

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SPECTRUM SOLUTIONS LLC
Petitioner,

v.

LONGHORN VACCINES & DIAGNOSTICS, LLC
Patent Owner.

IPR2021-00854
Patent 8,669,240 B2

Before GEORGIANNA W. BRADEN, WESLEY B. DERRICK, and
ROBERT A. POLLOCK, *Administrative Patent Judges*.

DERRICK, *Administrative Patent Judge*.

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

I. INTRODUCTION

On April 27, 2021, Spectrum Solutions LLC (“Petitioner”) filed a Petition for an *inter partes* review of claims 1–35 of U.S. Patent No. 8,669,240 B2 (“the ’240 patent,” Ex. 1001). Paper 1 (“Pet.”). Longhorn Vaccines & Diagnostics, LLC (“Patent Owner”) timely filed a Preliminary Response. Paper 6 (“Prelim. Resp.”). With our authorization (*see* Ex. 3001), Petitioner filed a Reply to the Preliminary Response (Paper 7, “Reply”); Patent Owner filed a corresponding Sur-Reply (Paper 10¹, “Sur-Reply”).

We have authority to determine whether to institute an *inter partes* review. *See* 35 U.S.C. § 314(b); 37 C.F.R. § 42.4(a). To institute an *inter partes* review, we must determine that the information presented in the Petition shows that there is “a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a). The Federal Circuit has interpreted the statute to require “a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition.” *PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018).

For the reasons provided below, we determine Petitioner has satisfied the threshold requirement set forth in 35 U.S.C. § 314(a). Thus, based on the information presented, we institute an *inter partes* review of claims 1–35 of the ’240 patent on all grounds.

¹ Patent Owner filed duplicative copies of its Sur-Reply as Papers 9 and 10, which, absent a word-for-word comparison, appear identical but for minor differences in formatting. In an abundance of caution, we expunged Paper 9 in favor of the second-filed copy. Patent Owner subsequently indicated that the expunged version contained a formatting error. Ex. 3003.

A. Real Parties-in-Interest

Petitioner identifies itself, Spectrum Solutions LLC, as a real party-in-interest. Pet. 1. Petitioner further identifies two companies having a financial interest in, or potentially substantially affected by the outcome of, this proceeding: its parent company, Spectrum Holdco LLC, and Spectrum Intermediate LLC. *Id.* Petitioner does not expressly identify those companies as real parties-in-interest.

Patent Owner identifies itself, Longhorn Vaccines & Diagnostics, LLC, as the real party-in-interest in this proceeding. Paper 3, 1.

B. Related Proceedings

The Parties identify a district court proceeding, *Longhorn Vaccines & Diagnostics, LLC v. Spectrum Solutions LLC*, C.A. No. 2:20-cv-00827 (D. Utah), as a related matter. Pet. 1; Paper 3, 1. The Parties also identify *inter partes* review proceedings challenging patents at issue in the district court proceeding: IPR2021-00847 (U.S. Pat. No. 8,084,443), -00850 (U.S. Pat. No. 8,293,467), -00851 (U.S. Pat. No. 8,415,330), -00857 (U.S. Pat. No. 9,212,399), and -00860 (U.S. Pat. No. 9,683,256). Pet. 1; Paper 3, 1.

C. The '240 Patent (Ex. 1001)

The '240 patent is titled “Biological Specimen Collection and Transport System and Method of Use” and is directed to “compositions for isolating populations of nucleic acids from biological, forensic, and environmental samples” that can be used in formulations to “kill[] pathogens, inactivat[e] nucleases, and releas[e] polynucleotides from other cellular components within the sample, and stabiliz[e] the nucleic acids prior to further processing or assay.” Ex. 1001, codes (54), (57).

The '240 patent states

In particular, the invention is directed to a one-step 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, and d) preserves the nucleic acids for subsequent isolation, detection, amplification, and/or molecular analysis.

Id. at 1:36–43. The '240 patent further discloses that “[t]he ability to achieve all of these desirable functions in a single-step formulation, . . . is a particularly marked advantage over that presently available.” *Id.* at 3:49–52.

