tube”), 38 (asserting that Yen-Lieberman meets the “agent that impedes cell lysis” requirement because “by instructing the collection of blood in an ACD tube, *Yen-Lieberman* necessarily describes the presence of glucose in the blood sample”). Thus, Petitioner does not appear to have used the Reexamination Office Action as a road map.

Patent Owner contends that Illumina had access to the papers filed by the other petitioners and by the Examiner in the reexamination. Patent Owner argues that “[t]hose papers gave Illumina a road map for preparing its own challenge.” Prelim. Resp. 49. Even if that was accurate, it is not the sort of alleged road-mapping about which *General Plastic* is primarily concerned. *General Plastic* at 17 (criticizing follow-on petitions that seek to “us[e] our [(i.e., the Board’s)] decisions as a roadmap, until a ground is found that results in the grant of review”); *see also id.* at 17 n.14 (citing cases that explain “a decision on a petition . . . is not simply part of a feedback loop by which a petitioner may perfect its challenges through a subsequent filing”) (citation omitted). We decline to weigh factor 3 in favor of denial here merely based on some substantive similarities in some of the grounds presented by unrelated petitioners.

Under the circumstances, Factor 3 weighs against discretionary denial of the Petition.

4. Factors 6 and 7

General Plastic Factors 6 and 7 relate to the Board’s resources and the requirement to issue a timely final written decision. *General Plastic* a 16. Patent Owner contends that we should deny institution because the Board’s

limited resources are generally better spent focusing on initial petitions as compared to follow-on petitions, and the Board can no longer realistically coordinate the schedules of Illumina's challenge with the earlier proceedings. Prelim. Sur-Reply 4; Prelim. Resp. 50.

To some extent, we agree with Patent Owner. Inasmuch as there are some similarities in the various petitioners' theories, it is arguably inefficient and wasteful to institute yet another trial—now three, counting Illumina's Petition—challenging substantially the same claims on those bases. And the opportunity for coordinated schedules has passed.

It is true that Illumina might have filed the Petition earlier and possibly allowed us to put its trial on the same schedule as the other ongoing proceedings against the '720 patent. Because it did not do so, it places a somewhat greater burden on Board resources. At the same time, the panel is already familiar with the '720 patent and certain prior art, so there are efficiencies gained.¹² And we perceive at present no specific obstacle to reaching a final written decision in this matter within one year from institution.

Altogether, on this record, Factors 6 and 7 are neutral to marginally weighing in favor of denial.

¹² In looking to overall efficiencies, it may well be inefficient for the Board, which is already familiar with the '720 patent and the prior art, to deny institution of Illumina's Petition on a discretionary basis, increasing inefficiencies for the district court in Delaware should it otherwise be inclined to grant a motion to stay pending resolution of the IPRs, which Illumina represents it will seek upon institution. *See General Plastic* at 16–17 (explaining that an objective of the AIA was to “provide an effective and efficient alternative to district court litigation”).

5. Conclusion

After considering all the *General Plastic* factors, we decline to deny the Petition on a discretionary basis. Factors 1 through 5 weigh against denial. Factors 6 and 7 are neutral to marginally weighing toward denial, which does not override the other factors on this record.

C. Analysis of the Fintiv Factors

1. Factor 1: Whether a Stay Exists or Is Likely to Be Granted if a Proceeding Is Instituted

Fintiv factor 1 recognizes that a stay of litigation pending resolution of the PTAB trial allays concerns about inefficiency and duplication of efforts, which strongly weighs against exercising the authority to deny institution. *Fintiv* at 6.

Petitioner represents that it will seek a stay in district court if we institute *inter partes* review. Pet. 55. Petitioner contends that given the timing, “there is a strong likelihood such a stay will be granted.” *Id.* Patent Owner responds that no motion to stay has been filed and therefore, this factor is neutral. Prelim. Resp. 52. We decline to speculate on how the court may rule on Petitioner’s yet-to-be-filed motion. Accordingly, this factor is neutral. *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 15 at 12 (PTAB May 13, 2020) (informative) (explaining that factor 1 generally “does not weigh for or against discretionary denial” when neither party has requested a stay).

2. Factor 2: Proximity of the Court’s Trial Date to the Board’s Projected Statutory Deadline

Fintiv factor 2 looks to the “proximity of the court’s trial date to the

Board’s projected statutory deadline.” *Fintiv* at 9. “If the court’s trial date is earlier than the projected statutory deadline, the Board generally has weighed this fact in favor of exercising authority to deny institution under NHK.” *Id.*

Petitioner represents that trial in the Illumina lawsuit is not scheduled to begin until September 11, 2023. Pet. 55. According to Petitioner, this supports declining to exercise our discretion to deny institution because a final written decision would precede trial in the Illumina lawsuit. *Id.*

Patent Owner does not dispute that our final written decision would precede trial in the Illumina lawsuit, but argues that our final written decision would come well after trial in three third-party lawsuits – i.e, the Natera lawsuit, the Quest lawsuit, and the Labcorp lawsuit (collectively, “the third-party lawsuits”). Prelim. Resp. 52–55; Prelim. Sur-reply 5. We address the Patent Owner’s arguments regarding third-party litigation, including issues of timing and overlap with respect to the third-party litigations in connection with *Fintiv* Factor 6. With respect to the Illumina lawsuit, we agree with Petitioner that the proximity of the court’s trial date to the Board’s projected statutory deadline weighs against exercising our discretion to deny institution because we expect to render a final written decision in this matter roughly eight months before any trial of Illumina’s lawsuit in Delaware.

3. Factor 3: Investment in the Parallel Proceeding by the Court and Parties

Fintiv factor 3 considers the “investment in the parallel proceeding by the court and parties,” including “the amount and type of work already

completed in the parallel litigation by the court and the parties at the time of the institution decision.” *Fintiv* at 9. For example, if, at the time of institution, the court in the parallel proceeding has issued “substantive orders related to the patent at issue in the petition” or “claim construction orders” this favors denial. *Id.* at 9–10.

