Trials@uspto.gov
571-272-7822

Paper 9
Entered: July 26, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GENEOSCOPY, INC.,
Petitioner,

v.

EXACT SCIENCES CORPORATION,
Patent Owner.

IPR2024-00459
Patent 11,634,781 B2

Before TINA E. HULSE, DAVID COTTA, and JAMIE T. WISZ, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

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

I. INTRODUCTION

Geneoscopy, Inc. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–20 of U.S. Patent No. 11,634,781 B2 (Ex. 1001, "the '781 Patent"). Paper 1 ("Pet."). Exact Sciences Corporation ("Patent Owner") filed a Preliminary Response to the Petition. Paper 6 ("Prelim. Resp."). We authorized additional briefing for the parties to address (1) discretionary denial under 35 U.S.C. § 325(d); and (2) discretionary denial under *General Plastic Industrial Co. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19 (PTAB Sept. 6, 2017) (precedential as to § II.B.4.i) ("*General Plastic*"). Ex. 3001. Petitioner filed a Reply to Patent Owner's Preliminary Response (Paper 7, "Pet. Reply") and Patent Owner filed a Sur-reply (Paper 8, "PO Sur-reply").

We have authority under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon considering the arguments and evidence presented in the papers, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of at least one claim challenged in the Petition and we decline to exercise our discretion to deny institution under 35 U.S.C. §§ 314(a) and 325(d). Accordingly, we institute an *inter partes* review of the challenged claims of the '781 Patent.

A. Real Parties-in-Interest

Petitioner identifies itself as the real party-in-interest. Pet. 2.

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

B. Related Matters

The parties identify *Exact Sciences Corporation v. Geneoscopy, Inc.*, No. 23-cv-1319-MN (D. Del.) as involving the '781 Patent. Pet. 2–3; Paper 4, 2.

C. The '781 Patent

The '781 Patent, entitled "Fecal Sample Processing and Analysis Comprising Detection of Blood," was filed as U.S. Application No. 17/936,335 on September 28, 2022, and claims priority to a series of continuation applications, including U.S. Application No. 16/634,607 ("the '607 Application"), and U.S. Provisional Application No. 61/149,581 ("the '581 Provisional"), which was filed on February 3, 2009. Ex. 1001, codes (54), (21), (22), (60), (63), 1:8–19. Thus, the earliest possible effective filing date of the '781 Patent is February 3, 2009, which we apply to our analysis in this Decision.

The '781 Patent relates to methods and kits for analysis of fecal samples. *Id.* at 1:30–31. According to the Specification, colorectal cancer ("CRC") is a leading cause of cancer-related deaths worldwide. *Id.* at 1:41–42. Most colon cancers arise from adenomatous polyps, which are usually asymptomatic. *Id.* at 1:46–52. Because of this, mass screening of asymptomatic patients is the cornerstone for detecting and eliminating these precursor lesions to reduce the risk of CRC. *Id.* at 1:52–55.

Colonoscopy is the primary screening test for CRC because of its high sensitivity and specificity and the ability to remove polyps if found. *Id.* at 1:65–2:1. The procedure, however, is invasive, costly, and has certain risks, such as infection and perforation of the bowel. *Id.* at 2:1–3. Fecal occult blood testing ("FOBT"), which tests for blood in the stool, is commonly used and less invasive and less expensive than colonoscopy. *Id.* at 2:4–12.

But because occult blood in stool can be indicative of different gastrointestinal disorders, further testing is necessary to detect CRC. *Id.* at 2:9–12. There are two types of FOBT: guaiac FOBT ("gFOBT"), which detects peroxidase activity of hemoglobin in fecal blood, and immunochemical FOBT ("iFOBT" or "FIT"), which uses anti-human hemoglobin antibodies to detect fecal blood. *Id.* at 2:13–34. Although the immunochemical procedure is more complicated and more expensive, iFOBT is more sensitive than gFOBT. *Id.* at 2:25–40.

The Specification also explains that recent developments in testing look specifically for mutations in DNA characteristic of colorectal neoplasia that are detectable in exfoliated epithelial cells in the stool. *Id.* at 2:44–47. The Specification explains that increased DNA methylation is an epigenetic alteration that is common in human cancers. *Id.* at 3:5–7. Aberrantly methylated DNA has also been proposed as a potential tumor marker for CRC detection. *Id.* at 3:7–9.

The '781 Patent further explains that, although combined assays for detecting CRC have been described, their approach targets either multiple protein markers or multiple DNA alterations. *Id.* at 3:41–43. According to the Specification, "[t]o date, immunochemical tests and DNA tests for CRC detection have been evaluated and compared on a separate basis only." *Id.* at 3:43–45.

The '781 Patent states that the invention "aims to improve the positive and negative predictive value and also the sensitivity and specificity of detection of colorectal cancer through non-invasive means." *Id.* at 6:42–45. Accordingly, the invention is based upon a combination of tests for detecting proteins and epigenetic modification markers in the same fecal sample. *Id.* at 6:49–53.

D. Illustrative Claim

Petitioner challenges claims 1–20 of the '781 Patent, of which claim 1 is the only independent claim. Claim 1 is illustrative and reproduced below:

> 1. A method of processing a freshly-collected fecal sample without freezing, the method comprising:
>
> a) collecting a fecal sample from a human subject, wherein the fecal sample is collected at home by the human subject by defecation directly into a sealable collection vessel;
>
> b) removing a portion of the fecal sample to a separate sealable container to produce a removed portion and a remaining portion of the fecal sample;
>
> c) combining the removed portion of the fecal sample in the separate sealable container with a buffer that prevents denaturation or degradation of blood proteins found in a fecal sample, and sealing the sealable container; and
>
> d) combining the remaining portion of the fecal sample in the sealable collection vessel with a stabilizing buffer, and sealing the sealable collection vessel.

Ex. 1001, 45:21–38.

E. The Asserted Grounds of Unpatentability

Petitioner asserts that claims 1–20 would have been unpatentable on the following grounds:

Claim(s) Challenged	35 U.S.C. §[1]	Reference(s)/Basis
1–9, 11, 14–20	103	Lenhard,[2] Vilkin,[3] Itzkowitz[4]
12, 13	103	Lenhard, Vilkin, Itzkowitz, Kanaoka[5]
10	103	Lenhard, Vilkin, Itzkowitz, Derks[6]
1–9, 11, 14–20	103	Shuber,[7] Vilkin
12, 13	103	Shuber, Vilkin, Kanaoka
10	103	Shuber, Vilkin, Derks

Petitioner also relies on the Declaration of Duncan Whitney, Ph.D. Ex. 1002. Patent Owner relies on the Declaration of Vadim Backman, Ph.D. Ex. 2001.