The '240 patent discloses an embodiment of the composition as including

- a) one or more chaotropes (each preferably present in the composition an amount from about 0.5 M to about 6 M);
- b) one or more detergents (each preferably present in the composition an amount from about 0.1% to about 1%);
- c) one or more chelators (each preferably present in the composition in an amount from about 0.01 mM to about 1 mM);
- d) one or more reducing agents (each preferably present in the composition in an amount from about 0.05 M to about 0.3 M); and
- e) one or more defoaming agents (each preferably present in the composition in an amount from about 0.0001% to about 0.3%).

Id. at 4:29–39 (added formatting). Additional, optional components include buffers, short-chain alkanols, and additional compounds or reagents, including nucleic acids. *Id.* at 5:28–67. The '240 patent also lists examples for each of chaotropes, detergents, chelators, reducing agents, defoaming agents, and other components. *Id.* at 4:38–5:65.

D. Claimed Subject Matter

Independent claims 1 and 35, reproduced below, are representative.

1. A aqueous composition comprising: a) one or more chaotropes; b) one or more detergents; c) one or more reducing agents; d) one or more chelators; and e) one or more buffers, each present in an amount sufficient to denature one or more proteins, inactivate one or more nucleases, kill one or more pathogens, or prevent one or more nucleic acids from degrading in a sample suspected of containing nucleic acids, when the sample is contacted with the composition.

Ex. 1001, 32:11–18.

35. A method for preparing one-step aqueous formulation adapted to obtain a population of polynucleotides from a biological sample suspected of containing nucleic acids, comprising contacting the sample with an amount of the one-step aqueous formulation effective to:

at least substantially kill or inactivate potentially-infectious pathogens in the sample;

lyse a portion of cells to release RNAs and/or DNAs from the sample; and

substantially inhibit or prevent the released polynucleotides in the sample from further hydrolysis or enzymatic degradation, modification, or inactivation,

so as to obtain the population of polynucleotides from the sample.

Id. at 36:4–17.

E. Asserted Challenges to Patentability

Petitioner challenges the patentability of claims 1–35 as follows

(Pet. 9):

Claims Challenged	35 U.S.C. §²	Reference(s)/Basis
1, 2, 5–11, 16, 21–30, 32, 33, 35	§ 102(b)	Birnboim, ³
1, 2, 4–14, 16, 21–30, 32, 33, 35	§ 103(a)	Birnboim
3	§ 103(a)	Birnboim, Chen, ⁴
15	§ 103(a)	Birnboim, Mori ⁵
16	§ 103(a)	Birnboim, Helftenbein ⁶
17	§ 103(a)	Birnboim, Chirgwin ⁷
18–20	§ 103(a)	Birnboim, Das, ⁸ Chen, Wagh ⁹
31	§ 103(a)	Birnboim

² The Leahy-Smith America Invents Act (“AIA”), Pub. L. No. 112–29, 125 Stat. 284, 287–88 (2011), revised 35 U.S.C. § 103 effective March 16, 2013. Petitioner treats the challenged patent as having an effective filing date prior to the effective date of the applicable AIA amendments, and this is not contested by Patent Owner. Accordingly, we refer to the pre-AIA versions of 35 U.S.C. §§ 102, 103.

³ Birnboim, US 2004/0038269 A1, published Feb. 26, 2004. Ex. 1003.

⁴ Chen et al., US 2007/0202511 A1, published Aug. 30, 2007. Ex. 1027.

⁵ Mori, WO 2005/111210 A1, published Nov. 24, 2005. Ex. 1011.

⁶ Helftenbein, US 6,776,959 B1, Aug. 17, 2004. Ex. 1019.

⁷ Chirgwin et al., “Isolation of Biologically Active Ribonucleic Acid from Sources Enriched in Ribonuclease,” *BIOCHEM.* 18:5294–99 (1979). Ex. 1015.

⁸ Das et al., US 2005/0123928 A1, published June 9, 2005. Ex. 1008.