Petitioner contends that “[t]here is still significant investment required in the district court litigation.” Pet. 55. Petitioner explains that “[c]laim construction, discovery, pre-trial motions, preparing for trial, going through the trial process, and engaging in post-trial motions practice, all lie in the future.” *Id.*

Patent Owner argues that “the parties and the district court have already invested significant effort in the Illumina Litigation and will invest quite a bit more by the time the Board issues its institution decision in January 2022.” Prelim. Resp. 56. Patent Owner explains that “[t]he parties have already exchanged infringement and invalidity contentions, exchanged claim terms for *Markman*, and will be in the middle of claim construction briefing at the time of the institution decision.” *Id.*

We agree with Petitioner that investment in the Illumina lawsuit, particularly as related to any validity issues, has not been substantial. Based on the scheduling order, fact discovery will not close until August 16, 2022. Ex. 2076, 6. The parties have exchanged preliminary infringement and invalidity contentions, but final contentions are not due until the summer of 2022. *Id.* at 5. Claim construction briefing has begun, but will not be completed until March 3, 2022, and a hearing is not scheduled until April 12, 2022. *Id.* at 10–11. Based on our review of the scheduling order, it

appears that most of the investment from the court and the parties in the Illumina lawsuit lies ahead. *See generally, id.*

Overall, this factor weighs against discretionary denial of the Petition.

4. Factor 4: Overlap between Issues Raised in the Petition and in the Parallel Proceeding

Fintiv Factor 4 considers whether “the petition includes the same or substantially the same claims, grounds, arguments, and evidence as presented in the parallel proceeding.” *Fintiv* at 12. If the issues in the Petition overlap substantially with those raised in the parallel proceeding, “this fact has favored denial.” *Id.* “Conversely, if the petition includes materially different grounds, arguments, and/or evidence . . . this fact has tended to weigh against exercising discretion to deny institution.” *Id.* at 12–13.

Patent Owner argues that there is “significant overlap between the claims challenged in the Petition and those asserted in the Illumina Litigation.” Prelim. Resp. 58. According to Patent Owner, “[a]ll seventeen Challenged Claims in the Petition are asserted in the Illumina Litigation.” *Id.* However, Patent Owner does not argue or direct us to evidence supporting that the arguments presented in the Petition overlap with those in the Illumina lawsuit. Prelim. Resp. 58–61; Prelim. Sur-reply 5. Moreover, Petitioner stipulates that “it will not pursue, in district court, invalidity based on any instituted IPR ground.” Prelim. Reply 4. This stipulation echoes the one cited in *Sand Revolution II, LLC v. Continental Intermodal Group-Trucking LLC*, IPR2019-01393, Paper 24 at

16 (PTAB June 16, 2020) (informative), which the Board determined weighed marginally against discretionary denial.

Given the absence of evidence of overlapping issues, and Petitioner's stipulation, we find that this factor weighs against exercising our discretion to deny institution.

5. Factor 5: Whether the Petitioner and the Defendant in the Parallel Proceeding Are the Same Party

Petitioner is the defendant in the Illumina lawsuit. Prelim. Resp. 59. Because our final written decision in this matter will likely precede the date for trial scheduled in the Illumina lawsuit by many months, this factor weighs against discretionary denial. *Google LLC v. Parus Holdings, Inc.*, IPR2020-00846, Paper 9 at 21 (PTAB Oct. 21, 2020) ("Here, . . . Petitioner is the defendant in the parallel proceeding. This fact could weigh either in favor of, or against, exercising discretion to deny institution, depending on which tribunal was likely to address the challenged patent first.").

6. Factor 6: Other Circumstances that Impact the Board's Exercise of Discretion, Including the Merits

Fintiv factor 6 looks to whether "other circumstances" exist that might "impact the Board's exercise of discretion, including the merits." *Fintiv* at 14.

Petitioner argues that this factor favors institution based on the "significant public interest against 'leaving bad patents enforceable.'" Pet. 56. Petitioner further argues that "it has presented strong grounds for anticipation and obviousness of the challenged claims." Prelim. Reply 5.

Patent Owner argues that the “merits of the instant Petition are far from strong.” Prelim. Resp. 62. Patent Owner further argues that the existence of “serially-filed petitions by similarly situated defendants . . . favors denial.” *Id.* In addition, Patent Owner argues that “trials are scheduled of the ’720 patent in *three* other litigations before the FWD would be due in this proceeding.” *Id.* at 52–53. According to Patent Owner the courts and the parties have made significant investments in these lawsuits and there is substantial argument between the arguments presented in the Petition and in these three third-party lawsuits. *Id.* at 52–57.

We begin by considering Petitioner’s argument that the merits are strong and that policy considerations against leaving “bad patents” enforceable counsel against discretionary denial. For the reasons discussed below, we find that Petitioner has met its institution burden. However, our determination is preliminary, and we are not prepared on this preliminary record to characterize the merits of Petitioner’s challenge as especially “strong,” or to characterize the ’720 patent as a “bad patent.” Accordingly, the merits are neutral for purposes of the *Fintiv* analysis.

We turn next to Patent Owner’s argument regarding the third-party petitions. We have considered Patent Owner’s arguments with respect to serially-filed petitions in the context of the *General Plastics* factors. For the reasons discussed *supra* § II.B, we are not persuaded that the existence of additional petitions challenging the ’720 patent merits denial.

Finally, we consider Patent Owner’s arguments regarding the third-party lawsuits. We consider each of the three pending third-party lawsuits in turn.

Considering the Natera lawsuit under the *Fintiv* rubric, *Fintiv* factor 2 (proximity to trial) weighs against denial or is at most neutral because we can only speculate as to when trial will occur given the recent cancellation of the trial date and transfer to a new judge. Ex. 3003; (order canceling trial); Ex. 3004 (docket report for Natera lawsuit). We agree with Patent Owner that *Fintiv* factor 3 (investment) arguably weighs against instituting trial on this Petition. The trial date in the Natera lawsuit was originally set for December, 13, 2021, and was taken off calendar shortly before the original trial date. *Id.* Given how close the case got to trial, we expect that the parties and the court made substantial investments in that proceeding.

With respect to the degree of overlap with the Natera Lawsuit, none of the art relied upon in the Petition is identified as a basis for invalidity in the Natera litigation. *Compare*, Pet. 5 with Ex. 2094. However, Patent Owner argues that because the Natera lawsuit includes Lee, and Lee collects blood samples in tubes containing acid citrate dextrose (“ACD”), the Petition and the Natera lawsuit will both “address and resolve the same key argument:” whether the dextrose component of acid citrate dextrose (“ACD”) meets the claim requirement for an “agent that impedes cell lysis.” Prelim. Resp. 59–61. We credit Patent Owner’s argument insofar as there does appear to be some substantive overlap, both as to anticipation and obviousness, in issues raised in the Petition and the Natera lawsuit. Although that overlap, along with the investment discussed above, weighs in favor of denial, that weight is diminished to a degree because Illumina is unrelated to Natera (*Fintiv* factor 5) and due to uncertainty about when and if trial in the Natera lawsuit will occur.