[1] The Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011), amended 35 U.S.C. § 103, effective March 16, 2013. Because the '781 Patent has an effective filing date before March 16, 2013, the pre-AIA version of § 103 applies. Our decision, however, would be the same under either version.

[2] Lenhard et al., *Analysis of Promoter Methylation in Stool: A Novel Method for the Detection of Colorectal Cancer*, 3 CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 142–49 (2005) (Ex. 1004, "Lenhard").

[3] Vilkin et al., *Performance Characteristics and Evaluation of an Automated-Developed and Quantitative, Immunochemical, Fecal Occult Blood Screening Test*, 100 AM. J. GASTROENTEROL. 2519–25 (2005) (Ex. 1005, "Vilkin").

[4] Itzkowitz et al., *Improved Fecal DNA Test for Colorectal Cancer Screening*, 5 CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 111–17 (2007) (Ex. 1006, "Itzkowitz").

[5] S. Kanaoka, US2006/0216714 A1, published Sept. 28, 2006 (Ex. 1007, "Kanaoka").

[6] Derks et al., *Promoter methylation precedes chromosomal alterations in colorectal cancer development*, 28 CELLULAR ONCOLOGY 247–57 (2006) (Ex. 1008, "Derks").

[7] Shuber et al., WO2005/113769 A1, published Dec. 1, 2005 (Ex. 1009, "Shuber").

II. ANALYSIS

A. Person of Ordinary Skill in the Art

Petitioner contends that a person of ordinary skill in the art at the time of the invention ("POSA") would have had "a Ph.D. in chemistry, biochemistry, biology, or a related field and at least five years of experience designing and performing diagnostic assays on fecal samples." Pet. 12 (citing Ex. 1002 ¶¶ 9–12).

Patent Owner disagrees. Prelim. Resp. 46–48. According to Patent Owner, a POSA would have had "a doctoral degree in medicine, chemistry, biochemistry, biology, or a related field and 1–2 years of experience in the processing and analysis of biological samples, including fecal samples." *Id.* at 47 (citing Ex. 2001 ¶ 43). Patent Owner also indicates that such a person could have been an individual or a member of a team of scientists addressing fecal sample processing and analysis. *Id.* Patent Owner notes that Petitioner's proposal in the Petition is significantly different from the proposal in its *ex parte* reexamination request, which merely required a bachelor's degree and several years of experience processing biological samples. *Id.* at 46; Ex. 1021, 7.[8] Patent Owner also contends that the level of skill set forth in the Petition requires an extraordinary level of skill within an overly narrow focus. Prelim. Resp. 47. Regardless, Patent Owner states that its expert, Dr. Backman, is a person of at least ordinary skill and the claims of the '781 Patent would not have been obvious under any of the parties' proposed definitions of the level of ordinary skill in the art.

[8] We cite to the page numbers of the exhibit for prosecution histories such as Exhibit 1021 and Exhibit 2003. Unless stated otherwise, we cite to the page numbers of the reference for all other exhibits.

We do not discern much of a substantive difference between the parties' respective definitions in this proceeding beyond the number of years of experience after obtaining a doctoral degree. *Compare* Pet. 12, *with* Prelim. Resp. 47. For purposes of this Decision, we adopt Patent Owner's definition as it appears to be reasonable and falls between Petitioner's definitions asserted in the reexamination request and in the Petition. Ex. 2001 ¶ 43. Moreover, Patent Owner's definition appears consistent with the prior art's demonstration of the level of ordinary skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985))). To the extent the parties continue to disagree on the level of ordinary skill in the art, they should brief the issue further during trial.

B. Claim Construction

In an *inter partes* review, the Board applies the same claim construction standard that would be used to construe claims in a civil action under 35 U.S.C. § 282(b). *See* 37 C.F.R. § 100(b). Under that standard, claim terms "are generally given their ordinary and customary meaning" as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–13 (Fed. Cir. 2005) (en banc).

Petitioner does not explicitly address claim construction in the Petition. *See generally* Pet.

Patent Owner states that it "does not believe that the Board must construe any claim terms in order to deny institution" and "reserves the right

to assert claim construction positions should the Board institute IPR." Prelim. Resp. 46.

At this stage of the proceeding, we agree with the parties that no construction of any claim term is necessary for purposes of our Decision. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

C. Asserted Obviousness Grounds over Lenhard, Itzkowitz, and Vilkin

Petitioner contends that claims 1–9, 11, and 14–20 would have been unpatentable as obvious over Lenhard, Itzkowitz, and Vilkin (Ground I). Pet. 20–43. Petitioner also argues that dependent claims 12 and 13 would have been unpatentable over Lenhard, Itzkowitz, Vilkin, and Kanaoka (Ground II) (Pet. 43– 46) and that dependent claim 10 would have been unpatentable over Lenhard, Itzkowitz, Vilkin, and Derks (Ground III) (Pet. 46–47). Patent Owner opposes. Prelim. Resp. 48–54.

Having considered the arguments and evidence presented by the parties, we determine that Petitioner has shown a reasonable likelihood of prevailing on its assertion that the challenged claims would have been unpatentable as obvious over the cited references.

1. Lenhard (Ex. 1004)

Lenhard is a journal article entitled "Analysis of Promoter Methylation in Stool: A Novel Method for the Detection of Colorectal Cancer" that appears to have been published in the journal *Clinical Gastroenterology and Hepatology* in 2005 and is therefore prior art under 35 U.S.C. § 102(b). Ex. 1004, 142. Patent Owner does not challenge the

prior art status of Lenhard at this stage of the proceeding. *See generally* Prelim. Resp.

