

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SPECTRUM SOLUTIONS, LLC,
Petitioner,

v.

LONGHORN VACCINES & DIAGNOSTICS, LLC,
Patent Owner.

IPR2021-00857
Patent 9,212,399

Before GEORGIANNA W. BRADEN, ZHENYU YANG, and
WESLEY B. DERRICK, *Administrative Patent Judges*.

BRADEN, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314, 37 C.F.R. § 42.4

Spectrum Solutions, LLC (“Petitioner”) filed a Petition (Paper 1, “Pet.”) requesting an *inter partes* review of claims 1–35 (the “challenged claims”) of U.S. Patent No. 9,212,399 (Ex. 1001, “the ’399 patent”). Longhorn Vaccines & Diagnostics, LLC (“Patent Owner”) filed a Preliminary Response (Paper 6, “Prelim. Resp.”). Petitioner filed a Reply to Patent Owner’s Preliminary Response (“Reply”) to which Patent Owner filed a Sur-Reply (“Sur-Reply”).

The Board has authority to determine whether to institute an *inter partes* review (“IPR”). See 35 U.S.C. § 314(b); 37 C.F.R. § 42.4(a). Under 35 U.S.C. § 314(a), authorization of an *inter partes* review requires the information in the Petition and the Preliminary Response to “show[] that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” For the reasons that follow, we institute an *inter partes* review as to the challenged claims of the ’399 patent on all challenges to patentability presented in the Petition.

I. BACKGROUND

A. *Real Parties in Interest*

Petitioner identifies Spectrum Solutions, LLC as the real party in interest. Pet. 1. Petitioner also identifies Spectrum Holdco, LLC and Spectrum Intermediate, LLC as having a financial interest in, or could be substantially affected by the outcome of this proceeding. *Id.* Patent Owner identifies Longhorn Vaccines & Diagnostics, LLC as the real party in interest. Paper 3 (Patent Owner’s Mandatory Notices), 2.

B. *Related Proceedings*

The parties identify the following infringement actions involving the ’399 patent: *Longhorn Vaccines & Diagnostics, LLC v. Spectrum*

Solutions LLC, C.A. No. 2:20-cv-00827 (D. Utah), filed November 20, 2020. Petitioner has also filed petitions for *inter partes* review of related U.S. Patents 8,084,443, 8,293,467, 8,415,330, 8,669,240, and 9,683,256. Pet. 1; Paper 3, 2.

C. The '399 Patent and Related Background

The '399 patent titled “Biological Specimen Collection and Transport System and Method of Use,” issued to Fischer et al., on Dec. 15, 2015, from U.S. Application No. 14/149,278, filed January 7, 2014, via a series of continuation actions first filed on October 1, 2009 and further claims priority to Provisional Application No. 60/976,728 filed on October 1, 2007.¹ Ex. 1001, codes (21), (45), (54), (60), (63), (72), 1:8–21.

1. Written Description

The '399 patent relates to “aqueous compositions for collection, transport, and storage of a biological specimen containing a population of nucleic acids in a single reaction vessel, which can then be purified and/or analyzed using conventional molecular biology methods.” Ex. 1001, 1:35–39. The '399 patent acknowledges that prior art methods existed, but states such methods could result in the degradation of nucleic acids, even when stored under freezing temperatures, and had the potential for exposure to infectious agents during collection, transfer, and testing. *Id.* at 1:55–2:36. The '399 patent also states that “clinical laboratory methods for pathogen detection were labor-intensive, expensive processes that required highly

¹ Petitioner claims the earliest possible priority date as October 1, 2007. Pet. 4. For the purposes of the institution decision, Patent Owner does not dispute the prior art status of any references. Prelim. Resp. 7.

knowledgeable and expert scientists with specific experience.” *Id.*
at 2:37–40.

Against this background, the ’399 patent purports to disclose “new and useful compositions . . . that may advantageously improve conventional collection, lysis, transport and storage methods for the preparation of nucleic acids from one or more biological sources.” *Id.* at 3:21–26. In particular, the ’399 patent discloses a one-step, aqueous composition that:

a) inactivates viruses or microbes in the sample, b) lyses the biological cells or tissues to free the nucleic acids from cellular debris and extraneous biomolecules, c) protects the nucleic acids from degradation by endonuclease activity, d) facilitates collection and handling of the sample at ambient temperatures, and e) preserves the nucleic acids for subsequent isolation, detection, amplification, and/or molecular analysis.

Id. at 3:41–51; *see id.* at 6:44–52.

The Specification further discloses exemplary compositions comprising a buffered solution of nuclease-free water containing:

a chaotrope, e.g., guanidine thiocyanate, guanidine hydrochloride, or guanidine isocyanate;

a detergent, e.g., sodium dodecyl sulfate (SDS), lithium dodecyl sulfate (LDS), sodium taurodeoxycholate (NaTDC), sodium taurocholate (NaTC), sodium glycocholate (NaGC), sodium deoxycholate (NaDC), sodium cholate, sodium alkybenzene sulfonate (NaABS), or N-lauroyl sarcosine (NLS);

a reducing agent, e.g., β -mercaptoethanol (β -ME), dithiothreitol (DTT), dimethylsulfoxide (DMSO), formamide, or phosphine (TCEP);

a chelator, e.g., EGTA, HEDTA, DTPA, NTA, EDTA, citrate anhydrous, sodium citrate, calcium citrate, ammonium citrate, ammonium bicitrate, citric acid, diammonium citrate, ferric ammonium citrate, or lithium citrate); and

a surfactant/ defoaming agent, e.g., a silicone polymer such as Antifoam A®, or a polysorbate such as Tween®.

Id. at 4:21–5:31. In certain embodiments, the composition further includes a short chain alkanol, e.g., methanol, ethanol, propanol, butanol, pentanol, hexanol (*id.* at 5:59–67) as well as buffer to control the pH of the solution (*id.* at 5:48–58).

According to the Specification, an exemplary composition containing the sample suspected of containing nucleic acids will:

stabilize the nucleic acids to the extent that they either remain at least substantially non-degraded (i.e., at least substantially stable) even upon prolonged storage of the composition at ambient, refrigerator, or sub-zero temperatures. It will be desirable that this stability provides that at least about 70%, at least about 85%, more preferably at least about 90%, more preferably at least about 95%, or even more preferably, at least about 98% of the polynucleotides contained within the stored sample will not be degraded upon prolonged storage of the sample. In certain embodiments, substantially all of the polynucleotides contained within the sample will be stabilized such that the original integrity of the polynucleotides is preserved during the collection, lysis, storage, and transport of the processed sample.

Id. at 9:63–10:11.

2. *Illustrative Claims*

As noted above, the Petition challenges independent claim 1, as well as dependent claims 2–35. Claim 1 illustrates the challenged subject matter at issue and is reproduced below.

1. A stock solution of an aqueous composition comprising:
 - a chaotrope,
 - a detergent,
 - a reducing agent,
 - a chelator, and

a buffer,
wherein the stock composition, when diluted with a sample
containing nucleic acids, nucleases and proteins,
denatures the proteins of the sample,
inactivates the nucleases of the sample,
kills pathogens that may be present in the sample, and
does not degrade the nucleic acids of the sample.

Ex. 1001, 31:44–50.

D. Asserted Challenges to Patentability and Evidence of Record

Petitioner asserts that claims 1–35 would have been unpatentable on the following basis:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1, 4, 6, 8, 10, 11, 16, 21–30, 32, 35	102	Birnboim ²
1, 2, 4–8, 10–14, 16, 21–30, 32, 35	103	Birnboim
3	103	Birnboim, Chen ³
9	103	Birnboim, Reed ⁴
15	103	Birnboim, Mori ⁵
16	103	Birnboim, Helftenbein ⁶
17	103	Birnboim, Chirgwin ⁷

² Birnboim, US 2004/0038269 A1, published Feb. 26, 2004 (“Birnboim,” Ex. 1003).

³ Chen et al., US 2007/0202511 A1, published Aug. 30, 2007. (“Chen,” Ex. 1027).

⁴ Reed et al., WO 00/77235 A1, published Dec. 21, 2000. (“Reed,” Ex. 1017).

⁵ Mori, WO 2005/111210 A1, published Nov. 24, 2005. (“Mori,” Ex. 1011).

⁶ Helftenbein, U.S. Patent No. US 6,776,959 B1, filed Aug. 12, 1999, issued Aug. 17, 2004. (“Helftenbein,” Ex. 1019).

⁷ Chirgwin et al., *Isolation of Biologically Active Ribonucleic Acid from Sources Enriched in Ribonuclease*, 18 Biochemistry 5294 (1979). (“Chirgwin,” Ex. 1015).