Patent Owner also cites its lawsuit against Labcorp as a source of overlap and duplication of efforts. Prelim. Resp. 57. Considering the Labcorp lawsuit under the *Fintiv* rubric, factor 2 is neutral. Although the parties have proposed moving the trial date for the Labcorp lawsuit to September 19, 2022, which would be four months before the due date of our final written decision, no firm date has been established; the September 19, 2022 trial date is only estimated. Ex. 3001 (Joint Proposed Schedule in Labcorp lawsuit); Ex. 3002 (docket report for Labcorp lawsuit). The proposed new schedule is unsigned by the court. *Id.* Although we usually take courts' trial schedules at "face value," that is not necessarily so with trial dates that are mere estimates. *See, e.g., Progenity, Inc. v. Natera, Inc.*, IPR2021-00279, Paper 12 at 29 (PTAB June 11, 2021) (concluding "there is no trial date scheduled for the parallel proceeding" based on an email from the court's clerk merely providing an estimated trial date); *Intel Corp., v. FG SRC LLC*, IPR2020-01449, Paper 13 at 15 (PTAB Mar. 3, 2021) (explaining that estimated trial dates are not firm trial dates). Therefore, "[w]hether the trial takes place before, contemporaneously with, or after our final written decision statutory deadline involves speculation." *Progenity*, IPR2021-00279 at 29.

With respect to Factor 3 for the Labcorp lawsuit, we find that investment in the litigation, particularly as related to any validity issues, has not been substantial. Even taking the unsigned, proposed scheduling order as a guide about case deadlines proposed therein, as of this institution decision, fact discovery opened on September 16, 2021, and will not close until April, 2022. Ex. 3001, 2–3. Expert discovery will not open until April,

and closes in June, at the earliest. *Id.* A *Markman* order has been entered but most of the investment from the court and the parties in the Labcorp lawsuit, especially on the invalidity issues, lies ahead.

With respect to Factor 4 for the Labcorp lawsuit, it is difficult to determine to what extent the arguments presented in the Petition overlap with those that will be developed in the Labcorp lawsuit. Patent Owner devotes a single sentence to addressing the alleged overlap, asserting that “[s]ignificant overlap also exists between the Petition and the LabCorp and Quest Litigations.” Prelim. Resp. 58 (citing Ex. 2055 (Quest’s Invalidity Contentions)). That does not persuade us of overlap to a degree that justifies weighing factor 4 in favor of denial, especially against Illumina as an unrelated party (factor 5).

Finally, Patent Owner cites the Quest lawsuit as a source of overlap and duplication of efforts. Prelim. Resp. 57. Considering the Quest lawsuit under the *Fintiv* rubric, factor 2 weighs against denial or is at most neutral because the case was recently transferred from the Western District of Texas to the Central District of California, and no trial date has been set by the new court. Ex. 3005 (docket from the Western District of Texas in Quest lawsuit); Ex. 3006 (docket from the Central District of California in the Quest lawsuit); *In re Quest Diagnostics Inc.*, 2021 WL 5230757.

Factor 3 weighs the same as in the Labcorp lawsuit because before it was transferred, the Quest lawsuit was before the same judge and on the same schedule as the Labcorp lawsuit, and the extent of ongoing investment by the transferee court on validity issues appears minimal.

With respect to factor 4, again, it is unclear to what extent the arguments presented in the Petition overlap with those that will be developed in the district court litigation. As with the Labcorp lawsuit, Patent Owner does not identify any areas of significant overlap between the grounds raised in Illumina's Petition and those being pursued by Quest in its lawsuit against Patent Owner. Prelim. Resp. 58. But even assuming that there is some degree of overlap, the weight given to such overlap is diminished because Quest and Illumina are unrelated and it is not apparent that trial in the new transferee court will precede a final written decision on Illumina's Petition.

Overall, we consider *Fintiv* factor 6 to be neutral.

7. Balancing the *Fintiv* Factors

We consider the above factors and take “a holistic view of whether efficiency and integrity of the system are best served by denying or instituting review.” *Fintiv* at 6. In our view, the facts weighing against exercising discretion to deny institution collectively outweigh those favoring denial and concerns about potential inefficiency or integrity of the system. For these reasons, we decline to exercise our discretion to deny institution under § 314(a).

III. ANALYSIS

A. *Principles of Law*

“In an [*inter partes* review], the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable.” *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) (citing 35 U.S.C. § 312(a)(3) (requiring *inter partes* review

petitions to identify “with particularity . . . the evidence that supports the grounds for the challenge to each claim”)).

To show anticipation under 35 U.S.C. § 102, each and every claim element, arranged as in the claim, must be found in a single piece of prior art. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359 (Fed. Cir. 2008).

To show obviousness under 35 U.S.C. § 103(a) the differences between the subject matter sought to be patented and the prior art are must be such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which that subject matter pertains. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations of nonobviousness when presented. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

B. Person of Ordinary Skill in the Art (“POSA”)

In determining the level of skill in the art, we consider the problems encountered in the art, the art’s solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field. *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986).

Petitioner proposes the following POSA definition:

[A POSA] would have had “a M.D. and/or Ph.D. in a related area such as genetics, biochemistry, molecular biology, cell biology,

or microbiology and at least one to two years of work in one of those related areas, [or] a Bachelor's degree in one of the foregoing areas and at least three to four years of work in that area.”

Pet. 12 (quoting Ex. 1020 ¶ 15). Petitioner additionally asserts that “[b]ased on this asserted level of skill, the POSA . . . would have had academic or industry experience collecting and analyzing cell-free nucleic acid, such as DNA, from blood samples.” *Id.* Patent Owner proposes substantially the same definition. Prelim. Resp. 11 (citing Ex. 2001 ¶ 32). To the extent there are minor differences in the proposals, Patent Owner's declarant testifies that such differences are not material and his “opinions . . . would not change if Dr. Levy's [i.e., Petitioner's] proposed level of ordinary skill were adopted.” Ex. 2001 ¶ 34.