According to Lenhard, the detection of tumor-derived genetic changes in stool is a promising new approach for CRC screening. *Id.* Lenhard describes a study involving the potential use of hypermethylated in cancer 1 ("HIC1") promoter methylation as a stool-based DNA marker. *Id.* at 143. According to Lenhard, the promoter of HIC1 frequently is methylated in CRC, but not in normal or aging colonic tissue. *Id.* Lenhard states that it has shown that "HIC1 promoter methylation can be detected frequently and with high specificity in stool samples from patients with CRCs." *Id.* Moreover, Lenhard states "[t]he combination of HIC1 methylation analysis with FOBT allowed for detection of two thirds of CRCs." *Id.* at 147. According to Lenhard, "[t]he combination of both assays resulted in increased detection rates for CRCs." *Id.*; *see also id.* at 146 (Table 4) (providing data for positivity rates of HIC1 assay, FOBT assay, and combination of the tests). Lenhard further states that "[a]lthough the combined test detected all localized cancers, no increase in sensitivity for adenoma was seen." *Id.*

Lenhard states that stool samples were collected preoperatively from patients with verified CRCs and before colonoscopy for patients with adenomas larger than one centimeter. *Id.* Samples were received within ten hours after defecation at the laboratory, subjected to gFOBT immediately on receipt, and then stored at -80°C until analyzed for methylated DNA. *Id.* at 143, 145.

2. Itzkowitz (Ex. 1006)

Itzkowitz is a journal article entitled "Improved Fecal DNA Test for Colorectal Cancer Screening" that appears to have been published in the

journal *Clinical Gastroenterology and Hepatology* in 2007 and is therefore prior art under 35 U.S.C. § 102(b). Ex. 1006. Patent Owner does not challenge the prior art status of Itzkowitz at this stage of the proceeding. *See generally* Prelim. Resp.

Itzkowitz explains that several studies have shown the feasibility of detecting colon tumor-specific products in stool. *Id.* at 111. The markers in these studies represent alterations of various genes. *Id.* Itzkowitz teaches that pilot studies have shown that several technical and conceptual advances could improve fecal DNA testing. *Id.* For example, adding a DNA-stabilizing buffer to the stool immediately on defecation was shown to prevent DNA degradation for several days and enhance the performance of a DNA integrity assay ("DIA"). *Id.* Also, promoter methylation has become recognized as a key pathway by which colon cancers develop. *Id.*

Itzkowitz describes a two-phase study. *Id.* at 112. Phase 1 involved analyzing stool samples from approximately 50 patients with CRC and 200 patients with normal colonoscopy to define suitable DIA cut-off values and to determine optimal markers for the new assay. *Id.* Phase 2, which is ongoing, was designed as a validation set in which an additional 125 patients with CRC and 200 patients with normal colonoscopy will be analyzed using the optimal marker panel from phase 1. *Id.*

Itzkowitz explains that subjects were given a special stool collection kit that is mounted on the toilet bowl. *Id.* Immediately after defecation, the subject added 250 ml of a DNA-stabilizing buffer to the stool specimen and then shipped the specimen at room temperature overnight to a laboratory for processing and analyzing. *Id.*

3. Vilkin (Ex. 1005)

Vilkin is a journal article entitled "Performance Characteristics and Evaluation of an Automated-Developed and Quantitative, Immunochemical, Fecal Occult Blood Screening Test" that appears to have been published in the *American Journal of Gastroenterology* in 2005 and is therefore prior art under 35 U.S.C. § 102(b). Ex. 1005. Patent Owner does not challenge the prior art status of Vilkin at this stage of the proceeding. *See generally* Prelim. Resp.

Vilkin explains that the standard guaiac fecal occult blood test ("gFOBT") is faulted for its low sensitivity for significant colorectal neoplasia (i.e., CRC and advanced adenomatous polyps ("AAP")), and low specificity due to nonspecificity for human hemoglobin ("Hb"). *Id.* at 2519. Vilkin explains that the introduction of central laboratory and office-developed, immunochemical fecal occult blood tests ("iFOBT") specific for human Hb improved specificity. *Id.* Vilkin describes a colonoscopy-controlled study that allowed for a detailed evaluation of an automated desktop instrument for quantitative, immunochemical determination of fecal occult blood. *Id.* at 2523.

Vilkin describes a fecal test sampling device shaped like a small test tube with a fecal probe that is inserted into the stool and then pushed back into the tube, through a membrane into a sample cup that includes a Hb stabilizing buffer. *Id.* at 2520. Vilkin explains that the samples are double-closed in ziplock bags and kept in the refrigerator until returned to the laboratory where they are kept at 4°C until development. *Id.*

4. Analysis of Claim 1

Petitioner asserts that the combination of Lenhard, Itzkowitz, and Vilkin teaches each limitation of claim 1 and a POSA would have had a

reason to combine the references with a reasonable expectation of success. On this record, we agree.

a) A method of processing a freshly-collected fecal sample without freezing, the method comprising

Petitioner asserts that to the extent the preamble is limiting, both Vilkin and Itzkowitz teach processing fecal samples without freezing. Pet. 26–27. Vilkin teaches refrigerating the sample and Itzkowitz teaches shipping the sample at room temperature. *Id.* (citing Ex. 1005, 2520; Ex. 1006, 112; Ex. 1002 ¶¶ 164–167). Thus, Petitioner asserts that both references teach processing freshly collected fecal samples without freezing.

b) collecting a fecal sample from a human subject, wherein the fecal sample is collected at home by the human subject by defecation directly into a sealable collection vessel

Petitioner asserts that Itzkowitz describes this limitation, as subjects were provided with a "special stool collection kit that is mounted on the toilet bowl." Pet. 27 (citing Ex. 1006, 112). Moreover, because the sample was "shipped at room temperature" to the laboratory, Petitioner asserts that a POSA would understand that the sample was collected at home in a container that must have been sealable. *Id.* (citing Ex. 1006, 112; Ex. 1002 ¶ 169). Moreover, Petitioner argues that direct defecation into a sealable container was a standard method for collecting stool samples before the priority date. *Id.* at 27–28 (citing Ex. 1002 ¶¶ 170–171).

c) removing a portion of the fecal sample to a separate sealable container to produce a removed portion and a remaining portion of the fecal sample

d) combining the removed portion of the fecal sample in the separate sealable container with a buffer that prevents

denaturation or degradation of blood proteins found in a fecal sample, and sealing the sealable container