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
18–20	103	Birnboim, Chen, Das ⁸ , Wanhg ⁹
31	103	Birnboim
31	103	Birnboim, Koller ¹⁰
33	103	Birnboim, Birnboim2006 ¹¹
34	103	Birnboim, Chirgwin, Farrell ¹²

Petitioner filed a Declaration from Richard F. Taylor, Ph.D. (Ex. 1002, “Dr. Taylor”) with its Petition. Patent Owner filed a Declaration from Louis DeFilippi, Ph.D. (Ex. 2010, “Dr. DeFilippi”).

II. PRELIMINARY MATTERS

A. *Legal Standards*

1. *Anticipation*

A claim is unpatentable under 35 U.S.C. § 102 if a prior art reference discloses every limitation of the claimed invention, either explicitly or inherently. *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047 (Fed. Cir. 1995). If the prior art reference does not expressly set forth a particular element of the claim, that reference still may anticipate if that element is “inherent” in its disclosure. *In re Robertson*, 169 F.3d 743 (Fed. Cir. 1999). To establish inherency, extrinsic evidence, when relied upon, “must make clear that the missing descriptive matter is necessarily present,” or inherent,

⁸ Das et al., US 2005/0123928 A1, published Jun. 9, 2005. (“Das,” Ex. 1008).

⁹ Wanhg et al., WO 2004/104181 A2, published Dec. 2, 2004. (“Wanhg,” Ex. 1022).

¹⁰ Koller, WO 91/02740 A1, published Mar. 7, 1991. (“Koller,” Ex. 1016).

¹¹ Birnboim et al., WO 2006/096973 A1, published Sept. 21, 2006. (“Birnboim2006,” Ex. 1023).

¹² Robert E. Farrell, Jr., Ph.D., “RNA Methodologies: A Laboratory Guide for Isolation and Characterization,” (3rd Ed., 2005). (“Farrell,” Ex. 1026).

in the single anticipating reference. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). “Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *Id.* at 1269 (quoting *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981)) (emphasis added).

Inherent anticipation, however, does not require recognition in the prior art. *Schering Corp. v. Geneva Pharmaceuticals*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (“*Continental Can* does not stand for the proposition that an inherent feature of a prior art reference must be perceived as such by a person of ordinary skill in the art before the critical date.”). Moreover, the reference must also “disclose[] within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim.” *Net MoneyIN, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008). Additionally, “the reference need not satisfy an ipsissimis verbis test.” *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009).

2. Obviousness

35 U.S.C. § 103(a) renders a claim unpatentable if the differences between the claimed subject matter and the prior art are 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 said subject matter pertains. See *KSR*, 550 U.S. at 406. Tribunals resolve obviousness based on 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 skill in the art; and (4) where in evidence, so-called secondary considerations. See *Graham v. John Deere Co.*, 383 U.S. 1,

17–18 (1966). Prior art references must be “considered together with the knowledge of one of ordinary skill in the pertinent art.” *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994) (citing *In re Samour*, 571 F.2d 559, 562 (CCPA 1978)).

B. Burden of Proof

“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”)). This burden of persuasion never shifts to Patent Owner. *See Dynamic Drinkware, LLC v. Nat’l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015) (discussing the burden of proof in *inter partes* review). Furthermore, Petitioner cannot satisfy its burden of proving obviousness by employing “mere conclusory statements.” *In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016).

Thus, to prevail in an *inter partes* review, Petitioner must explain how the proposed combinations of prior art would have rendered the challenged claims unpatentable. At this preliminary stage, we determine whether the information presented in the Petition shows there is a reasonable likelihood that Petitioner would prevail in establishing that one of the challenged claims is unpatentable. Additionally, the Supreme Court held that a decision to institute under 35 U.S.C. § 314(b) may not institute review on less than all claims challenged in the petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1355–56 (2018). Moreover, in accordance with USPTO Guidance, “if the PTAB institutes a trial, the PTAB will institute on all challenges raised in

the petition.” *See Guidance on the Impact of SAS on AIA Trial Proceedings* (April 26, 2018) (available at <https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial>) (“USPTO Guidance”).

C. Level of Ordinary Skill in the Art

In determining whether an invention would have been obvious at the time it was made, we consider the level of ordinary skill in the pertinent art at the time of the invention. *Graham*, 383 U.S. at 17. “The importance of resolving the level of ordinary skill in the art lies in the necessity of maintaining objectivity in the obviousness inquiry.” *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991).

Relying on the testimony of Dr. Taylor, Petitioner contends that A person of ordinary skill in the art (“POSA”) would have had (1) a Ph.D. in microbiology, molecular biology, biochemistry, or related discipline; (2) at least two years of post-graduate experience in the area of nucleic acid extraction and analysis; and (3) experience with the development or use of nucleic acid extraction formulations, and the literature concerning nucleic acid extraction and analysis. Ex. 1002, ¶¶37–38.

Pet. 9.

At this stage of the proceeding, Patent Owner does not contest Petitioner’s definition of a person of ordinary skill in the art. Prelim. Resp. 7. For the purposes of this Decision on Institution, we agree with Petitioner’s proposed level of ordinary skill in the art, which is not substantively opposed by Patent Owner and appears to comport with the teachings of the ’399 patent and asserted prior art.

D. Claim Construction

In an *inter partes* review, the Board construes each claim “in accordance with the ordinary and customary meaning of such claim as

understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” 37 C.F.R. § 42.100(b). Under the same standard applied by district courts, claim terms have their plain and ordinary meaning as would have been understood by a person of ordinary skill in the art at the time of the invention and in the context of the entire patent disclosure.

Phillips v. AWH Corp., 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc).

“There are only two exceptions to this general rule: 1) when a patentee sets out a definition and acts as his own lexicographer, or 2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution.” *Thorner v. Sony Comput. Entm’t Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012).

Petitioner contends that we should apply the plain and ordinary meaning of “stock solution” as meaning “a formulated supply of solution for future use.” Pet. 7. Patent Owner does not dispute Petitioner’s definition of “stock solution” nor request that we construe any other claim at this time, but reserves its right to do so. Prelim. Resp. 7.

At this stage of the proceeding, we apply the plain and ordinary meaning of “stock solution” as Petitioner proposes. We note that Patent Owner implicitly relies on narrow constructions of “kills pathogens” and “without degrading nucleic acids.” As these terms may be critical to our final determination but have not been briefed by either party, we provisionally apply their plain and ordinary meaning.

III. ANALYSIS AND DISCUSSION

A. *Alleged Anticipation of Claims 1, 4, 6, 8, 10–11, 16, 21–30, 32 and 35 over Birnboim*

Petitioner relies on Birnboim to allege anticipation of claims 1, 4, 6, 8, 10–11, 16, 21–30 and 35. Pet. 7. Patent Owner opposes and disputes that Birnboim establishes every element of the challenged claims of the '399 patent. Prelim. Resp. 8. The burden remains on Petitioner to sufficiently demonstrate a reasonable likelihood the challenged claims are unpatentable. *See Dynamic Drinkware*, 800 F.3d at 1378. For reasons that follow, we determine Petitioner has shown a reasonable likelihood of demonstrating that the challenged claims were anticipated in view of Birnboim under 35 U.S.C. § 102.

1. *Overview of Birnboim (Exhibit 1003)*

Birnboim discloses “compositions and methods for preserving nucleic acids at room temperature for extended periods of time and for simplifying the isolation of nucleic acids,” most particularly, DNA or RNA from sputum or saliva. Ex. 1003 ¶¶ 2, 27. According to Birnboim, nucleic acid isolated can be that of the sputum or saliva donor or “from a bacterium or a virus that is residing in the buccal, nasal, or respiratory passages of the subject.” *Id.* ¶ 27; *see id.* ¶ 43 (defining “nucleic acid” as meaning “a chain of the nucleotides, including deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), typically found in chromosomes, mitochondria, ribosomes, bacteria, or viruses”); ¶ 18 (“The nucleic acid to be preserved can be . . . viral RNA.”); ¶ 27 (“If the nucleic acid is RNA, desirably it is mRNA or viral RNA.”) ¶ 45 (discussing quantitation of “high molecular weight nucleic acid (DNA, RNA, mRNA, or viral RNA)”); claims 7, 16.

Birnboim discloses stock solutions (“nucleic acid preserving compositions”) for use in a one-step method to lyse nucleic acid-containing cells or viruses, release the nucleic acids into the composition, inactivate nucleases in the sample, and stabilize the extracted nucleic acid for future analysis. *See generally id.* ¶¶ 11, 22, 27, 64, 114–122. Birnboim further teaches “inclusion of an inhibitor of ribonuclease in the composition of the invention . . . when the nucleic acid to be preserved is RNA, desirably mRNA, or when the nucleic acid to be preserved is from a virus or a bacterium.” *Id.* ¶ 22; *see also id.* ¶ 68 (stating that in addition to the use of various denaturing agents, “reagents such as heparin, heparian sulfate, or oligo(vinylsulfonic acid) . . . are known to inhibit the action of deoxynucleases and /or ribonucleases”).