The parties are in substantial agreement on the POSA level, and we adopt Petitioner's proposal for this Decision. Our determinations below would not change if we adopted Patent Owner's minimally different level.¹³

C. Claim Construction

We interpret a claim “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b).” 37 C.F.R. § 42.100(b) (2020). Under this standard, we construe the claim “in accordance with the ordinary and customary meaning of such

¹³ We adopted a somewhat differently phrased definition for the POSA in the Quest and Labcorp cases based on the parties' positions in those matters. *See, e.g.*, IPR2021-00791, Paper 20 at 38–40; IPR2021-01026, Paper 11 at 30–32. On this record, we do not see that such differences are material or would alter the outcome of this Decision.

claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” *Id.*

Petitioner does not identify any claim terms as needing construction. Pet. 21–22. Patent Owner argues that in applying Landes and Yen-Lieberman to the challenged claims, Petitioner interprets the claims too broadly. Prelim. Resp. 12. In particular, Patent Owner argues that Petitioner’s interpretation of the claims to encompass anticoagulant chelators, such as ACD [acid citrate dextrose] and EDTA, is “impermissibly broad.” *Id.* at 13.

At this point in the proceeding, we do not find it necessary to construe the claims to determine whether they encompass anticoagulant chelator compounds such as EDTA and ACD because Petitioner relies on glucose, not an anticoagulant chelator such as ACD or EDTA, as the “agent that impedes cell lysis.” Pet. 28 (“Thus, *Landes* describes a method of isolating cell-free nucleic acid, such as DNA, from a sample that comprises ‘an agent that impedes cell lysis’, *i.e.*, glucose.”); *id.* at 38 (“Thus, *Yen-Lieberman* described a method of isolating cell-free nucleic acid from a sample that comprises ‘an agent that impedes cell lysis,’ *i.e.*, glucose.”).

We recognize that the glucose in Landes and Yen-Lieberman is introduced to the samples as a component of ACD, a known anticoagulant. Ex. 1043 ¶ 49 (testimony of Dr. Levy that “*Landes* . . . discusses the same method as is claimed in the ’720 patent, where ‘an agent that impedes cell lysis’ is present in a sample through the glucose ingredient present in the

ACDA^[14] blood collection tube”). However, the challenged claims use the transitional phrase “comprising.” Ex. 1001, 535:15–21 (reciting “[a] method for detecting a free nucleic acid, wherein said method *comprises*: (a) isolating free nucleic acid from a non-cellular fraction of a sample, wherein said sample *comprises*. . .”) (emphasis added). Accordingly, the challenged claims do not exclude the presence of additional elements beyond those recited in the claim. *Exergen Corp. v. Wal-Mart Stores, Inc.*, 575 F.3d 1312, 1319 (Fed. Cir. 2009) (“The claim uses the term ‘comprising,’ which is well understood in patent law to mean ‘including but not limited to.’”).

Consistent with the use of the transitional term “comprising,” we do not understand Patent Owner to argue that the sample cannot contain an anticoagulant. Rather, we understand Patent Owner to argue that one cannot satisfy the claim element requiring “an agent that impedes cell lysis” by pointing solely to an anticoagulant. As Petitioner does not do so, we do not find it necessary to construe the claims at this stage of the proceeding. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (“[W]e need only construe terms ‘that are in controversy, and only 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))); *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’”).¹⁵

¹⁴ According to Dr. Levy, Landes uses the acronym ACDA to refer to Becton Dickinson’s Acid Citrate Solution A. Ex. 1043 ¶ 33.

¹⁵ As understood, Patent Owner’s position also does not account adequately

The parties are, of course, welcome to brief the proper construction of the claim term “agent that impedes cell lysis,” or any other claim term, to the extent they contend that construction is necessary to resolve the issues presented in this proceeding.

D. Overview of the Asserted Prior Art

1. Landes (Exhibit 1003)

Landes is an international patent application that published July 31, 2003. Ex. 1003, code (43). Landes claims priority to a U.S. provisional patent application (No. 60/349,877) that was filed January 18, 2002 (hereafter “the Landes Provisional” (Ex. 1006)).

Landes relates generally to non-invasive methods used to distinguish circulating fetal DNA from maternal DNA in samples from maternal blood, and thereby to detect fetal aneuploidies and alleles. Ex. 1003, code (57). Landes teaches, for example, that “maternal serum or plasma may be a relatively rich source of fetal DNA based on PCR determinations,” that it “has been shown that fetal DNA can be consistently detected in maternal serum as early as 7 weeks,” and that such DNA increases during gestations. *Id.* at 2:19–25 (disclosing that “the lowest fetal DNA concentration in plasma as measured by PCR was greater than 20 fetal cell equivalents per mL of maternal blood with some instances where fetal DNA constituted as much as 5% of the total DNA in plasma”).

Landes discloses a plasma separation and fetal DNA isolation

at this stage for a compound that may have a more than one functionality (e.g., chelation and cell membrane stabilization).

protocol where maternal blood is first collected into ACDA tubes from Becton, Dickinson. *Id.* at 10:26–12:6. Landes teaches that, following centrifugation and plasma removal, DNA can be isolated from the plasma sample using commercially available kits. *Id.* The DNA may then be treated with bisulfite to distinguish fetal and maternal DNA,¹⁶ and the nucleotide sequence of interest may subsequently be amplified (e.g. via fetal-specific PCR) and analyzed. *Id.* at 12:9–15:3.

2. Marx (Exhibit 1029)

Marx is an article entitled “Reducing white cells in platelet units. Ex. 1029, 743. It published in 1991 and generally relates to techniques that aim to prepare platelet rich plasma samples with reduced white blood cell contamination. *Id.* Marx teaches, for example, “an effective method of significantly decreasing the WBC content” of platelet units is to prepare a sample “with reduced centrifugation time and with the braking programs disengaged.” *Id.*; *see also id.* at 746 (“[N]o brakes gave much more reasonable yields . . . as well as low WBC contamination.”).

3. Yen-Lieberman (Exhibit 1033)

Yen-Lieberman is an article entitled “Diagnosis of Human Cytomegalovirus Disease,” that appears in the Clinical Microbiology

¹⁶ Landes teaches that isolated DNA may be treated “with a reagent which differentially modifies methylated and non-methylated DNA, e.g., bisulfite,” which recognizes that fetal DNA is generally “hypomethylated relative to adult DNA.” Ex. 1003, 8:22–28 (explaining that “[o]ne means of generating fetal-specific PCR products is to identify loci that are unmethylated in fetal DNA and methylated in adult/maternal DNA.”).