Petitioner asserts that the combination of Lenhard and Vilkin teaches these limitations. Petitioner asserts that Lenhard describes removing a portion of a patient's stool sample to test for blood proteins using gFOBT and then testing the remaining portion for tumor-derived DNA. Pet. 28 (citing Ex. 1004, 143–45). Petitioner further asserts that it would have been obvious to replace the gFOBT of Lenhard with the iFOBT of Vilkin given the numerous advantages of iFOBT over gFOBT described by Vilkin. *Id.* at 29. Moreover, Petitioner asserts that in Vilkin, the patient removes a portion of the fecal sample using a fecal test device that seals the sample in the sealable container along with an amount of hemoglobin stabilizing buffer. *Id.* at 29–31 (citing Ex. 1005, 2520; Ex. 1002 ¶¶ 173–178).

e) combining the remaining portion of the fecal sample in the sealable collection vessel with a stabilizing buffer, and sealing the sealable collection vessel

Petitioner asserts that the combination of Lenhard and Itzkowitz teaches this limitation, because a POSA would have been motivated to combine the DNA stabilizing buffer of Itzkowitz with the remaining portion of the fecal sample of Lenhard to "preserve the integrity of the DNA in that portion of the sample when it was shipped to a diagnostic laboratory for analysis." Pet. 31 (citing Ex. 1006, 112). Moreover, according to Petitioner, a POSA would have understood that the collection vessel containing the remaining portion and buffer would be sealed before shipping. *Id.* at 31–32 (citing Ex. 1002 ¶ 181).

On this record, we find Petitioner has shown sufficiently that the combination of Lenhard, Itzkowitz, and Vilkin teaches each limitation of the claims for the reasons stated by Petitioner. At this stage of the proceeding,

we are not persuaded by Patent Owner's arguments to the contrary. In its Preliminary Response, Patent Owner attacks the references individually rather than considers them in combination, as is required in an obviousness analysis. *Bradium Techs. LLC v. Iancu*, 923 F.3d 1032, 1050 (Fed. Cir. 2019) ("A finding of obviousness . . . cannot be overcome by 'attacking references individually where the rejection is based upon the teachings of a combination of references.'") (quoting *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986)). For example, Patent Owner asserts that Lenhard does not describe "at-home collection, or separation into separate sealed containers, or the addition of stabilizing buffers, or processing of the samples without freezing." Prelim. Resp. 48 (citing Ex. 1004; Ex. 2001 ¶¶ 47–52). Patent Owner also argues that Vilkin does not suggest "home separation of the sample and addition of buffer to each of the removed and remaining portions in separate sealable containers." *Id.* at 49. And Patent Owner argues that Itzkowitz "does not suggest the home collection processes of the claims, let alone testing a single sample using both FOBT and DNA tests." *Id.* at 50. We are not persuaded by Patent Owner's attacks on each reference individually, as Petitioner relies on the combination of cited references for those limitations of the claim, as explained above.

f) Reason to combine Lenhard, Itzkowitz, and Vilkin with a reasonable likelihood of success

Petitioner asserts that it would have been obvious for a POSA to use the iFOBT of Vilkin and the fecal collection and DNA stabilization process of Itzkowitz in the screening method of Lenhard to arrive at the claimed method. Pet. 20–21. Specifically, Petitioner argues that Lenhard provides the reason to combine the references, because it teaches that "[t]he combination of HIC1 methylation analysis with FOBT allowed for the

detection of two thirds of CRCs" and that combining the tests "increased detection rates for CRCs" and "detected all localized cancers." *Id.* at 21 (citing Ex. 1004, 143, 147).

Although Lenhard does not expressly disclose the use of the claimed buffers, Petitioner asserts it would have been obvious to replace the gFOBT in Lenhard with the iFOBT of Vilkin, which stabilized the stool sample in a buffer to prevent blood protein degradation. Pet. 21–22 (citing Ex. 1005, 2519–20). According to Petitioner, a POSA would have had a reason to modify Lenhard's assay to use Vilkin's iFOBT, because Vilkin teaches numerous advantages of iFOBT over gFOBT, which were known in the art, including iFOBT's higher sensitivity and its ability to quantify the blood proteins so a physician could choose the Hb threshold level for a patient. *Id.* at 22–23 (citing Ex. 1002 ¶¶ 143–147).

As for combining Itzkowitz, Petitioner asserts that a POSA would have had a reason to improve Lenhard's assay by directly defecating into a sealable container, as was done in Itzkowitz and generally well known in the art, and by adding a stabilization buffer to the sample so it could be shipped to a laboratory without freezing. Pet. 24 (citing Ex. 1002 ¶¶ 148–158).

Petitioner asserts that a POSA would have had a reasonable expectation of successfully combining the references to reach the claimed invention because "it amounts to the routine performance, in combination, of two well-established prior art tests that already had been shown to work on fecal samples." *Id.* at 26 (citing Ex. 1002 ¶ 161).

Patent Owner disagrees, arguing that a POSA would have been discouraged from combining iFOBT with nucleic acid-based testing because the increased sensitivity came with a reduction in specificity. Prelim. Resp. 50–51 (citing Ex. 2001 ¶¶ 50, 73). Patent Owner further notes that Lenhard

concludes that combining HIC1 with a few additional methylation markers is preferred as it may be highly sensitive and specific for detection of CRCs and adenomas. *Id.* at 51 (citing Ex. 1004, 7). In other words, Patent Owner argues that Lenhard does not suggest combining HIC1 testing with FOBT. *Id.* Moreover, Patent Owner argues that a POSA would have known that the combination of gFOBT and nucleic acid-based testing in Lenhard was not as sensitive or specific as either iFOBT alone or other fecal nucleic acid-based tests and would therefore have had no reason to add to the cost and complexity of combining the two different types of tests. *Id.* at 53 (citing Ex. 2001 ¶ 83). Finally, Patent Owner argues that a POSA would have had no way to predict without testing whether a combination of different tests would result in improved performance. *Id.* at 54 (citing Ex. 2001 ¶ 84).