Birnboim explains:

When sputum is mixed with a composition of the present invention, cells are disrupted, nucleic acids are liberated from the cells, membranous material is solubilized, proteins are stripped from the nucleic acids, and protein digestion begins If transferred to a laboratory soon after collection, incubation at 55° C. for 4 to 16 hours is sufficient to allow the activated protease to digest the majority of protein to small peptides or amino acids. Under such conditions, nucleic acids and polysaccharides remain relatively intact.

Once digestion is complete, nucleic acid isolation can be performed using any technique known in the art.

Id. ¶¶ 84–85.

Example 1 discloses an embodiment wherein a subject spits saliva into a collection tube which is mixed with an equal volume of stock solution. *Id.* ¶¶ 107–109. Once the container is capped and the contents shaken, the nucleic acid is “in an intermediate preserved state” and “can be maintained

in a frozen state or at any temperature up to about 60 °C.” *Id.* ¶ 110.

Alternatively, “[t]he container can be mailed back to the testing lab at room temperature.” *Id.* ¶ 111.

Example 3 discloses the collection and extraction of DNA using a stock solution comprising “33 mM TRIS-HCl, 0.67 M urea, 0.67 M LiCl, 0.6% sodium dodecyl sulfate, 3.3 mM CDTA, 30% ethanol, and 0.25 M sodium ascorbate, all adjusted to a final pH of 8.0.” *Id.* ¶¶ 114–122. In Example 4, Birnboim subjects the DNA to agarose gel electrophoresis and ethidium bromide staining, noting “the characteristic band of chromosomal DNA present in all samples.” *Id.* ¶ 117, Fig. 1; *see also id.* ¶ 13 (disclosing preferred reducing agents erythiorbate, N-acetylcysteine, dithiothreitol, 2-mercaptoethanol and, “most desirably. . . ascorbic acid”), ¶ 25 (disclosing that isolated DNA is preferably stable for “more than 60 days” and “when . . . the composition does not contain ascorbic acid, the DNA is stable for more than 60 days, and desirably more than 360 days”).

2. *Analysis of Birnboim as Applied to Challenged Independent Claim 1*

a. *“A stock solution of an aqueous composition”*

Claim 1’s preamble recites “a stock solution of an aqueous composition” Ex. 1003, 41:44. Petitioner contends that if the preamble of claim 1 were limiting, then Birnboim plainly discloses the limitation. Pet. 17.

“Whether to treat a preamble term as a claim limitation is determined on the facts of each case in light of the claim as a whole and the invention described in the patent.” *Am. Med. Sys., Inc. v. Biolitec, Inc.*, 618 F.3d 1354, 1358 (Fed. Cir. 2010) (internal quotation marks omitted). “Absent clear reliance on the preamble in the prosecution history, or in situations where it

is necessary to provide antecedent basis for the body of the claim, the preamble generally is not limiting.” *Symantec Corp. v. Computer Assoc. Int’l, Inc.*, 522 F.3d 1279, 1288 (Fed. Cir. 2008) (internal quotation marks omitted). Furthermore, where “the body of the claim fully and intrinsically sets forth the complete invention, including all of its limitations, and the preamble offers no distinct definition of any of the claimed invention’s limitations, but rather merely states, for example, the purpose or intended use of the invention, then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation.” *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999). Yet, when the limitations in the body of the claim rely upon or derive essential structure from the preamble, then the preamble acts as a necessary component of the claimed invention and is limiting. See *Eaton Corp. v. Rockwell Int’l Corp.*, 323 F.3d 1332, 1339 (Fed. Cir. 2003).

Patent Owner does not at this time directly dispute Petitioner’s contention that Birnboim discloses a stock solution of an aqueous composition, but does dispute that Birnboim discloses *the* aqueous composition as claimed. See Prelim. Resp. 8.

Based on the current record, which shows that the Birnboim discloses a “stock solution of an aqueous composition,” we are satisfied Petitioner has shown that Birnboim meets the preamble to the extent it is limiting.

b. “a chaotrope, a detergent, a reducing agent, a chelator, and buffer”

Claim 1 recites “A stock solution of an aqueous composition comprising: a chaotrope, a detergent, a reducing agent, a chelator, and a buffer” Ex. 1003, 41:44–46.

Petitioner contends Birnboim teaches this limitation by disclosing “stock solutions with the same components in the same amounts claimed by the ’399 patent to achieve the same claimed purpose.” Pet. 12.

Petitioner argues that Birnboim discloses denaturing agents that “lyse cells, denature proteins, and inactivate nucleases.” In addition to providing antimicrobial properties. Pet. 13 (citing Ex. 1003 ¶¶ 41, 64, 68, 84).

According to Petitioner, the ’399 patent discloses these same reagents disclosed by Birnboim under the labels chaotrope or detergent. *Id.* Petitioner points out that Birnboim, in its illustrative examples, discloses the same specific reagents present in the claims of the ’399 patent. *Id.* For example, Birnboim discloses urea, sodium dodecyl sulfate and guanidinium thiocyanate as denaturing agents, which the ’399 patent claims as a chaotrope, a detergent, and a chaotrope respectively. *Compare* Ex. 1003 ¶¶ 20, 68, *with* Ex. 1001, 4:44–47; 31:65–66, 32:24–25. Additionally, Petitioner argues Birnboim discloses reducing agents, chelating agents, and buffers. Pet. 14.

In response, Patent Owner argues that Birnboim fails to disclose the claimed aqueous composition of the ’399 patent because Birnboim fails to teach the use of chaotropes and detergents as separate components. Prelim. Resp. 9. Specifically, Patent Owner contends that Birnboim uses the term “denaturing agent” in a broad manner, and the mere presence of both chaotropes and detergents within the category of “denaturing agents” fails to disclose the use of a chaotrope combined with a detergent. *Id.* at 9–10. Patent Owner, however, does not appear to dispute that Birnboim discloses a buffer, a chelator, and a reducing agent. *See generally* Prelim. Resp.

On the present record, we do not find Patent Owner’s argument persuasive. Birnboim discloses a variety of denaturing agents, several of which are directly claimed within the ’399 patent, and states that denaturing agents may be used “alone or in combination [with one another]”. Ex. 1003 ¶ 68. Based on the explicit disclosure of Birnboim, we find Petitioner’s argument regarding a stock solution comprising a chaotrope, a detergent, a chelating act, a reducing agent and a buffer to be adequate for institution. Additionally, we credit Dr. Taylor’s testimony regarding the wide-spread and well-known nature of the combination of reagents specified in claim 1 of the ’399 patent. Ex. 1002, 19–22.

Accordingly, at this stage of the proceeding and based on the record before us, we are satisfied Petitioner has shown adequately for the purposes of institution that Birnboim discloses the challenged claim limitations of a stock solution containing the aforementioned reagents as required by challenged claim 1.

- c. *“wherein the stock composition, when diluted with a sample containing nucleic acids, nucleases and proteins, denatures the proteins of the sample inactivates the nucleases of the sample kills pathogens that may be present in the sample does not degrade the nucleic acids of the sample”*

Claim 1 recites “wherein the stock composition, when diluted with a sample containing nucleic acids, nucleases and proteins, denatures the proteins of the sample inactivates the nucleases of the sample kills pathogens that may be present in the sample does not degrade the nucleic acids of the sample.” Ex. 1003, 4:44–50.

Petitioner contends Birnboim anticipates this limitation because Birnboim’s disclosed denaturing agents denature proteins, inactivate

nucleases, and kill pathogens via the lysing of cells. Pet. 21. Furthermore, Petitioner contends that Birnboim does not degrade the nucleic acids of the sample due to the presence of: (1) the chelating agents that provide antimicrobial activity; (2) reducing agents that prevent nucleic acid degradation; and (3) buffers, which stabilize the pH to prevent nucleic acid degradation. *Id.*

Patent Owner first contends that Birnboim does not anticipate the '399 patent as the '399 patent fails to “expressly disclose killing pathogens with its composition.” Prelim. Resp. 11 (citing Ex. 2001 ¶ 32 (Dr. DeFilippi testifies that “Birnboim nowhere discloses killing pathogens as a step in the obtaining of DNA, RNA, or, more generally, nucleic acids.”)). Patent Owner argues that Birnboim does not teach the killing of pathogens because Birnboim references the risk of infection in a sample as well as “antimicrobial substances” such as chelating agents, or denaturing agents like ethanol disclosed by Birnboim as used for the purpose of “inhibiting microbial growth.” Rather, Patent Owner contends Birnboim teaches the use of a microbial agent in a “bacteriostatic” fashion, i.e. inhibiting pathogen cell division without killing the pathogen. See Prelim. Resp. 12–13. For this argument, Patent Owner relies on the testimony of Dr. DeFilippi that ethanol is not sufficient to kill pathogens except in very high percentages and that 30% ethanol is not sufficient to have a bactericidal effect. Prelim. Resp. 13–14 (citing Ex. 2001¶ 21). Patent Owner then argues that even if Birnboim’s disclosure addresses inhibiting microbial growth, it limits its discussion to bacteria, and fails to disclose other possible pathogens, such as spores, viruses or fungi. *Id.* at 14.