Newsletter. Ex. 1033. The article is dated July 15, 2000. Yen-Lieberman is a review of the “methodological aspects of newer and current commercially available tests” for detecting human cytomegalovirus (“HCMV”). *Id.* at 105. One of the tests discussed is the AMPLICOR CMV test, which “uses PCR nucleic acid amplification for qualitative detection of HCMV DNA in plasma separated from anticoagulated whole blood (EDTA or ACD anticoagulants).” *Id.* at 107. Yen-Lieberman teaches that “[t]he detection of circulating HCMV DNA in plasma or whole blood predicts the subsequent development of HCMV disease.” *Id.* at 108 (internal citations omitted). “Additionally, quantitation of the amount of HCMV DNA in blood is a useful clinical tool to monitor patients on therapy.” *Id.*

4. Gocke (Exhibit 1034)

Gocke is an issued U.S. Patent, entitled “Detection of Extracellular Tumor-Associated Nucleic Acid in Blood Plasma or Serum Using Nucleic Acid Amplification Assays.” Ex. 1034 code (54). It issued on December 5, 2000. *Id.* at code (45). Gocke discloses “detection of specific extracellular nucleic acid in plasma or serum fractions of human or animal blood.” *Id.* at code (57). Gocke states that the methods disclosed therein can be used to detect “[n]ucleic acid from any biological source, including but not limited to . . . viral . . . nucleic acid.” *Id.* at 7:57–60.

E. Ground 1: Anticipation by Landes

Petitioner asserts that claims 1, 3–8, 21, and 24 are unpatentable as anticipated by Landes. Pet. 22–32. We provided an overview of Landes above. Petitioner shows, based on this preliminary record, where each of the

limitations of the challenged claims is disclosed in Landes. *Id.* Petitioner’s assertions above are backed by the cited prior art and by the testimony of its declarant, Dr. Levy. *Id.*; *see also* Ex. 1043 ¶¶ 41–60. On this preliminary record, we determine that Petitioner’s arguments and evidence are sufficient for purposes of institution. We focus our discussion on Patent Owner’s arguments.

1. Patent Owner’s argument that Petitioner has not established that Landes is prior art

Petitioner contends that Landes properly claims, and is entitled to, the priority benefit of the Landes Provisional (Ex. 1006), filed on January 18, 2002. Pet. 16–19. In furtherance of its position, Petitioner provides a chart, breaking down each element of the claims in Landes and providing citations for disclosure in the Landes Provisional that allegedly provides support under 35 U.S.C. § 112, first paragraph, for each of the claims. *Id.* at 17–19. In addition, Petitioner contends that “each of the anticipatory statements in *Landes* relied on in the following sections were carried forward verbatim from the ’877 [Landes] provisional.” *Id.* at 19; *see, e.g., id.* at 22–36 (citing corresponding disclosures in both Ex. 1003 (Landes) and Ex. 1006 (Landes Provisional) for each limitation of the challenged claims).

Patent Owner responds that Petitioner has not shown that Landes is prior art as of its provisional filing date. Prelim. Resp. 22–26. According to Patent Owner, Petitioner’s “conclusory assertions” do not show that the claims of Landes have § 112 support in the Landes Provisional. *Id.* at 22–24, 26 (asserting that Petitioner cites large portions of the disclosure). Patent

Owner notes that, even if the claims of Landes appear verbatim in the Landes Provisional, that does not necessarily mean that the description requirement under § 112 is met. *Id.* at 24–25 (citing *Ariad Pharms., Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1349 (Fed. Cir. 2010)).¹⁷ Patent Owner also contends that *in ipsius verbis* claim language in the Landes Provisional does not necessarily show that Landes’s claims are enabled. *Id.* at 25. In support, Patent Owner points out that claims 1 and 2 of Landes were rejected for lack of enablement during prosecution and that the application was ultimately abandoned. *Id.* (citing Ex. 2078, 6–12).

To determine whether a later published patent application is entitled to the priority date of an earlier filed provisional application from which it claims priority, we ask two questions. First, whether at least one claim of the patent application is supported by the description of the relied-upon provisional application. *Dynamic Drinkware, LLC V. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1382; *Lyft, Inc. v. Ikorongo Tech LLC*, IPR2021-00422, Paper 10 at 10–12 (PTAB Aug. 19, 2021) (hereafter “*Lyft*”) (explaining, with citation to the MPEP and Board decisions, that “the provisional application must provide sufficient [§ 112] support for at least one claim in the reference patent or published application”). Second, whether the

¹⁷ In *Ariad*, appellant argued that the “original claims identify whatever they state” leaving only the question of whether applicant had enabled use of the invention, but the court “disagree[d] that this is always the case.” *Ariad*, 598 F.3d at 1349 (explaining that, “[a]lthough many original claims will satisfy the written description requirement, certain claims may not” and giving, as an example, claims that recite a broad genus of compounds without sufficient disclosure of representative species).

provisional application supports the disclosure relied upon for prior art purposes in the reference patent application. *Lyft* at 11.¹⁸

This second question or requirement is often established if the relied-upon disclosures in the reference patent application appear in substantially the same form in the provisional application. *Lyft* at 13 (“In a case in which a provisional application is shown to have identical or nearly identical disclosure to the portions of an application or patent relied upon, this may be enough.”). Petitioner has met this second requirement because the disclosures of Landes and the Landes Provisional appear to be nearly identical. Petitioner argues that Landes’s disclosures cited as meeting the limitations of the challenged claims appear verbatim in the Landes Provisional (Pet. 19) and Patent Owner provides no argument to the contrary. Patent Owner’s argument is, instead, aimed at the first requirement—whether Landes’s claims have § 112 support in the Landes

¹⁸ In *Lyft*, the Board found that petitioner had not met its burden on the second requirement. Among other things, the reference patent application and the provisional application in that case had materially different disclosures; the relationship between those documents, and satisfaction of the relevant claim limitations by such disclosures was entirely unclear in the petition, such that the Board could not determine the relationship itself from the record. *Lyft* at 13–16. Here, in contrast, the disclosures of Landes and the Landes Provisional are virtually identical, only the first requirement is contested, and, notwithstanding the breadth of Petitioner’s citations, we are able to ascertain the relevance of those cited portions of the specification to the issue of § 112 support without difficulty. It may have been prudent for Petitioner to include a more detailed discussion to accompany its citations but, on this record and without persuasive argument in opposition, we determine Petitioner met its burden to proceed to trial relative to the prior art status of Landes. We discuss further below.