At this stage of the proceeding, we are persuaded that Petitioner has shown sufficiently that a POSA would have had a reason to modify the assay of Lenhard to combine Vilkin's iFOBT and Itzkowitz's collection process and DNA stabilization buffer with a reasonable expectation of success. Lenhard expressly states that "[t]he combination of [HIC1 methylation analysis with gFOBT] resulted in increased detection rates for CRCs" and includes data that supports this statement. *See* Ex. 1004, 147, 146 (Table 4); *see also id.* at 143 ("The combination of HIC1 methylation analysis with FOBT allowed for the detection of two thirds of CRCs."). We find these positive statements and supporting data in Lenhard are sufficient to provide a "rational underpinning" to combine the gFOBT and DNA test at this stage of the proceeding. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). Moreover, we are persuaded on this record that Vilkin's explanation of the benefits of iFOBT over gFOBT provide a reason to replace Lenhard's gFOBT with Vilkin's iFOBT assay. *See* Ex. 1005, 2519. And we agree at

this stage of the proceeding that a POSA would have had a reason to improve Lenhard's assay by requiring a patient to directly defecate into a sealable container and add a stabilization buffer to the sample so it could be shipped to a laboratory without freezing, as described in Itzkowitz. *See* Ex. 1002 ¶¶ 148–158.

On this record, we are not persuaded by Patent Owner's arguments to the contrary. Although Lenhard concluded that combining different nucleic acid tests may allow for more sensitive and specific detection of CRCs and adenomas, that does not teach away from combining FOBT and DNA tests. The Federal Circuit instructs that the reason to combine need not coincide with the preferred or most desirable combination described in the prior art to provide motivation for the invention. *See Gen. Elec. Co. v. Raytheon Techs. Corp.*, 983 F.3d 1334, 1351 (Fed. Cir. 2020) (holding the Board erred in finding no motivation to combine where the art merely suggested a preference for a different engine and did not teach away from the claimed invention) (citing *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004) ("[O]ur case law does not require that a particular combination must be the preferred, or the most desirable, combination described in the prior art in order to provide motivation for the current invention.")).

Moreover, even if the combined tests in Lenhard were not as sensitive or specific as either Vilkin's iFOBT alone or other fecal nucleic acid tests, Patent Owner misses the point. First, the claims do not require a particular level of sensitivity or specificity. *See* Ex. 1001, 45:20–47:4. Second, we are persuaded on this record that a POSA would have sought to improve the combined assay of Lenhard by using Vilkin's iFOBT given the advantages of iFOBT over gFOBT taught by Vilkin, including increased specificity, lack of diet restrictions, and Hb quantification. *See* Ex. 1005, 2519; *see also*

Ex. 1002 ¶¶ 143–147. Regardless, conclusive proof of efficacy is not required to show obviousness. *See Hoffmann-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1331 (Fed. Cir. 2014) ("Conclusive proof of efficacy is not necessary to show obviousness. All that is required is a reasonable expectation of success.").

Accordingly, having considered the parties' respective evidence and arguments, we find on this record that Petitioner has shown a reasonable likelihood of prevailing on its assertion that claim 1 would have been unpatentable as obvious over the combination of Lenhard, Itzkowitz, and Vilkin.[9]

5. Analysis of Remaining Claims 2–20

Petitioner asserts that the combination of Lenhard, Itzkowitz, and Vilkin teaches each limitation of claims 2–9, 11, and 14–20, that the combination of Lenhard, Itzkowitz, Vilkin, and Kanaoka teaches each limitation of claims 12 and 13, and that the combination of Lenhard, Itzkowitz, Vilkin, and Derks teaches each limitation of claim 10. Pet. 32–47. At this stage of the proceeding, Patent Owner does not separately argue those challenges beyond that addressed above. *See generally* Prelim. Resp.

Accordingly, we have considered the arguments and evidence presented by the parties, and find Petitioner has shown sufficiently that the combination of the cited references teaches each limitation of the claims and that a POSA would have had a reason to combine the references according

[9] We note that Patent Owner has not presented any evidence of secondary considerations of nonobviousness at this stage of the proceeding. We will consider that evidence, if presented, in our Final Written Decision when determining the obviousness of the claims.

to the claimed invention with a reasonable expectation of success for the reasons stated by Petitioner. *See* Pet. 32–47; Ex. 1002 ¶¶ 184–234.

D. Asserted Obviousness Grounds over Shuber and Vilkin

Petitioner contends that claims 1–9, 11, and 14–20 would have been obvious over Shuber and Vilkin (Ground IV). Pet. 47–62. Petitioner also asserts that claims 12 and 13 would have been obvious over Shuber, Vilkin, and Kanaoka (Ground V) (Pet. 62–64) and that claim 10 would have been obvious over Shuber, Vilkin, and Derks (Ground VI) (Pet. 65). Patent Owner opposes. Prelim. Resp. 55–60.

Having considered the arguments and evidence presented by the parties, we determine that Petitioner has shown a reasonable likelihood of prevailing on its assertion that the challenged claims would have been unpatentable as obvious over the cited references.

We incorporate our analysis and findings of Vilkin here.

1. Shuber (Ex. 1009)

Shuber is a PCT application entitled "Method for Stabilizing Biological Samples for Nucleic Acid Analysis," which was published on December 1, 2005, and is therefore prior art under 35 U.S.C. § 102(b). Ex. 1009, codes (43), (54). Patent Owner does not challenge the prior art status of Shuber at this stage of the proceeding. *See generally* Prelim. Resp.

Shuber relates to methods for preparing nucleic acid-containing biological samples for an assay to detect nucleic acid markers indicative of cancer. *Id.* at 1:11–13. According to Shuber, contacting a patient sample with a stabilization solution stabilizes the DNA so that intact nucleic acids indicative of diseased cells are more effectively detected in a nucleic acid integrity assay. *Id.* at 2:7–9. Shuber explains that a stabilization solution "may be particularly useful when samples are not refrigerated or frozen" and

if a sample "is obtained at a remote location and mailed or delivered to a testing center." *Id.* at 10:10–14. In one aspect of the invention, a stool sample may be directly deposited into a sealable container and a stabilization solution may be added to the container, after which the container may be sealed for storage/shipping. *Id.* at 29:8–19.