As an initial matter, “a reference . . . is prior art for all that it teaches,” and we decline to dismiss the express teachings of Birnboim because they may not be the main focus of its disclosure. *See Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551 (Fed. Cir. 1989) (citation omitted).

Additionally, Patent Owner appears to equate the claim language, “kill[ing] pathogens,” with complete sterilization of a sample “to prevent ‘dissemination of live infections pathogens.’” Prelim. Resp. 15 (citing Ex. 1001, 2:23–26, 6:46–49; Ex. 2001 ¶ 7); *see also id.* at 11 (asserting the Birnboim “does not require lysing all or even most of the cells in a sample”). On their face, however, the claims do not require killing every potential pathogen in a sample. *See In re Self*, 671 F.2d 1344, 1348 (CCPA 1982) (holding that such “arguments fail from the outset because . . . they are not based on limitations appearing in the claims”); *see also* Ex. 1001, 26:10–28:61 (the ’399 patent itself disclosing killing bacteria only in Examples 7 and 8, whereas Example 9 specifically states “kill or inactive microorganisms in the sample.”). Birnboim expressly teaches the isolation of nucleic acids from bacteria and viruses. *See* Ex. 1003 ¶¶ 18, 22, 27, 30. The reference does not appear to suggest that such isolation is non-destructive, we presume that at least some of these potential pathogens are “killed” in the extraction process according to the ordinary meaning of the term.

Considering the present record as whole, Petitioner persuades us that compositions taught or suggested in Birnboim kill at least *some* bacteria and/or viruses. To be clear, we do not read the challenged claims as suggesting that *every* pathogenic agent including, for example, prions and bacterial spores, must be so susceptible, nor that the addition of stock

solution should clear an entire sample of all such agents. *See e.g.*, Ex. 2003 (CDC Guidance), 9–10, 34, 102 (discussing difficulty of eliminating bacterial spores and prions as opposed to, for example, lipid encapsulated viruses and vegetative bacteria); Sur-reply 3 (Patent Owner noting that some strains of gram negative bacteria “were not sensitive to 0.05% SDS *relative to control bacteria*” (citing Ex. 1044, 8) (emphasis added); *see also* Ex. 2001 ¶ 22 (Dr. DeFilippi testifying that “Birnboim fails to kill pathogens” because it only references “bacteriostatic” and “bactericidal” components and does not teach killing “any pathogen including fungi, spores, or viruses”).¹³

To the extent Patent Owner implies that we should assign some special meaning to the “kills pathogens” requirement of the claim element, Patent Owner neither raises this issue in the claim construction portion of its brief, nor anywhere proposes a specific construction of the term. *See* Prelim. Resp. 7 (“Claim Construction”), 16–19. And although Patent Owner points to the purported “purpose and value” of stock solutions disclosed in the ’399 Patent as killing pathogens “to facilitate safe handling” of biological samples, and evidence that a commercial embodiment showed “effectiveness . . . in killing methicillin-resistant *Staphylococcus aureus*,” Patent Owner provides insufficient reasoned argument why we should import such limitations into the challenged claims. Prelim. Resp. 17–19

¹³ On page 1 of its Reply, Petitioner contends Dr. DeFilippi admitted that “[Birnboim] does not teach killing of anything but bacteria”) (citing Ex. 2001 ¶ 22). Although Patent Owner reasonably argues that we should read this portion of Dr. DeFillippi’s report indicating that “that the word ‘bactericidal’ itself . . . ‘does not teach the killing of anything but bacteria,’” Birnboim, nevertheless, expressly teaches compositions comprising antimicrobial agents, that “can be bacteriostatic, bactericidal or both.” Sur-reply 1; Ex. 1042 ¶ 21.

(citing e.g., Ex. 1001, 2:24–28, 3:41–51, 6:46–49, 9:31–40, 14:64–15:4, 16:3–5, 27:25–67). Accordingly, we decline to do so on the instant record. *See SuperGuide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004). (“Though understanding the claim language may be aided by the explanations contained in the written description, it is important not to import into a claim limitations that are not a part of the claim.”).

Patent Owner similarly contends that Ground 1 fails because “Birnboim does not disclose a stock solution of an aqueous composition that perform the functional limitations of claim 1 using the claimed reagents.” Prelim. Resp. 20 (heading capitalization normalized) (“nothing in Birnboim teaches using the claimed aqueous composition, as opposed to utilizing additional unclaimed substances, to kill pathogens”); Sur-reply 3–4.

Patent Owner argues, for example, that although Birnboim teaches the use of antimicrobial agents, and preferably ethanol, the stock solution of Example 3 contains only 30% ethanol which, Patent Owner asserts, “is not sufficient to have a bactericidal effect, much less kill viruses or vegetative bacteria.” Prelim. Resp. 13 (citing Ex. 1003 ¶¶ 21, 64, 73, 115; Ex. 2001 ¶¶ 21, 25–26; Ex. 2003). In this respect, Patent Owner states that Birnboim teaches the use of such agents “in a way that is merely “bacteriostatic,” and that “an antimicrobial agent is bacteriostatic if it inhibits cell division *without affecting the viability of the inhibited cell*,” i.e. without killing the cell. *Id.* (citing Ex. 1003 ¶ 21).

Patent Owner also argues that the lithium chloride and NaOAc in the stock solution of Example 3, are not recited in challenged claim 1, suggesting that these unclaimed reagents “were important for one or more of the functions of denaturing proteins, inactivating nucleases, and preventing

degradation of nucleic acids,” as required by the claim. *Id.* at 23–24 (citing Ex. 2001 ¶ 19). Patent Owner further argues that Birnboim relies on proteases to digest proteins, and “states in Example 4 that the enzyme proteinase K is added to the solution of Example 3 to prepare the solution for precipitating DNA.” *Id.* at 22–23 (citing Ex. 1003 ¶¶ 26, 83, 84, 117; Ex. 2001 ¶¶ 41, 44, 45, 47). Thus, Patent Owner argues, addition of proteinase K to digest proteins as a subsequent step in Example 4 demonstrates that the composition of Example 3 does not “denature proteins” because, if it did, the composition of Example 3 would have denatured the proteinase K added in Example 4, rendering it inoperable.” *Id.* at 23 (citing Ex. 2001 ¶¶ 45, 47).

As an initial matter, Patent Owner’s reference to bacteriostatic antimicrobial agents in paragraph 21 of Birnboim omits much from that passage. In particular, Birnboim states that

An antimicrobial agent can be bacteriostatic, bactericidal or both. . . . An antimicrobial agent is bactericidal if it causes cell death. Cell death is commonly detected by the absence of cell growth in liquid growth medium (e.g., absence of turbidity) or on a solid surface (e.g., absence of colony formation on agar). Those of skill in the art know that a substance or group of substances which is bacteriostatic at a given concentration may be bactericidal at a higher concentration.

Ex. 1003 ¶ 21. Accordingly, Birnboim not only teaches the use of bactericidal agents, but indicates that their efficacy can be tested using the same type of assays employed in the ’399 patent. *See* Ex. 1001, 26:38–28:45) (colony forming assay testing bactericidal effect on *Staphylococcus aureus* strain ATCC33592).

Moreover, and as discussed at the beginning of this section, we do not read Petitioner’s arguments with respect to Birnboim as being limited to the

exemplary composition of Example 3. *See, e.g.*, Ex. 1003 ¶ 21 (“most desirably the composition includes ethanol”) ¶ 20 (“the alcohol is 10%-60% of the total composition volume”). Nor, with respect to the stock solution of Example 3, does the preliminary record make clear that the 30% ethanol component alone, is responsible (or even necessary) for killing viruses or bacteria, or that one of ordinary skill in the art reading Birnboim would understand that protease, lithium chloride, and NaOAc are required to perform the functions of the claim.