⁹ Wagh et al., WO 2004/104181 A2, published Dec. 2, 2004. Ex. 1022.

Claims Challenged	35 U.S.C. § ²	Reference(s)/Basis
31	§ 103(a)	Birnboim, Koller ¹⁰
34	§ 103(a)	Birnboim, Chirgwin, Farrell ¹¹

In support of its patentability challenge, Petitioner relies on the Declaration of Richard F. Taylor, Ph.D. (Ex. 1002). In support of its position, Patent Owner relies on the Declaration of Louis DeFilippi, Ph.D. (Ex. 2001).

II. ANALYSIS

A. *Level of Ordinary Skill in the Art*

In determining the level of skill in the art, we consider the type of problems encountered in the art, the prior art solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field. See *Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986); see also *Orthopedic Equip. Co. v. U.S.*, 702 F.2d 1005, 1011 (Fed. Cir. 1983).

Petitioner asserts that

A person of ordinary skill in the art . . . 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

¹⁰ Koller, WO 91/02740, published Mar. 7, 1991. Ex. 1016.

¹¹ Robert E. Farrell, Jr., Ph.D., “RNA Methodologies: A Laboratory Guide for Isolation and Characterization,” (3rd Ed., 2005). Ex. 1026.

extraction formulations, and the literature concerning nucleic acid extraction and analysis.

Pet. 7 (citing Ex. 1002 ¶ 38). Patent Owner does not dispute Petitioner's proposed definition at this stage. Prelim. Resp. 7.

For purposes of this Decision, at this stage of the proceeding, we accept Petitioner's proposed definition of the person of ordinary skill in the art, which is not substantively opposed by Patent Owner and appears to be consistent with the level of skill in the art reflected in the prior art of record and the disclosure of the '240 patent. *Cf. Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) ("the prior art itself [may] reflect[] an appropriate level" as evidence of the ordinary level of skill in the art) (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp.*, 755 F.2d 158, 163 (Fed. Cir. 1985)).

B. Claim Construction

In an *inter partes* review, we construe the challenged claims under the framework set forth in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc). See 37 C.F.R. § 42.100(b). Under this framework, claim terms generally are given their ordinary and customary meaning as would be understood by one with ordinary skill in the art in the context of the specification (including other claims), the prosecution history, and even extrinsic evidence including expert and inventor testimony, dictionaries, and learned treatises, although extrinsic evidence is less significant than the intrinsic record. *Phillips*, 415 F.3d at 1312–19. Usually, the specification is dispositive, and it is the single best guide to the meaning of a disputed term. *Id.* at 1315.

Only those claim terms that are in controversy need to be construed, and only to the extent necessary to resolve the controversy. *Nidec Motor*

Corp. v. Zhongshan Broad Ocean Motor Co., 868 F.3d 1013, 1017 (Fed. Cir. 2017); *see also U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1568 (Fed. Cir. 1997) (holding claim construction is not necessary when it is not “directed to, or has been shown reasonably to affect, the determination of obviousness”).

Neither Petitioner nor Patent Owner offer any position on the construction of any claim term. *See* Pet.; Prelim. Resp. 7.

On this record, and for purposes of this Decision, we decline to construe any claim terms beyond the limited extent we do so below in our analysis, because it is not necessary to do so in reaching our decision on institution.

C. Principles of Law

Petitioner challenges claims under 35 U.S.C. §§ 102 and 103. A claim is anticipated under § 102 only if each limitation in the claim is found in a single prior art reference, arranged as recited in the claim. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008). A claim is unpatentable under 35 U.S.C. § 103 if “the differences between the subject matter sought to be patented 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.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) if in evidence, objective evidence of nonobviousness, i.e., secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

A party that petitions the Board for a determination of unpatentability based on obviousness must show that “a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.” *In re Magnum Oil Tools International, Ltd.*, 829 F.3d 1364, 1381 (Fed. Cir. 2016) (quotations and citations omitted). “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) as “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) (citing *Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1326–27 (Fed. Cir. 2008)) (discussing the burden of proof in *inter partes* review).