2. Analysis

For this set of Grounds, Petitioner relies on Shuber instead of Lenhard and Itzkowitz. That is, Petitioner asserts that the combination of Shuber and Vilkin teaches each limitation of claim 1 and that it would have been obvious for a POSA to combine the fecal DNA assay of Shuber with the iFOBT assay of Vilkin to arrive at the claimed methods with a reasonable expectation of success. Pet. 47–55. Unlike Lenhard, however, Shuber does not expressly combine FOBT and nucleic acid tests or suggest that combining the tests may result in increased sensitivity of detecting CRC. Petitioner does, however, rely on the statements discussed above in Lenhard—along with other prior art—to argue that the benefits of combining stool DNA and blood protein assays was well understood in the art. Pet. 48–50 (citing, e.g., Ex. 1004, 143, 147, Table 4; Ex. 1011,[10] 112; Ex. 1012,[11] 40; Ex. 1002 ¶¶ 240–245). Petitioner also asserts that successfully combining the assays of Shuber and Vilkin "requires no more tha[n] the use of routine methods to perform [] a pair of well-established

[10] Nishikawa et al., *A simple method of detecting K-ras point mutations in stool samples for colorectal cancer screening using one-step polymerase chain reaction/restriction fragment length polymorphism analysis*, 318 CLINICA CHIMICA ACTA 107–12 (2002) (Ex. 1011, "Nishikawa").
[11] Kutzner et al., *Non-invasive detection of colorectal tumours by the combined application of molecular diagnosis and the faecal occult blood test*, 229 CANCER LETTERS 33–41 (2005) (Ex. 1012, "Kutzner").

assays on separate portions of a fecal sample." *Id.* at 50–51 (citing Ex. 1002 ¶ 246).

Patent Owner disagrees, arguing that the art did not provide a reason to combine DNA and iFOBT tests with a reasonable expectation of success. Prelim. Resp. 55–60. Patent Owner asserts that Petitioner takes the statements in the prior art out of context and that nothing in the art suggests combining DNA and iFOBT tests to improve the sensitivity of CRC diagnosis. *Id.* at 59 (citing Ex. 2001 ¶¶ 76–83). Patent Owner also asserts that Petitioner's arguments that piece together the limitations as arranged in the claims suffer from impermissible hindsight. *Id.* at 60.

For the same reasons explained above with respect to the reason to combine Lenhard, Itzkowitz, and Vilkin, we find on this record that Petitioner has shown sufficiently that a POSA would have had a reason to combine the DNA assay of Shuber with the iFOBT of Vilkin in view of Lenhard's finding that combining the DNA and FOBT tests increased detection rates for CRCs and the various suggestions in the art to combine fecal DNA assays with FOBT assays. *See* Ex. 1004, 147 (stating that "[t]he combination of [HIC1 methylation analysis with gFOBT] resulted in increased detection rates for CRCs."); Ex. 1011, 112 (stating its fecal DNA assay "should provide a more sensitive and specific tool for mass screening of colorectal cancer than is currently available, especially if used in combination with fecal occult blood testing and other methods for detecting genetic abnormalities"); Ex. 1012, 40 ("The combined applications of [the fecal DNA test and FOBT] together led to a significantly higher sensitivity than the application of any of the methods alone."). On this record, we are not persuaded by Patent Owner's argument that the statements from Nishikawa (Ex. 1011) and Kutzner (Ex. 1012) are taken out of context and

insufficient to provide a reason to combine fecal DNA tests with FOBT tests. Both references suggest a benefit in combining the two types of tests, which is sufficient at this stage of the proceeding. *See Outdry Techs. Corp. v. Geox S.p.A.*, 859 F.3d 1364, 1370–71 (Fed. Cir. 2017) ("Any motivation to combine references, whether articulated in the references themselves or supported by evidence of the knowledge of a skilled artisan, is sufficient to combine those references to arrive at the claimed process."). As for the reasonable expectation of success, on this record, we agree with Petitioner that combining the two tests according to the claimed methods amounts to no "more than the predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417.

Thus, having considered the parties' respective arguments and evidence, we are persuaded that Petitioner has shown a reasonable likelihood of prevailing on its assertion that the challenged claims would have been unpatentable over the asserted combinations of Shuber, Vilkin, Kanaoka, and Derks.

Having found Petitioner has met its burden to institute trial on at least one claim, we now address Patent Owner's request that we exercise our discretion under 35 U.S.C. §§ 325(d) and 314(a) to deny institution.

III. DISCRETIONARY DENIAL UNDER 35 U.S.C. § 325(d)

Patent Owner urges us to exercise our discretion to deny institution under 35 U.S.C. § 325(d). Prelim. Resp. 18–38. Petitioner opposes. Pet. Reply 1–6. For the reasons discussed below, we decline to exercise our discretion under § 325(d).

A. Legal Standards

Under § 325(d), we have discretion to deny a petition that presents the same or substantially the same prior art or arguments as previously presented to the Office. *See* 35 U.S.C. § 325(d).

In performing an analysis under § 325(d), the Board uses a two-part framework:

> (1) We consider whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and
>
> (2) If either condition of the first part of the framework is satisfied, we consider whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential).

To help us evaluate the *Advanced Bionics* framework, we consider a number of non-exclusive factors, as set forth in the decision in *Becton, Dickinson and Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential) ("the *Becton, Dickinson* factors"):

> (a) the similarities and material differences between the asserted art and the prior art involved during examination;
>
> (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
>
> (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
>
> (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;

> (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
>
> (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Becton, Dickinson, IPR2017-01586, Paper 8 at 17–18.

According to *Advanced Bionic*s, *Becton*, *Dickinson* factors (a), (b), and (d) relate to whether the same or substantially the same art or arguments previously were presented to the Office, and factors (c), (e), and (f) relate to whether the petitioner has demonstrated a material error by the Office. *Advanced Bionics*, IPR2019-01469, Paper 6 at 9–11.

B. Relevant Prosecution History

The '781 Patent application was a continuation of the '607 Application, which was filed on June 27, 2017. Ex. 1001, code (63). During prosecution of the '607 Application, the Examiner issued a number of office actions rejecting the claims as obvious, including an obviousness rejection over the combination of Wang, Liang, Olek, and Kutzner.[12] Ex. 2003, 640. The '607 Application issued as U.S. Patent No. 11,845,991 on December 19, 2023. Prelim. Resp. 8.

The '781 Patent application was filed on September 28, 2022. Ex. 1001, code (22). The only rejection issued by the Office during prosecution of the '781 Patent was based on obviousness-type double patenting over the '607 Application. Ex. 1020. Patent Owner filed a terminal disclaimer and the '781 Patent issued on April 25, 2023.

[12] Only Kutzner (Ex. 1012) appears to be of record in this proceeding. We, therefore, rely on the Examiner's description and quotations from the Wang, Liang, and Olek references for purposes of this Decision.