Finally, with respect to Patent Owner’s assertion that adding proteinase K to the solution of Example 3 “would have denatured the proteinase K added in Example 4, rendering it inoperable,” we note that this step involved diluting the stock solution of Example 3 with “an equal volume of saliva,” and then treating a 0.25 mL portion of that sample with proteinase K. Prelim. Resp. 23 (citing Ex. 2001 ¶¶ 40–45, 47; Ex. 1003 ¶¶ 83, 117). In asserting that the proteinase K would have been rendered inoperable, Patent Owner fails to account for factors such as the amount and effect of dilution on stability of the proteinase K, the time course of any inactivation, or the rate and extent of proteolysis expected prior to any such inactivation. *See e.g.*, Ex. 1003 ¶ 69 (Birnboim’s teaching that “a balance must be struck between the concentration of denaturing agents that will, on the one hand, inhibit deoxyribonucleases or ribonucleases and denature other proteins in saliva and, on the other hand, not significantly inhibit the proteolytic enzymes”). Accordingly, it is of little moment whether denaturants in the stock solution might *eventually* render the proteinase K component of Example 4 inoperable. And though Patent Owner cites paragraphs 45 and 47 of Dr. DeFilippi’s testimony in support of its position,

those passages do not even reference proteases, let alone the understanding of one of ordinary skill in the art with respect to the addition of proteinase K in Example 4. *See* Prelim. Resp. 23 (citing Ex. 2001 ¶¶ 45, 47). As such, Patent Owner’s arguments are both unsupported and unpersuasive on this preliminary record.

Patent Owner’s arguments also are undercut by its assertion before the district court that:

It is common knowledge to one skilled in the art that an aqueous composition that comprises a) one or more chaotropes; b) one or more detergents and/or surfactants; c) one or more reducing agents; d) one or more chelators; and e) one or more buffers [all components of the stock solution in Birnboim’s Example 3] serves the purpose of denaturing proteins, inactivating nucleases, killing pathogens, and not degrading nucleic acid of a sample suspected of containing pathogens when the sample is contacted with the composition.

Ex. 1007 ¶ 17. Petitioner contends that Patent Owner’s statement before the district court are inconsistent with its representations in the present case. Pet. Reply 4–5. Patent Owner responds that its argument are consistent because the district court complaint refers to “what is known in the art today *as a result* of Patent Owner’s disclosures.” PO Sur-reply 3–4.

Considering the arguments and evidence presently before us, we find Petitioner’s reading more plausible, particularly in light of Birnboim’s disclosure of compositions comprising all the named ingredients and the general skill in the art regarding methods and reagents for isolating nucleic acids. Accordingly, we infer that the above reference to the “common knowledge [of] one skilled in the art” encompasses the knowledge of one of ordinary skill in the art as of the filing date of the ’399 patent. *See* Ex. 1007 ¶¶ 14, 266. As such, we are hard pressed to credit Patent Owner’s arguments

that Birnboim alone, or in combination with other asserted references, fails to teach or suggest a “stock solution, [that] when combined with a biological sample suspected of containing a pathogen, denatures proteins, inactivates nucleases, and kills pathogens all without degrading nucleic acids of the sample,” as set forth in claim 1. We invite the parties to explore these issues further at trial.

As Patent Owner points out, Petitioner does not expressly invoke inherency to establish that the stock solutions taught or suggested by the prior art kill pathogens. Prelim. Resp. 12–13, fn.3, 18. Addressing inherency, nevertheless, Patent Owner states that Birnboim’s disclosure of denaturing agents as “antimicrobial substances” (¶ 64) or for inhibiting microbial growth (¶ 73) “would not *necessarily* kill pathogens.” Prelim. Resp. 19. Patent Owner further states it submitted evidence that both the sodium dodecyl sulfate (SDS) that Birnboim includes in Example 3 as a “denaturing agent” and the chelator CDTA that Birnboim includes in Example 3 would not *necessarily* be expected to be bactericidal (killing pathogens). *Id.* at 30 (citing Ex. 2001 ¶¶ 29, 31).

Relying on the testimony of Dr. DeFilippi, Patent Owner points to its “submitted evidence” that the SDS in Birnboim’s “Example 3 would not necessarily be expected to be bactericidal.” Prelim. Resp. 30 (citing Ex. 2001 ¶¶ 29, 31, 33–35; *see* Reply 3–4. Dr. DeFilippi asserts, for example that “[b]acteria are known to degrade SDS.” Ex. 2001 ¶ 29 (citing Ex. 2006 “Shahbazi”).¹⁴ Shahbazi, however, is a bioremediation study showing that

¹⁴ Shahbazi, et al. “Screening of SDS-degrading bacteria from car wash wastewater and study of the alkylsulfatase enzyme activity,” 5(2) Iranian journal of microbiology 153–158 (2013).

bacteria isolated from car wash waste water could degrade low concentrations of SDS. Ex. 2006, Abstract, 154 (screening media comprising 1.5 mM SDS), 156–157 (reporting degradation of 7 mM SDS by “a consortium *Acinetobacter calcoaceticus* and *Pantoea agglomerans*”).

Dr. DeFilippi also points to Woldringh¹⁵ as evidence that SDS “is quite poor as a lysis agent,” insofar as it reports that “[d]uring prolonged SDS interaction” only “25% of the ribonucleic acid and 40% of the deoxyribonucleic acid were released from [bacterial] cells.” Ex. 2001 ¶¶ 29–30 (quoting Ex. 2007, Abstract). Woldringh, however, was studying the controlled dissolution of the *E.coli* plasma membrane using 0.05% SDS, a “comparatively low concentration of detergent” and substantially lower than the 0.60% SDS used in Birnboim’s Example 3. Ex. 2007, 801; Ex. 1003 ¶ 115.

As Petitioner points out, however, even at this low concentration of SDS, Woldringh reported dissolution of bacterial plasma membranes and the release of nucleic acids indicating that, “the cells are, of course, dead.” Reply 3 (citing Ex. 2007, 801 (Abstract), 807, 809, Figs. 2, 12); *see also id.* at 3–4 (quoting Ex. 1044 (McDaniel))¹⁶ (citing Woldringh for the proposition that “SDS has been shown more than 40 years ago to cause *significant bacterial membrane damage* with subsequent *release of DNA*,

¹⁵ Woldringh et al., (1972). “*Effects of treatment with sodium dodecyl sulfate on the ultrastructure of Escherichia coli*,” 111(3) J. Bacteriol, 801–813 (1972). (Ex. 2007). Exhibit 2007 includes a series of thumbnails followed by the complete, full-size article. We cite to the native pagination of the latter.

¹⁶ McDaniel, et al., “*A Putative ABC Transporter Permease is Necessary for Resistance to Acidified Nitrite and EDTA in Pseudomonas aeruginosa under Aerobic and Anaerobic Planktonic and Biofilm Conditions*,” 7(291) Frontiers in Microbiol. 1–14 (April 2016). (Ex. 1044).

RNA and protein”).¹⁷ Thus, irrespective of whether Patent Owner’s above-quoted statement before the district court refers to the state of the art before or after the filing date of the ’399 patent, it would appear at odds with Patent Owner’s position that Birnboim’s stock solution lacks any of the functionality recited in the claim. Nevertheless, as noted above, we invite the parties to further explore the inherency and obviousness arguments and their factual underpinnings at trial.

Patent Owner further argues that even if Birnboim’s “Example 3 composition may have liberated nucleic acids from native human cells [this] does not establish that the same composition would necessarily have been effective either to extract nucleic acids from pathogens or to kill pathogens and render a sample safe for transportation and evaluation.” Prelim. Resp. 30; Sur-reply 1–2. Moreover, Patent Owner argues, “even if it were able to extract DNA from a single “bacterium or virus,” it fails to teach or disclose a solution as claimed that kills pathogens, for example to facilitate safe handling and transport of the collected specimen,” or “necessarily prevent[s] degradation of nucleic acids.” Prelim. Resp. 31–33 (citations omitted).

¹⁷ Patent Owner appears to assert that McDaniel’s determination that some strains of *Pseudomonas aeruginosa* “were not sensitive to 0.05% SDS relative to control bacteria,” contradicts Petitioner’s contention that 0.05% SDS kills *e. coli* as shown by Woldringh. Sur-reply 3 (citing Ex. 1044). This argument is unavailing insofar as Patent Owner does not explain how one of ordinary skill in the art would understand McDaniel’s statement that the *P. aeruginosa* strains were “not sensitive . . . relative to control bacteria.” More to the point, we do not read the claims to require complete sterilization of a sample, nor efficacy against every potential species of pathogen, as discussed more fully above.

Throughout these arguments, Patent Owner implicitly relies on narrow constructions of “kills pathogens” and “without degrading nucleic acids” that have not been briefed or argued by either party. For the purpose of institution, however, we apply the plain and ordinary meaning. As such, Birnboim’s instruction to isolate nucleic acid “from a bacterium or a virus that is residing in the buccal, nasal, or respiratory passages of the subject,” necessarily “kills pathogens.” See Ex. 1003 ¶ 27.

Accordingly, at this stage of the proceeding and based on the record before us, we are satisfied Petitioner has adequately shown for the purposes of institution that Birnboim discloses claim limitation of the killing of pathogens sufficiently.