D. Asserted Anticipation by Birnboim

Petitioner asserts that Birnboim anticipates claims 1, 2, 5–11, 16, 21–30, 32, 33, and 35. Pet. 9–35. Patent Owner disputes Petitioner’s challenge. Prelim. Resp. 7–36. Based on this record, we determine Petitioner has met its burden to establish a reasonable likelihood of prevailing on this ground for at least one claim.

1. Birnboim (Ex. 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 “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. *See id.* ¶¶ 11, 22, 27, 64, 114–122. Birnboim further teaches that the composition also reduces the viscosities of samples facilitating the extraction and recovery of nucleic acids. *See id.* ¶ 11 (stating the composition “contains an agent that rapidly reduces the viscous properties of mucin, greatly facilitating the extraction of nucleic acids contained within”), ¶ 64 (“The composition of the invention can also include one or more reducing agents, which can reduce sample viscosity, thereby making nucleic acid recovery an easier process.”).

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 “nucleic acid-preserving 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 treats a portion of samples prepared using the nucleic acid-preserving solution with proteinase K, removes insoluble matter by centrifugation, and precipitates the DNA with ethanol prior to subjecting the DNA to agarose gel electrophoresis and ethidium bromide staining to find “the characteristic band of chromosomal DNA present in all samples.” *Id.* ¶ 117, Fig. 1. In Examples 5 and 6, Birnboim prepares “minimally purified DNA” from samples prepared using the nucleic acid-preserving solution by centrifuging the samples to remove insoluble material and precipitating the DNA with ethanol prior to using polymerase chain reactions to detect the DNA. *Id.* ¶¶ 118–121.

2. Analysis

For purposes of this Decision, we focus on the independent claims, and particularly claim 1. Petitioner provides a detailed analysis of where each element of claim 1 is found in Birnboim. Pet. 13–19. Specifically, Petitioner asserts that Birnboim’s Example 3 discloses an aqueous composition comprising the one or more chaotropes, one or more detergents, one or more reducing agents, one or more chelators, and one or more buffers, as recited in the claim. *Id.* at 13–18. Petitioner also asserts that “Birnboim’s reagents are present in an amount sufficient to perform the claimed functions.” *Id.* at 18–23 (heading capitalization normalized and underlining omitted).

Patent Owner counters that Birnboim does not disclose the claimed composition because it does not teach “the use of chaotropes and detergents as individual and separate components.” Prelim. Resp. 9–11. Patent Owner also contends Birnboim does not expressly disclose killing pathogens with its composition. *Id.* at 11–20. Patent Owner further asserts Birnboim does not disclose “a composition as-claimed with the claimed reagents ‘present in an amount sufficient to perform’ the functional claim limitations” of claim 1. *Id.* at 20–32 (heading capitalization normalized and emphasis omitted).

On this record, and at this stage of the proceeding, Petitioner has shown sufficiently Birnboim discloses each limitation of claim 1. See Pet. 17–18 (table showing “Birnboim Example 3 discloses each of claim 1’s limitations (a)-(e) together in an aqueous composition”), 18–19 (pointing to Birnboim’s Examples 4–6 as confirming the amounts of the compounds used in the composition in Example 3 perform the functions recited in claim 1). We address below Patent Owner’s counterarguments, which do

not undermine the adequacy of Petitioner's showing for purposes of trial institution.

Patent Owner argues that Birnboim neither teaches “the use of chaotropes and detergents as individual and separate components” nor explains why denaturing agents urea and SDS were selected for the exemplary composition in Example 3. Prelim. Resp. 9–11. Patent Owner's argument is unavailing.

As Patent Owner acknowledges, the exemplary composition in Birnboim's Example 3 includes “a denaturing agent that works as a chaotrope (urea) and a second denaturing agent that works as a detergent (SDS).” Prelim. Resp. 11. It is of no import that Birnboim refers to these reagents generally as “denaturing agents” where it is not contested that urea is a chaotrope and SDS is a detergent. *Id.* Furthermore, Birnboim's identification of these reagents generally as “denaturing agents” (Ex. 1003 ¶¶ 20, 68) does not matter because, based on this record, it is apparent that an ordinarily skilled artisan would understand the identity of chaotropes and detergents and their use for isolating nucleic acid.