On May 22, 2023, Petitioner filed a request for *ex parte* reexamination of the '781 Patent, which was granted on June 29, 2023. Ex. 1021; Ex. 1022. Petitioner asserted fourteen proposed rejections (two anticipatory and 12 obviousness based) that applied eight different references, including an obviousness rejection based on the combination of Ahlquist,[13] De Luca,[14] and Olson.[15] Ex. 1021, 13–18. On October 18, 2023, the Office issued a Notice of Intent to Issue an *Ex Parte* Reexamination Certificate. Ex. 1023. The Examiner stated that the closest prior art of record was U.S. Patent No. 5,952,178, U.S. Patent No. 5,741,650, De Luca, Olson, and WO2005/014154. Ex. 1023, 2. The Examiner stated that the art fails to reasonably teach or suggest the limitations of claim 1. *Id.* at 2–3. The Examiner further stated that "[n]one of the references of record reasonably suggest collection at home with each of the fecal portions sealed in separate containers, each with a buffer therein as required by independent claim 1." *Id.* at 3.

C. Analysis

1. Whether the same or substantially the same art was previously presented

According to the first step of *Advanced Bionics*, Patent Owner asserts that the same or substantially the same art as Lenhard, Shuber, Itzkowitz, and Vilkin was previously presented to the Office. Prelim. Resp. 22–31.

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[13] Ahlquist et al., *Stool DNA and Occult Blood Testing for Screen Detection of Colorectal Neoplasia*, 149 ANN. INTERN. MED. 441–50 (2008) (Ex. 1044, "Ahlquist").
[14] De Luca et al., EP 1 366 715 A1, published Dec. 3, 2003 (Ex. 2006, "De Luca").
[15] Olson et al., *DNA Stabilization Is Critical for Maximizing Performance of Fecal DNA-Based Colorectal Cancer Tests*, 14 Diagn. Mol. Pathol. 183–91 (2005) (Ex. 1025, "Olson").

The parties do not dispute that primary references Lenhard and Shuber were listed on an Information Disclosure Statement during prosecution of the '781 patent and are cited on the face of the patent. *See* Ex. 2004, 141, 143;[16] Ex. 1001, code (56). Patent Owner also argues—and Petitioner does not dispute—that Itzkowitz 2008,[17] which was also cited during prosecution and is on the face of the '781 Patent (Ex. 2004, 142; Ex. 1001, code (56)), is cumulative of Itzkowitz. Prelim. Resp. 28–29; *see generally* Pet. Reply 1–6. Thus, the only issue in dispute is whether substantially the same art as Vilkin, which is included in all of Petitioner's grounds, was previously presented to the Office.

Patent Owner asserts that Vilkin is "substantively indistinguishable" from De Luca, which Petitioner relied on during the reexamination. Prelim. Resp. 25. Patent Owner argues that, like Vilkin, De Luca discloses a sealable tube for collecting a test portion of a fecal sample to be used in iFOBT tests, where buffer is introduced into the tube. *Id.* at 25–26 (citing Ex. 1022, 7; Ex. 2006, Abstract, ¶¶ 5, 19). Vilkin, however, expressly states that the collection device contains "Hb stabilizing buffer." Ex. 1005, 2520. De Luca, on the other hand, merely states that the collection device contains "a buffer solution" without specifying whether it was a buffer that prevents denaturation or degradation of hemoglobin. Ex. 2006 ¶ 19.

In its Sur-reply, Patent Owner argues that De Luca discloses the buffer limitation at least as much as Vilkin, because De Luca "discloses a

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[16] The parties agree that reference US 2008/0124714 A1 (Shuber et al.) cited during prosecution is the same reference as Shuber (Ex. 1009). Prelim. Resp. 9 n.2; Pet. 67.

[17] Itzkowitz et al., *A Simplified, Noninvasive Stool DNA Test for Colorectal Cancer Detection*, 103 AM. J. GASTROENTEROL. 2862–70 (2008) (Ex. 1055, "Itzkowitz 2008").

buffer solution that may contain 'specific' stabilizers for analytes such as hemoglobin." PO Sur-reply 3 (citing Ex. 2006 ¶¶ 1, 42). We note, however, that De Luca is not as clear as Patent Owner represents. De Luca generally states that the invention relates to a device "for collection of [feces] samples particularly for laboratory immunological tests, for qualitative or quantitative determination of one or more analytes, such as [hemoglobin], Helicobacter pylori and the like." Ex. 2006 ¶ 1. De Luca later separately states that a buffer solution is introduced into the device and the buffer "can be, for example, a solution with a pH between 7 and 9 with specific stabilizers." *Id.* ¶ 42. Thus, unlike Vilkin, which expressly states the device contains "Hb stabilizing buffer," De Luca does not indicate what the "specific stabilizers" in its buffer are for.[18] Accordingly, given these differences, we are not persuaded that De Luca is substantially the same as Vilkin.

Patent Owner also argues that Vilkin is substantially the same as Levi, which was cited during prosecution of the '781 Patent. Prelim. Resp. 28–29. Patent Owner asserts that Levi is a later publication covering "essentially the same work by the same group as Vilkin." *Id.* at 29 (emphases omitted). Patent Owner states that, like Vilkin, Levi describes an automated iFOBT that was more efficient than gFOBTs. *Id.* (citing Ex. 2007, 5). We are not persuaded. The mere fact that Levi and Vilkin generally describe the same work by the same group does not mean their disclosures are the same. We agree with Petitioner that Levi does not describe the fecal collection device with a blood protein stabilization buffer or separate sealable container for

[18] Moreover, we note that in its reexamination request, Petitioner did not cite paragraph 42 of De Luca, which describes the "specific stabilizers." *See* Ex. 1021, 90–91 (citing De Luca ¶¶ 1, 15, 19, 32 for limitation 1(c)).

which Petitioner relies on Vilkin. Pet. Reply 3 (citing Ex. 2007). Thus, on this record, we are not persuaded that Levi is substantially the same as Vilkin, either.