3. *Analysis of Birnboim as Applied to Challenged Dependent Claims 4, 6, 8, 10–11, 16, 21–30, 32 and 35.*

Petitioner contends dependent claims 4, 6, 8, 10–11, 16, 21–30, 32 and 35 of the ’399 patent are unpatentable as anticipated under 35 U.S.C. § 102 in view of Birnboim and provides specific arguments for each claim. Pet. 22–36. Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. See *Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claims 4, 6, 8, 10–11, 16, 21–30, 32 and 35. At this stage of the proceeding, we are persuaded that Petitioner’s analysis as supported by Dr. Taylor’s testimony is sufficient for institution regarding the specific limitations recited in these claims. Accordingly, we conclude Petitioner has established a reasonable

likelihood it would prevail in showing that the challenged dependent claims would have been anticipated under 35 U.S.C. § 102 in view of Birnboim.

B. Alleged Obviousness of Claims 1, 2, 4–8, 10–14, 16, 21–30, 32, 35 over Birnboim

Petitioner relies on teachings of Birnboim to allege claims 1, 2, 4–8, 10–14, 16, 21–30, 32, 35 of the '399 patent are unpatentable under 35 U.S.C. § 103 in view of Birnboim. *See* Pet. 36–46. Patent Owner opposes and argues that Petitioner fails to show on what basis any missing elements of claim 1 can be found in Birnboim. Prelim. Resp. 33. The burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378. 35 U.S.C. § 103(a) renders a claim unpatentable if the differences between the claimed subject matter and the prior art are 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 said subject matter pertains. *See KSR*, 550 U.S. at 406. Tribunals resolve obviousness based on 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 skill in the art; and (4) where in evidence, so-called secondary considerations. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). Prior art references must be “considered together with the knowledge of one of ordinary skill in the pertinent art.” *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994) (citing *In re Samour*, 571 F.2d 559, 562 (CCPA 1978)).

For reasons that follow, we determine Petitioner has shown a reasonable likelihood of demonstrating that the challenged claims would have been obvious in view of Birnboim under 35 U.S.C. § 103.

1. Analysis of Birnboim as Applied to Challenged Independent Claim 1

Petitioner contends that both the '399 patent and Birnboim: (1) are in the same field of endeavor; (2) have the same objective; (3) accomplish their objective through performing the same several basic functions; (4) employ a combination of the same well known-reagents; (5) use those reagents in accordance with their well understood functions to achieve the desired objective; and (6) achieve the same result. Pet. 38. Therefore, according to Petitioner the '399 patent uses a combination of familiar elements according to known methods and would have been obvious as it yields predictable results. *Id.* (citing KSR, 550 U.S. at 401).

Patent Owner does not address Petitioner's arguments directed toward specific claims, but argues that Petitioner fails to provide proper analysis as to why the '399 patent would have been obvious in light of Birnboim. Prelim Resp. 33. Instead, according to Patent Owner, Petitioner simply assumes the '399 patent is anticipated by Birnboim and ignores that Birnboim fails to disclose the killing of pathogens, a key objective of the '399 patent. *Id.* at 34. Petitioner's and Patent Owner's arguments are the same or similar to the arguments made for independent claim 1 with regard to anticipation. *See generally* Pet.; Prelim. Resp.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged independent claim 1. Because we determine Petitioner has met its burden of establishing a reasonable likelihood that it will prevail in showing claim 1 to be anticipated by Birnboim, and Patent Owner does not presently rely on objective indicia of non-obviousness, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that challenged independent claim 1

would have been obvious under 35 U.S.C. § 103 in view of Birnboim. *See Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542 (Fed. Cir. 1983) (quoting *In re Fracalossi*, 681 F.2d 792, (CCPA 1982)) (“a disclosure that anticipates under § 102 also renders the claim invalid under § 103, for ‘anticipation is the epitome of obviousness.’”).

2. *Analysis of Birnboim as Applied to Challenged Dependent Claims 2, 4–8, 10–14, 16, 21–30, 32, 35*

Petitioner contends dependent claims 2, 4–8, 10–14, 16, 21–30, 32, and 35 of the ’399 patent are unpatentable as obvious under 35 U.S.C. § 103 in view of Birnboim and provides specific arguments for each claim.

Pet. 22–36. Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claims 2–4, 8–10, 14–16, 22–24, 28, and 29. At this stage of the proceeding, we are persuaded that Petitioner’s analysis as supported by Dr. Taylor’s testimony is sufficient for institution regarding the specific limitations recited in these claims. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claims would have been obvious under 35 U.S.C. § 102 in view of Birnboim.

C. *Alleged Obviousness of Claim 3 over Birnboim and Chen*

1. *Overview of Chen*

Chen discloses extraction compositions and methods for the isolation of small RNA molecules from a biological sample. Ex. 1027, code (57).

Chen discloses aqueous solutions designed to preserve nucleic acids. *Id.* The

aqueous solution includes: a chaotrope, a metal agent, a pH buffer, a detergent, a reducing agent, an anti-foaming agent, and a bulking agent. *Id.* ¶¶ 12–27. A suitable reducing agent disclosed by Chen includes “tris(2-carboxyethyl)phosphine” (“TCEP”).

2. *Analysis of Birnboim and Chen as Applied to Challenged Dependent Claim 3*

Claim 3 depends from claim 2 and recites “the stock solution of claim 2, wherein the reducing agent comprises tris(2-carboxyethyl)phosphine” also known as TCEP. Birnboim does not disclose TCEP as a reducing agent. *See* Ex. 1002; *see generally* Ex. 1003.

Petitioner contends dependent claim 3 of the ’399 patent is unpatentable as obvious under 35 U.S.C. § 103 in view of Birnboim in combination with Chen. Pet. 47–48. Petitioner further argues that it was well known that TCEP was a desirable reducing agent for aqueous solutions directed at preserving nucleic acids. *Id.* at 48. According to Petitioner, claim 3 is “merely the predictable result of a simple substitution of known elements[]” and therefore would have been obvious. *Id.* (citing *KSR*, 550 U.S. at 416). Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 3. At this stage of the proceeding, we are persuaded that Petitioner’s analysis as supported by Dr. Taylor’s testimony is sufficient for institution regarding the specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in

showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim and Chen.

D. Alleged Obviousness of Claim 9 over Birnboim and Reed

1. Overview of Reed

Reed discloses solutions and methods for isolating nucleic acids from biological materials. Ex.1017, code (57). Reed further discloses including a surfactant as part of the solution promotes “solubilization of contaminating proteins,” with polysorbates as a preferred surfactant. *Id.* at 15:15–18 (“preferred surfactants are non-ionic detergents such as . . . polysorbates.”).

2. Analysis of Birnboim and Reed as Applied to Dependent Claim 9

Claim 9 depends from claim 1 and recites, “The stock solution of claim 1, further comprising a surfactant that comprises a silicone polymer, a polysorbate, or any combination thereof.” Ex. 1001, 41:45–47.

Petitioner contends claim 9 of the ’399 patent is unpatentable as obvious under 35 U.S.C. § 103 in view of Birnboim in combination with Reed. Pet. 49–50. Petitioner further argues that the use of surfactants in nucleic acid stabilization was well-known in the prior art, and that Reed discloses using such a surfactant, a polysorbate, as a “preferred surfactant.” Pet. 49; Ex. 1017, 15:15–18. Therefore, according to Petitioner, a person of ordinary skill in the art at the time of the alleged invention would have been motivated to use a polysorbate surfactant as disclosed in Reed in combination with Birnboim’s stock solution with a reasonable expectation of success, rendering claim 9 obvious. Pet. 50. Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 9. At this stage of the proceeding, we are persuaded that Petitioner’s analysis as supported by Dr. Taylor’s testimony is sufficient for institution regarding the specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim and Reed.

E. Alleged Obviousness of Claim 15 over Birnboim and Mori

1. Overview of Mori

Mori discloses the isolation of nucleic acids from a test sample (e.g., bodily fluids, plants, animals, bacteria, viruses, and cultured cells) by treating the sample with a “nucleic acid-solubilizing reagent,” which “dissolves cell membranes and nuclear membrane, and solubilizes nucleic acid.” Ex. 1011, 57:14–22. Exemplary nucleic acid-solubilizing reagents may include “a chaotropic salt, a surfactant, a defoaming agent, a protease and a nucleic acid stabilizing agent.” *Id.* at 58:19–21; *see also id.* at 63:6–24 (indicating that the nucleic acid stabilizing agent assists in inactivating nuclease activity).

According to Mori, preferred chaotropic salts are guanidine hydrochloride, guanidine isothiocyanate and guanidine thiocyanate (*id.* at 61:11–14); the nucleic acid stabilizing agent is a reducing agent, and preferably a mercapto compound (*id.* at 63:21–22); and the defoaming agent may be any number of silicon-, alcohol-, ether-, fatty oil-, fatty acid-phosphate ester-, amine-, or amide-based compounds, “preferably in a range of 0.1 to 10% by weight.” *Id.* at 64:9–25.