Provisional. Prelim. Resp. 24–26.

Based on the current record, we find that Petitioner has met its institution burden in establishing that Landes is entitled to claim the priority benefit of the Landes Provisional and, thus, is prior art to the '720 patent. On the matter of written description support under § 112, the claims of Landes (claims 1–4) appear unchanged in the Landes Provisional (claims 1–4). *Compare* Ex. 1003, 22–23, *with* Ex. 1006, 21–22. Petitioner also provides citations to the specification of the Landes Provisional that, while broad, correspond to several disclosed alternative embodiments, and the various working examples (Materials and Methods and Experimental Examples 1–5) that describe and explain how to carry out the methods claimed. Pet. 17–19 (citing, e.g., Ex. 1006, 8:7–9:27, and 10:1–20:12). Patent Owner cites precedents for the proposition that, in some circumstances, the presence of the same claim language in an original disclosure may not be enough to satisfy the description requirement. Prelim. Resp. 23–24. But Patent Owner provides neither specific argument nor evidence that this is one of those circumstances. If Patent Owner believes there is some particular deficiency with respect to Landes's claims and the written description requirement, Patent Owner leaves it unsaid.

Patent Owner's position relative to whether the claims of Landes are enabled under § 112 based on the Landes Provisional is a closer call. Here, at least, Patent Owner cited a rejection for lack of enablement of claims 1 and 2 during Landes's prosecution as possibly illustrating some gap in the disclosure of Landes or the Landes Provisional. Prelim. Resp. 26. Petitioner's cited evidence is, however, not limited to claims 1 and 2 of

Landes or the Landes Provisional—independent claims 3 and 4 are also identified, and those claims were *not* rejected for lack of enablement. Ex. 2078, 12–16 (rejecting claims 3 and 4 for anticipation and obviousness, but not under § 112, first paragraph). It is not necessary that all the reference’s claims be supported or enabled by the disclosure of the provisional under § 112 for the reference to receive the priority benefit of the provisional’s filing date. *Lyft* at 10–11; *Ex parte Mann*, 2016 WL 7487271, at *6 (PTAB Dec. 21, 2016); MPEP § 2136(I) (9th ed. rev. 10.2019 (June 2020)). And Petitioner has identified the working examples in the Landes Provisional, which provide further guidance on using the various methods described and claimed in Landes.¹⁹ See Pet. 18–19 (citing, e.g., Ex. 1006, 10:1–20:12). Patent Owner provides no argument on why such disclosures are insufficient in enabling at least claim 3 or 4 of Landes.

For the reasons above, Patent Owner’s argument about the prior art status of Landes is unavailing on this record. Petitioner is reasonably likely to prevail in establishing that Landes is prior art to the ’720 patent.

2. Patent Owner’s argument that Petitioner has not established that Landes discloses an “agent that impedes cell lysis”

Patent Owner argues that Petitioner has failed to show that Lee discloses the use of an “agent that impedes cell lysis,” as recited in each of the challenged claims. Prelim. Resp. 27–33. More specifically, Patent

¹⁹ *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (identifying factors relevant to the enablement inquiry including guidance provided and whether working examples are present in the disclosure).

Owner argues that Petitioner relies on “Landes’s disclosure of ACD in blood collection tubes as allegedly meeting the ‘agent that impedes cell lysis’” and that “Petitioner failed to show that ACD is the claimed agent.” Prelim. Resp. 27–28. We do not find this argument persuasive because it is not clear that it accurately characterizes Petitioner’s contentions.

Although Petitioner does not rely on ACD itself as corresponding to the claimed “agent that impedes cell lysis,” Petitioner does rely on dextrose, a component of ACD. *Id.* at 24–28. For the reasons discussed in Section III.C, we are not persuaded that the claims exclude anticoagulants, like ACD, from being present in the sample.

Patent Owner argues that Petitioner’s proof is lacking because it “focuses solely on dextrose in isolation, but ACD is a compound comprised of multiple components” that “work together in the composition to provide ACD’s anticoagulant properties.” Prelim. Resp. 29. According to Patent Owner, “Petitioner’s focus only on properties that dextrose might have if added independently to a sample does not show what happens when the compound ACD is added to a sample in Landes’s blood collection tubes.” *Id.* at 29–30. Patent Owner contends that other references categorize ACD as an anticoagulant without mentioning that ACD can serve as a membrane stabilizer. *Id.* at 30–31.

Patent Owner’s arguments may have merit, but would be better evaluated on a full record at trial. The current record supports that dextrose is present in solution in ACD. Ex. 1043 ¶ 24 (testimony of Dr. Levy that “ACD tubes contain dextrose”); *see also*, Ex. 2001 ¶ 137 (testimony of Dr. Prestwich describing ACD has having three components, one of which is

dextrose); Ex. 2071 (FDA label for ACD, identifying ACD as a “solution of citric acid, sodium citrate, and dextrose.”). The current record further supports that dextrose is a form of glucose. Ex. 1043 ¶ 24 (testimony of Dr. Levy that “[d]extrose is the naturally-occurring dextrorotatory form of glucose, and is often referred to as glucose”). Finally, the record at present supports that glucose is a membrane stabilizer that impedes cell lysis. *See, e.g.*, Ex. 1001 at 6:49–56 (specification of the ’720 patent, stating: “An agent that stabilizes cell membranes may be added to the maternal blood sample to reduce maternal cell lysis including but not limited to . . . glucose.”); *id.* at 11:57–63 (specification of the ’720 patent, stating: “An agent that stabilizes cell membranes may be added to the sample including but not limited to . . . glucose.”); *see also*, Ex. 2001 ¶ 138 (Dr. Prestwich testimony that “glucose by itself . . . is a membrane stabilizer in the context of the ’720 Patent invention because it functions to stabilize membranes by maintaining the health of cells and strengthening the cell membrane”); Ex. 1011, 15–16 (“[G]lucose . . . had the most marked effect on inhibiting [cell] lysis on storage.”).