Finally, Patent Owner asserts that Wang and Liang, which were asserted during prosecution of the '607 Application, are substantially the same as Vilkin. Prelim. Resp. 31 (citing Ex. 2003, 640). Patent Owner argues that Wang teaches a collection device that is mixed with a "preserving fluid" and shipped unfrozen to a testing lab. *Id.* Patent Owner also argues that Liang teaches a method for collecting fecal samples, which includes inserting a sampling wand into a test apparatus that contains "an appropriate assay buffer." *Id.* (citing Ex. 2003, 641). We are not persuaded that a generic reference to a "preserving fluid" in Wang and an "appropriate assay buffer" in Liang is substantially the same as Vilkin's express reference to "hemoglobin stabilizing buffer." *Compare* Ex. 2003, 640, 641, *with* Ex. 1005, 2520.

Accordingly, on this record, we find that the same or substantially the same art as Vilkin was not previously presented to the Office. We next determine whether the same or substantially the same arguments were previously presented to the Office.

2. Whether the same or substantially the same arguments were previously presented

Patent Owner argues that the Petition makes effectively the same argument as it made during reexamination and the Examiner made during prosecution of the '607 Application. Prelim. Resp. 32–34. Specifically, Patent Owner argues that the rejection over Ahlquist, De Luca, and Olson during reexamination and Wang, Liang, Olek, and Kutzner during the '607

Application prosecution substantially overlaps with Petitioner's arguments here. *Id.*

Again, we are not persuaded. We agree with Petitioner that none of the reexamination references teaches that combining a DNA assay with an FOBT assay improves assay sensitivity over either test alone. Pet. Reply 2. Although Ahlquist teaches performing DNA tests and FOBT tests separately, Ahlquist never combines the two tests or suggests combining the two tests like Lenhard does. *See* Ex. 1044. We also agree with Petitioner that the rejection over Wang, Liang, Olek, and Kutzner was very different than any of the Grounds asserted in the Petition. Pet. Reply 3. Because of the differences in the references, the '607 Application traversed the rejection by arguing that the references fail to teach direct defecation into a sealable vessel, use of a blood protein stabilization buffer, and use of a DNA stabilizing buffer. Ex. 2003, 721–723. As shown above, Petitioner has shown sufficiently that the combination of asserted references teaches each of those limitations.

Accordingly, on this record, we find that the same or substantially the same arguments in the Petition have not been previously presented to the Office.

Because the first step of *Advanced Bionics* has not been met, we need not consider the second step of whether Petitioner has shown that the Office erred. As such, we decline to exercise our discretion to deny institution under 35 U.S.C. § 325(d).

IV. DISCRETIONARY DENIAL UNDER 35 U.S.C. § 314(a)

Patent Owner also argues that we should deny institution under *General Plastic* because Petitioner previously sought reexamination of the '781 Patent. Prelim. Resp. 38–45. Petitioner opposes. Pet. Reply at 6–8.

Institution of an *inter partes* review under 35 U.S.C. § 314(a) is discretionary. *See Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. 261, 273 (2016) (citing § 314(a) and stating "the agency's decision to deny a petition is a matter committed to the Patent Office's discretion"); *see also Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (explaining that under § 314(a), "the PTO is permitted, but never compelled, to institute an IPR proceeding"). In *General Plastic*, the Board considers several factors in determining whether to exercise its discretion under § 314(a) to deny institution when a party files multiple or "follow-on" petitions challenging the same patent as a previous petition. *See General Plastic*, 15–16.

Here, there were no prior petitions challenging the '781 Patent. Rather, Patent Owner urges us to extend the rationale of *General Plastic* and exercise our discretion to deny institution under § 314(a) because of Petitioner's prior *ex parte* reexamination request. Patent Owner reasons that extending *General Plastic* is justified, because this case presents a unique situation where the previous reexamination was made by the same party and involved substantially the same arguments and prior art. Prelim. Resp. 38–39. Patent Owner further argues that applying *General Plastic* to the facts of this case is justified where, as here, there have been repeated attacks on the patent by Petitioner and that AIA proceedings should not be used as tools for harassment. *Id.* at 40.

We are not persuaded that the facts and circumstances of this case warrant extending *General Plastic* to Petitioner's prior *ex parte* reexamination request. As explained above in our analysis under § 325(d), we disagree with Patent Owner that the previous reexamination involved substantially the same arguments and prior art. And although Petitioner may have known of the decision in the *ex parte* reexamination proceeding before

filing the Petition, the Statement of Reasons for Patentability and/or Confirmation consists of just two sentences stating that the cited references do not teach the limitations of claim 1. *See* Ex. 1023, 2–3. Moreover, Patent Owner chose not to respond to the *ex parte* reexamination request before the Examiner issued the decision. Prelim. Resp. 7 (citing Ex. 1023, 4). Thus, despite Patent Owner's arguments to the contrary, Petitioner could likely not use the reexamination decision or any statements from Patent Owner as a roadmap to cure any deficiencies for its Petition.

Given the facts and circumstances of this case, we are not inclined to extend the holding of *General Plastic* to Petitioner's prior *ex parte* reexamination request. As such, we decline to exercise our discretion to deny institution under 35 U.S.C. § 314(a).

V. CONCLUSION

For the foregoing reasons, we determine that Petitioner has established a reasonable likelihood of prevailing on its assertion that at least one of the challenged claims of the '781 Patent is unpatentable. Accordingly, we institute an *inter partes* review of claims 1–20 of the '781 Patent on each of the grounds raised in the Petition.

Our determination in this Decision is not a final determination on the construction of any claim term or the patentability of any challenged claim and, thus, leaves undecided any factual issues necessary to determine whether sufficient evidence supports Petitioner's contentions by a preponderance of the evidence in the final written decision. *See TriVascular, Inc. v. Samuels*, 812 F.3d 1056, 1068 (Fed. Cir. 2016) (noting that "there is a significant difference between a petitioner's burden to establish a 'reasonable likelihood of success' at institution, and actually proving invalidity by a preponderance of the evidence at trial") (quoting

35 U.S.C. § 314(a) and comparing § 316(e)). Any argument not raised in a timely Patent Owner Response to the Petition, or as permitted in another manner during trial, shall be deemed waived.

VI. ORDER

In consideration of the foregoing, it is hereby

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 1–20 of U.S. Patent No. 11,634,781 B2 is instituted with respect to all challenged claims and all grounds set forth in the Petition; and

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

FOR PETITIONER:

Brendan Jones
bjones@foleyhoag.com

FOR PATENT OWNER:

James Glass
Sandra Haberny
jimglass@quinnemanuel.com
sandrahaberny@quinnemanuel.com