With respect to the surfactant, Mori teaches thus use of a wide variety of compounds including an anionic surfactant, an amphoteric surfactant and, preferably, either a nonionic or cationic surfactant. *Id.* at 61:18–21.

Nonionic surfactants include a polyoxyethylene alkyl phenyl ether-based surfactant, a polyoxyethylene alkyl ether-based surfactant, and fatty acid alkanolamide, and the preferable one is a polyoxyethylene alkyl ether-based surfactant. Among the polyoxyethylene (POE) alkyl ether surfactant, POE decylether, POE lauryl ether, POE tridecyl ether, POE alkylenedecyl ether, POE sorbitan monolaurate, POE sorbitan monooleate, POE sorbitan monostearate, tetraoleic polyoxyethylene sorbit, POE alkyl amine, and POE acetylene glycol are more preferred. *Id.* at 61:22–62:4.

Cationic surfactants include cetyl trimethyl ammonium bromide, dodecyl trimethyl ammonium chloride, tetradecyl trimethyl ammonium chloride, cetyl pyridinium chloride. *Id.* at 62:5–7. With respect to surfactant concentration, Mori states: “The concentration of the surfactant in the nucleic acid-solubilizing reagent is preferably from 0.1 to 20% by weight.” *Id.* at 62:8–10.

2. *Analysis of Birnboim and Mori as Applied to Dependent Claim 15*

Claim 15 depends from claim 1 and recites, “The stock solution of claim 1, further comprising a defoaming agent that comprises a silicon polymer or a polysorbate.” Ex. 1001, 32:61–63. Petitioner contends that the use of defoaming agents to reduce foaming in nucleic acid preserving solutions was well-known in the prior art. Pet. 52. Petitioner further argues, a person of ordinary skill in the art at the time of the invention would have expected success in using a defoaming agent along with the stock solution disclosed by Birnboim. *Id.* at 53. Therefore, according to Petitioner, an

ordinarily skilled artisan would have had reason to use a defoaming agent disclosed by Mori, in combination with Birnboim's stock solution and have a reasonable expectation of success in doing so, thus rendering claim 15 obvious. *Id.* Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 15. At this stage of the proceeding, we are persuaded that Petitioner's analysis as supported by Dr. Taylor's testimony is sufficient for institution regarding the specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim and Mori.

F. Alleged Obviousness of Claim 16 over Birnboim and Helftenbein

1. Overview of Helftenbein

Helftenbein discloses an aqueous solution containing: a chaotrope, a buffer, a reducing agent and a detergent intended for use to stabilize nucleic acids extracted from cells. Ex. 1019, 2:32–63. Helftenbein discloses the extraction of nucleic acids from human blood cells as a particularly suited use. *Id.* at code (57).

2. Analysis of Birnboim and Helftenbein as Applied to Dependent Claim 16

Claim 16 depends from claim 1 and recites “further comprising a population of isolated polynucleotides that comprises RNA, DNA or a combination thereof.” Ex. 1001, 32:63–65. Petitioner contends that claim 16 of the '399 patent is unpatentable as obvious under 35 U.S.C. § 103. Pet. 54.

Petitioner argues that Helftenbein discloses the use of carrier DNA or RNA in a solution designed to extract nucleic acids as a positive control, while Birnboim discloses a stock solution of an aqueous composition for the extraction of nucleic acids. *Id.* According to Petitioner an ordinarily skill artisan would have been motivated to use carrier RNA or DNA, i.e. isolated populations of polynucleotides, in a stock solution analogous to claim 1 of the '399 patent. *See id.* In view of Helftenbein, Petitioner contends a person of ordinary skill in the art at the time of the alleged invention would have been motivated to combine Birnboim's disclosure and Helftenbein's disclosure with a reasonable expectation of success, thus rendering claim 16 obvious. *Id.*

Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 16. At this stage of the proceeding, we are persuaded that Petitioner's analysis as supported by Dr. Taylor's testimony is sufficient for institution regarding the specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim and Helftenbein.

G. Alleged Obviousness of Claim 17 over Birnboim and Chirgwin

1. Overview of Chirgwin

Chirgwin is a research article that discloses a method for the isolation of intact RNA from biological samples using an aqueous solution including

a strong denaturing agent and a reductant along with other reagents.

Ex. 1015, 1. The use of guanidinium thiocyanate and 2-mercaptoethanol are disclosed. *Id.* at 1, Experimental Procedure.

2. *Analysis of Birnboim and Chirgwin as Applied to Dependent Claim 17*

Claim 17 depends from claim 1 and recites “the stock solution of claim 1, which, when diluted for use, comprises: a) about 4 M guanidine thiocyanate; b) about 30 mM sodium citrate; c) about 0.25% (wt./vol.) sodium dodecyl sulfate; d) about 0.25% (wt./vol.) N-lauroyl sarcosine, sodium salt; e) about 0.1 M 2-mercaptoethanol; and f) about 0.1% silicon polymer (wt./vol).” Ex. 1001, 32:66–33:4.

Petitioner contends claim 17 of the ’399 patent would have been obvious under 35 U.S.C. § 103. Pet. 55. Petitioner argues that only insubstantial differences exist between the composition disclosed by claim 17 and the composition disclosed by Chirgwin. *Id.* at 57. Petitioner further argues that that ’399 patent is a compilation of well-known reagents in the field used according to their well-understood functions and accordingly, it would have been obvious to integrate the use of Chirgwin’s disclosed reagents, which are well-known, with Birnboim’s stock solution. *Id.* In doing so, an ordinarily skilled artisan at the time of the invention would have had a reasonable expectation of success and a motivation to combine Birnboim and Chirgwin, rendering claim 17 obvious.

Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 17. At this

stage of the proceeding, we are persuaded that Petitioner's analysis as supported by Dr. Taylor's testimony is sufficient for institution regarding the specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim and Chirgwin.

H. Alleged Obviousness of Claims 18–20 over Birnboim, Chen, Das, and Wangh

1. Overview of Das

Das discloses a method for extracting bacterial DNA from a biological sample. Ex. 1008, code (57), ¶ 38. One particular embodiment involves collecting a sputum sample and using a modified buffer to lyse all specimen cells. *Id.* at ¶ 38. Das' disclosed embodiments include a lysis buffer containing: guanidinium isothiocyanate, N-lauryl sarcosyl, guanidinium isothiocyanate, 2-mercaptoethanol, EDTA, and a buffer. *Id.* ¶¶ 62–68.

2. Overview of Wangh

Wangh discloses solutions and method for the preparation of nucleic acids to make them available for subsequent uses such as detection, modification or manipulation with or without amplification. Ex. 1022. 1:1–5. Wangh's disclosed solutions include many of the same classes of reagents as disclosed by Birnboim, such as detergents, chaotropes, and reducing agents. *See id.* at ¶¶ 11–20.

3. Alleged Obviousness of Birnboim, Chen, Das, and Wangh as Applied to Dependent Claims 18–20.

Claims 18–20 depend from claim 1 and recite specific reagents for claim 1's stock solution. Ex. 1001, 33:5–24. Petitioner contends that claims 18–20 are unpatentable as obvious under 35 U.S.C. § 103. Pet. 59.

Petitioner argues that Birnboim discloses the stock solution of claim 1 and that Das, Chen, and Wangh disclose the claimed reagents and concentrations of claims 18–20. *Id.* at 59–61. Petitioner further argues that because the prior art discloses the claimed reagents and concentration, it would have been obvious for a POSA to employ them as a “matter of routine optimization.” *Id.* at 61.

Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claims 18–20. At this stage of the proceeding, we are persuaded that Petitioner’s analysis as supported by Dr. Taylor’s testimony is sufficient for institution regarding the specific limitations recited in these claims. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claims would have been obvious under 35 U.S.C. § 103 in view of Birnboim, Chen, Das, and Wangh.

I. Alleged Obviousness of Claim 31 over Birnboim and Koller

1. Overview of Koller

Koller discloses “methods and compositions for isolation of nucleic acids. . . .” Ex. 1016, code (57). Koller’s compositions include a chaotrope, a detergent, a reducing agent, and a salt. *Id.* at 7:1–3.

2. Analysis of Birnboim and Koller as applied to Dependent Claim 31.

Claim 31 depends from claim 21 and recites “wherein less than about 5% of the population of polynucleotides contained in the sample is degraded after the stock solution comprising the sample has been stored at a

temperature from about 10° C. to about 40° C. for a period of about 7 to about 30 days.” Ex. 1001, 34:8–12. Petitioner contends that claim 31 of the ’399 patent is unpatentable as obvious under 35 U.S.C. § 103. Pet. 62. Petitioner argues that the ’399 patent does not disclose how to achieve the desired preservation levels of nucleic acids, e.g. how to ensure a percentage of the sample “will not be degraded upon prolonged storage. . . .” *Id.* (citing Ex. 1001, 10:12–45).