Patent Owner faults Petitioner for focusing “only on the hypothetical presence of dextrose alone” (Prelim. Resp. 29), but the current record supports that dextrose is introduced into Landes’s blood samples as one component in a three component solution (*see e.g.*, Ex. 2071, 1). We do not find support in the current record for the proposition that the dextrose component of Landes’s ACD solution will act differently on the cells in Landes’s sample simply because it is introduced to the blood in a solution with two other components. We recognize Dr. Prestwich’s testimony that

“the components of ACD work together to prevent coagulation” with dextrose functioning to “counter-balance the sodium citrate in order to maintain the isotonicity of the sample environment.” Ex. 2001 ¶ 138. But Dr. Prestwich’s testimony does not speak to whether the isotonicity-maintenance function of dextrose in ACD would preclude dextrose from also acting to stabilize membranes, as taught in the ’720 patent. *Id.* Absent evidence to support that dextrose would function differently as a cell membrane stabilizer when it is introduced in solution with other components than when it is introduced alone, for purposes of institution, the presence of dextrose as a component of ACD in Landes’s blood samples is sufficient to support that Landes discloses an “agent that impedes cell lysis.”

Patent Owner also contests Petitioner’s anticipation theory to the extent it is based on inherency. Prelim. Resp. 31–32. At this stage, however, we determine that Petitioner has made a threshold showing that dextrose/glucose in Landes’s tubes would necessarily function as a cell-membrane stabilizer. As discussed above, the evidence in support includes at least the ’720 patent, which lists glucose as providing the claimed functionality.²⁰ Whether Landes intended or recognized ACDA’s function as an anticoagulant and not, explicitly, as a cell-membrane stabilizer is not decisive. First, Landes, like the methods disclosed and claimed in the ’720 patent is directed to the same purpose—non-invasive methods for isolating cell-free fetal DNA from maternal samples and detecting sequences of fetal genetic material (e.g., alleles of interest) in those samples, which may be

²⁰ *Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1369 (Fed. Cir. 2012) (analyzing inherency based on disclosures of the “patent itself”).

used to determine if genetic abnormalities are present. *See, e.g.*, Ex. 1003, Abstr., 3:1–4:6; Ex. 1001, Abstr., 1:30–39, 472:66–473:5. Second, recognition of an inherent functionality (here, inhibition of cell lysis by glucose in ACD) within the prior art itself is not necessary. *See MEHL/Biophile Int’l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999) (“Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art.”) (citations omitted).

3. Patent Owner’s argument that Petitioner has not established that Landes does not disclose “detecting the presence or absence of the free nucleic acid”

Patent Owner argues that Petitioner has not established that Landes discloses “detecting the presence or absence of the free nucleic acid” as required by each of the challenged claims. Prelim. Resp. 33–35. According to Patent Owner, “Landes modifies DNA to distinguish fetal DNA from maternal DNA” and thus the DNA detected in Landes is not “isolated free DNA or sequences therein, but rather the ‘primary sequence differences’ created after free DNA is isolated.” *Id.* at 34. Patent Owner explains that Landes treats isolated fetal DNA with bisulfite, which “reacts differently with methylated and unmethylated loci in DNA such that ‘unmethylated Cs in DNA undergo oxidative deamination, resulting in C to U transitions.’” *Id.* (quoting Ex. 1003, 8:28–9:3). Based on this alteration in DNA sequence, Patent owner argues: “Landes discloses only isolating free DNA and detecting a ***different modified DNA*** product, not ‘isolating free nucleic acid

from a non-cellular fraction of a sample’ and ‘detecting the presence or absence of *the free nucleic acid*’ as claimed.” *Id.* at 35. On the present record, Patent Owner’s argument does not persuade us that Petitioner’s showing is insufficient to support institution.

The preliminary record supports Patent Owner’s assertion that Landes treats isolated free DNA with bisulfite and that this results in C to U transitions in the treated DNA. Ex. 1003, 8:23–9:3. However, treatment with bisulfite is simply the manner in which Landes detects the targeted free DNA. *Id.* at 8:28–29 (“Another means to detect fetal-specific DNA is to identify loci that are methylated in fetal DNA and unmethylated in adult/maternal DNA. Loci of this type are differentially reactive with bisulfite.”). Patent Owner does not presently argue that the challenged claims should be construed as limited to a particular manner of detecting free DNA and, on the present record, we do not discern a basis for so limiting the claims. We recognize that treatment with bisulfite causes C to U transitions in the treated DNA, but the treated DNA still provides information about the presence or absence of, for example, aneuploidies or alleles in the free fetal DNA. *See e.g.*, Ex. 1003, 3:1–3 (“The present invention provides several non-invasive methods for detecting fetal alleles and aneuploidies.”). For purposes of institution, this is sufficient to show that Landes teaches “detecting the presence of absence of the free nucleic acid.”

For the reasons above, Petitioner has established a reasonable likelihood that it will prevail in showing at least one of the challenged claims is unpatentable as anticipated by Landes.

F. Ground 2: Obviousness over the combination of Landes and Marx

Petitioner asserts that claim 22 would have been obvious over the combination of Landes and Marx. Pet. 33–36. Petitioner provides documentary and testimonial evidence to back its assertions. *Id.*; *see also* Ex. 1043 ¶¶ 62–66). Patent Owner does not provide arguments beyond the arguments it presented in connection with Petitioner’s Ground 1. For the reasons discussed above, those arguments do not persuade us that Petitioner’s showing is insufficient to support institution. Also, if trial is instituted it must be instituted on all challenged claims and grounds. *See SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1354 (2018).

G. Ground 3: Anticipation by Yen-Lieberman

Petitioner asserts that claims 1, 3–6, and 24 are anticipated by Yen-Lieberman. Pet. 36–41. Petitioner cites the testimony of Dr. Levy as support for its assertions. Ex. 1043 ¶¶ 79–96. We provided an overview of Yen-Lieberman above. We focus our remaining discussion on this ground on Patent Owner’s arguments.

1. Patent Owner’s argument that Petitioner has not established that Yen-Lieberman is prior art

Patent Owner argues that “the Petition does not establish Yen-Lieberman as prior art for Grounds 3–5.” Prelim. Resp. 43. Patent Owner concedes that “Yen-Lieberman bears a date of July 15, 2000 and a copyright date of 2000,” but argues that “Petitioner has failed to provide any evidence that Yen-Lieberman was publicly accessible as of either of those dates.” *Id.*

We find that, for purposes of institution, Yen-Lieberman bears sufficient indicia of public accessibility.