According to Petitioner, because the ’399 patent fails to disclose how to achieve this goal, and because Birnboim discloses using the same reagents as the ’399 patent, a person of ordinary skill in the art at the time of the alleged invention would have recognized that Birnboim would not cause more than 5% degradation of the isolated nucleic acids as recited by claim 31. *Id.* at 62–63. Petitioner further argues that Koller, in utilizing a similar composition, disclosed that the “isolated DNA was essentially intact and . . . not degraded.” *Id.* at 63 (citing Ex. 1016, 23:10–15). Because an ordinarily skill artisan would have understood Koller’s disclose of nucleic acids as not degraded, and would have reasonably expected success in combining this information with the disclosed composition of Birnboim, claim 31 would have been obvious in view of Birnboim and Koller. *Id.* at 64.

Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 31. At this stage of the proceeding, we are persuaded that Petitioner’s analysis as supported by Dr. Taylor’s testimony is sufficient for institution regarding the

specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim and Koller.

J. Alleged Obviousness of Claim 33 over Birnboim and Birnboim2006

1. Overview of Birnboim2006

Birnboim2006 discloses compositions for extracting and preserving nucleic acids from degradation at room temperature. Ex. 1023, Field of the Invention. Birnboim2006 discloses gathering a sample for nucleic acid isolation from the inside of a patient's cheek using a "buccal swab." *Id.* at 1023.

2. Analysis of Birnboim and Birnboim2006 as Applied to Dependent Claim 33

Claim 33 depends from claim 32 and recites, "The sample collection system of claim 32, furthering comprising a swab, curette, or culture loop." Ex. 1001, 34:17–18. Petitioner contends claim 32 is unpatentable as obvious under 35 U.S.C. § 103. Pet. 64–65. Petitioner argues that Birnboim discloses a collection vessel, while Birnboim2006 discloses a buccal swab. *Id.* at 65 (citing Ex. 1023, 2). Therefore, a person of ordinary skill in the art would have been motivated to use Birnboim2006's buccal swab with Birnboim's disclosed collection vessel and solution with a reasonable expectation of success rendering claim 32 obvious. *Id.*

Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 33. At this stage of the proceeding, we are persuaded that Petitioner's analysis as supported by Dr. Taylor's testimony is sufficient for institution regarding the specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim and Birnboim2006.

K. Alleged Obviousness of Claim 34 over Birnboim, Chirgwin, and Farrell

1. Overview of Farrell

Farrell is a laboratory guide describing the isolation and characterization of ribonucleic acids. Ex. 1026, Title. Farrell discloses that it was widely known that nucleases, which are enzymes that degrade nucleic acids, should be purged from solutions when trying to isolate RNA. *Id.* at 48–49. Farrell discloses that numerous compounds have been used to inhibit RNase activity including, vanadyl ribonucleoside complexes, RNasin, heparin, iodoacetate, polyvinyl (dextran) sulfate, cationic surfactant, macaloid and bentonite clays, and hydrogen peroxide. *Id.* at 50–53.

Farrell further states that “stock solutions and buffers prepared in the laboratory can be treated, directly or indirectly, with the potent chemical RNase inhibitor DEPC” or diethylpyrocarbonate. *Id.* at 55. Farrell notes that “DEPC is an efficient, nonspecific inhibitor of RNase,” but “must be destroyed completely” since “[e]ven trace amounts of residual DEPC will result in chemical modification of the base adenine” and, thus, should not be added directly to cell suspensions or lysates containing RNAs to be purified. *Id.* at 55. Farrell discloses that there additional “legitimate reasons” not to

use DEPC in that laboratory and that making solutions with nuclease-free water is a more desirable alternative for solutions that isolate nucleic acids.

Id. at 57. In this respect, Farrell states:

A suitable alternative to DEPC treatment of water to render it nuclease-free is to simply buy nuclease-free water from one's favorite vendor. For those laboratories affiliated with hospitals, it is interesting to note that water labeled "sterile water for irrigation," is free of contaminants and is good for RNA work. Purified RNA may be rehydrated in this water and stored at -80°C . This water is also excellent for making dilutions of nuclease-free stock solutions.

Id.

2. *Analysis of Birnboim, Chirgwin and Farrell as Applied to Dependent Claim 34*

Claim 34 discloses a method of preparing the stock solution of claim 1. Ex. 1001, 34:19–46. Claim 34 recites 8 steps, 4 of which are optional and need not be considered for the purpose of obviousness analysis. *See In re Johnston*, 435 F.3d 1381, 1384 (Fed. Cir. 2006); Ex. 1001, 34:19–46. The limitations recited by claim 34 are: [a] combining one or more chaotropes with nuclease-free water at a temperature of about 20C to 90C; [b] combining the dissolved one or more chaotropes with one or more reducing agents, one or more chelators and one or more detergent to form an intermediate composition; [d] combining a sufficient amount of buffer to the intermediate composition so as to maintain a pH of about 5 to 7; [f] increasing the temperature of the second intermediate composition to about 60 °C to 95 °C for about 1 to 30 minutes and lowering the temperature to ambient conditions. *Id.*

Petitioner contends that claim 34 is unpatentable as obvious under 35 U.S.C. § 103. Pet. 66. Petitioner argues that Chirgwin satisfies limitations

[a] and [b] via disclosing the mixing of a chaotrope, a chelator, a reducing agent, and a detergent in deionized water. *Id.* at 67. Petitioner also relies on the testimony of Dr. Taylor that it would have been obvious as a design choice to combine the chaotrope (guanidinium thiocyanate) with water, prior to the other reagents at room temperature, then raise the temperature to dissolve the reagents. *Id.* (citing Ex. 1002 ¶ 294). Petitioner further argues that Farrell discloses that DEPC had become undesirable for nucleic acid isolation due to its carcinogenic properties. *Id.* 68 (citing Ex. 1026, 55, 57). According to Petitioner, Farrell also discloses nuclease-free water as a desirable alternative to DECP treated water, which a person of ordinary skill in the art at the time of the invention would have been motivated to use in the composition taught by Birnboim. *Id.*

Additionally, Petitioner argues that in light of Chirgwin, it would have been obvious for an ordinarily skill artisan to include a buffer to obtain a pH between 5 and 7 in the solution, because Chirgwin discloses adjusting the pH of its nucleic acid isolation solution to 7, and Birnboim discloses the use of a buffer to maintain a pH between 5 and 7. *Id.* (citing Ex. 1003, ¶ 19; Ex. 1015, 5295) ([for RNA preservation,] “a pH from about 5.0 to about 7.0, desirably from about 6.5 to about 6.8 can be used.”). Therefore, according to Petitioner, Birnboim, in combination with Chirgwin, satisfies limitation [d]. *Id.* at 68.

Finally, regarding limitation [f] Petitioner argues that Chirgwin discloses warming and stirring the solution, followed by returning the solution to room temperature. *Id.* According to Petitioner, it would have been obvious to raise the temperature of the solution to between 65 °C and 95 °C as it was an obvious consideration to dissolve the reagents.

Therefore, according to Petitioner, Birnboim meets this limitation and claim 34 would have been obvious. *Id.* at 68–69.

Patent Owner does not address the additional limitations of the dependent claims at this time, but the burden remains on Petitioner to demonstrate unpatentability. *See Dynamic Drinkware*, 800 F.3d at 1378.

We have considered carefully all arguments and supporting evidence in light of the limitations recited in challenged dependent claim 34. At this stage of the proceeding, we are persuaded that Petitioner’s analysis as supported by Dr. Taylor’s testimony is sufficient for institution regarding the specific limitations recited in this claim. Accordingly, we conclude Petitioner has established a reasonable likelihood it would prevail in showing that the challenged dependent claim would have been obvious under 35 U.S.C. § 103 in view of Birnboim, Chirgwin, and Farrell.

IV. CONCLUSION

After considering the evidence and arguments presented in the Petition and the Preliminary Response, we determine Petitioner has demonstrated a reasonable likelihood that it would prevail with respect to its unpatentability challenges. Accordingly, we institute an *inter partes* review on all of the challenged claims and all of the grounds presented in the Petition. At this stage of the proceeding, we have not made a final determination as to the patentability of these challenged claims.

V. ORDER

Accordingly, it is

ORDERED that, pursuant to 35 U.S.C. § 314, *inter partes* review is instituted as to all the challenged claims of the ’399 patent with respect to all grounds of unpatentability presented in the Petition; and

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FURTHER ORDERED that *inter partes* review is commenced on the entry date of this Order, and 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.

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