A petitioner in an *inter partes* review may challenge the claims of a patent “*only* on the basis of prior art consisting of patents or printed publications.” 35 U.S.C. § 311(b) (emphasis added). “[A]t the institution stage, the petition must identify, with particularity, evidence sufficient to establish a reasonable likelihood that [a] reference was publicly accessible before the critical date of the challenged patent and therefore that there is a reasonable likelihood that it qualifies as a printed publication.” *Hulu, LLC v. Sound View Innovations, LLC*, IPR2018-01039, Paper 29 at 13 (PTAB Dec. 20, 2019) (precedential). Although “indicia on the face of a reference, such as printed dates and stamps,” are not “per se . . . sufficient at the institution stage,” they “are considered as part of the totality of the evidence.” *Id.* at 17–18.

The facts of the *Hulu* case are instructive here. In *Hulu*, the reference at issue—Dougherty—included the following indicia on the face of the reference: “a copyright date of 1990, a printing date of November 1992, and an ISBN date of 8/94.” *Id.* at 19. In addition, the reference was “a textbook from an established publisher . . . and a well-known book series.” *Id.* The panel concluded that this was “sufficient evidence to establish a reasonable likelihood that Dougherty is a printed publication that a publisher made available to the pertinent public prior to the October 1995 critical date.” *Id.* at 19–20.

Here, Yen-Lieberman bears the following indicia on the face of the reference: 1) it is dated July 15, 2000, 2) it states that it was copyrighted

in 2000 by Elsevier Science Inc., 3) it states that it is volume 22, number 14 of the Clinical Microbiology Newsletter, and 4) it states that it is “issued twice monthly in one indexed volume per year by Elsevier Science Inc” at a subscription price of \$198. Ex. 1033, 1, 2. The information on the face of the Yen-Lieberman reference is similar to that found sufficient for purposes of institution in *Hulu*. In both cases, the references bear copyright dates, printing dates, and purport to have been issued by an established publisher. We find that, for purposes of institution, this information is sufficient to establish a reasonable likelihood that Yen-Lieberman is prior art to the ’720 patent.

2. Patent Owner’s argument that Petitioner has not established that Yen-Lieberman discloses an “agent that impedes cell lysis”

Like Landes, Yen-Lieberman discloses the collection of blood in a tube containing ACD. Ex. 1033, 107. As with Grounds 1 and 2, which relied on Landes, Petitioner contends that the dextrose component of ACD meets the claim requirement for an “agent that impedes cell lysis.” Pet. 38. As with Grounds 1 and 2, Patent Owner argues that Petitioner has not established that the dextrose component of ACD meets the claim requirement for an “agent that impedes cell lysis.” Prelim. Resp. 36–41. For the same reasons discussed *supra* § III.E.2, on the current record, Patent Owner’s arguments do not persuade us that Petitioner has not sufficiently shown that the dextrose component of ACD meets the claim requirement for an “agent that impedes cell lysis.”

3. Patent Owner’s argument that Petitioner has not established that Landes does not disclose “isolating free nucleic acid from a noncellular fraction of a sample”

Patent Owner argues that Petitioner has not established that Yen-Lieberman discloses “isolating free nucleic acid” as required by each of the challenged claims. Prelim. Resp. 41–42. According to Patent Owner, “Petitioner does not cite to any disclosure in Yen-Lieberman’s brief discussion of the AMPLICOR test that describes how plasma is processed or otherwise handled to allow for detection of the target cell-free DNA, and particularly does not disclose any step of isolating cell-free DNA as part of that processing.” *Id.*

Patent Owner’s argument has some appeal in that Yen-Lieberman does not expressly mention “isolating” free nucleic acid. *See*, Ex. 1033. However, Dr. Levy testifies that Yen-Lieberman’s description of an AMPLICOR CMV test that “uses PCR nucleic acid amplification for qualitative detection of HCMV DNA in plasma separated from anticoagulated whole blood” is an “example” of “isolating cell-free nucleic acid from a noncellular fraction of a sample.” Ex. 1033 ¶ 69. We find that we would benefit from a more fully developed record in resolving the question of whether Yen-Lieberman discloses “isolating free nucleic acid.” In this regard, we note that, for the reasons discussed *supra* § III.E, Petitioner’s Ground 1 meets the reasonable likelihood standard for institution, and if trial is instituted it must be instituted on all challenged claims and grounds. *See SAS*, 138 S. Ct. at 1354 (2018).

H. Ground 4: Obviousness over the combination of Yen Lieberman and Gocke

Petitioner asserts that claims 7–9, 21, and 25–30 would have been obvious over the combination of Yen-Lieberman and Gocke. Pet. 41–51. Petitioner provides documentary and testimonial evidence to back its assertions. *Id.*; *see also* Ex. 1043 ¶¶ 79–96). Patent Owner does not provide arguments beyond the arguments it presented in connection with Petitioner’s Ground 3. Prelim. Resp. 36–43. For the reasons discussed above, those arguments do not persuade us that Petitioner’s showing is insufficient to support institution. Also, if trial is instituted it must be instituted on all challenged claims and grounds. *See SAS*, 138 S. Ct. at 1354 (2018).

I. Ground 5: Obviousness over the combination of Yen Lieberman and Gocke and Marx

Petitioner asserts that claim 22 would have been obvious over the combination of Yen-Lieberman, Gocke, and Marx. Pet. 51–53. Petitioner provides documentary and testimonial evidence to back its assertions. *Id.*; *see also* Ex. 1002 ¶¶ 98–101). Patent Owner does not provide arguments beyond the arguments it presented in connection with Petitioner’s Ground 3. Prelim. Resp. 36–43. For the reasons discussed above, those arguments do not persuade us that Petitioner’s showing is insufficient to support institution. Also, if trial is instituted it must be instituted on all challenged claims and grounds. *See SAS*, 138 S. Ct. at 1354 (2018).

IV. CONCLUSION

On this preliminary record, Petitioner has established a reasonable likelihood of prevailing in showing that at least one of the challenged claims

is unpatentable based on the grounds advanced in the Petition.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that the Petition is *granted*, and we institute *inter partes* review of claims 1, 3–9, 21, 22, and 24–30 based on the grounds asserted in this Petition;

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is given of the institution of trial, which will commence on the entry date of this Decision.

IPR2021-01271
Patent 7,727,720 B2

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