For example, as Dr. Taylor points out, Koller (Ex. 1016) teaches “nucleic acid releasing compositions containing a chaotrope, detergent, reducing agent, and chelator salt that could keep nucleic acids stable for months.” Ex. 1002 ¶ 53 (citing Ex. 1016, 7:1–5). According to Koller, “[t]he chaotropic component of the nucleic acid releasing composition is both an effective protein denaturant and a strong inhibitor of nucleases. The effect of a chaotropic agent on growing cells is an almost instantaneous dissolution of the cells.” Ex. 1016, 7:19–23. Koller teaches urea is a useful chaotropic agent. *Id.* at 7:23–25. Koller also teaches that for the nucleic acid releasing composition, it is “beneficial to incorporate a surface-active

anionic detergent to further aid in lysis and disruption of the cells,” and that SDS is such a detergent. *Id.* at 8:8–15. Thus, we are persuaded that an ordinarily skilled artisan would have understood the individual properties and uses of urea as a chaotrope and SDS as a detergent for isolating nucleic acid. *See* Pet. 4–7 (State of the Prior Art).

Patent Owner points out that the exemplary composition of Birnboim’s Example 3 includes ethanol and other “unexplained components . . . not claimed in the composition of claim 1, including LiCl and NaOAc.” Prelim. Resp. 11. Patent Owner is correct; but that does not undercut Petitioner’s anticipation argument. Challenged claim 1 is directed to an aqueous composition “comprising” five categories of reagents. Because of the open-ended transition phrase “comprising,” we agree with Petitioner that “[t]he claimed composition includes the listed reagents but does not exclude others.” Reply 4. Indeed, just like the exemplary composition in Example 3 of Birnboim, challenged claim 11, which indirectly depends from claim 1, recites ethanol (as the recited alkanol). Ex. 1001, 33:33–37. Furthermore, claim 12, depending from claim 11, recites that the alkanol can be “present in an amount from about 1 to about 25% (vol./vol.).” *Id.* at 33:38–40.

Patent Owner argues that although Birnboim teaches the use of antimicrobial agents, and preferably ethanol, the composition of Example 3 includes only 30% ethanol, which, Patent Owner asserts, “is not sufficient to have a bactericidal effect, much less to kill viruses or vegetative bacteria.” Prelim. Resp. 14 (citing Ex. 2001 ¶¶ 21, 25–26). In addition, Patent Owner argues that SDS in Birnboim’s Example 3 “would not *necessarily* be expected to be bactericidal.” *Id.* at 27–28 (citing Ex. 2001 ¶¶ 29, 31, 33–35). Dr. DeFilippi testifies that SDS “is quite poor as a lysis agent,” because “[d]uring prolonged SDS interaction” only “25% of the ribonucleic acid and

40% of the deoxyribonucleic acid were released from the cells.” Ex. 2001 ¶¶ 29–30 (citing Ex. 2007¹²). Thus, according to Dr. DeFilippi, an ordinarily skilled artisan “would not rely on SDS in [an] aqueous composition to ‘kill pathogens’ in a sample because the composition would not render the sample safe for handling or transport.” *Id.* ¶ 30. We do not find Dr. DeFilippi’s testimony to bear the weight required of it.

Exhibit 2007 shows “the structural alterations . . . occur[red] in *E. coli* during its interaction with a comparatively low concentration of detergent, i.e. with 0.05% SDS.” Ex. 2007, 5. This concentration is substantially lower than the 0.6% SDS used in Birnboim’s Example 3. Ex. 1003 ¶ 115. Nevertheless, as Petitioner argues, even at this low concentration of SDS, there was reported dissolution of bacterial plasma membranes and release of nucleic acids, indicating that, “the cells are, of course, dead.” Reply 3 (citing Ex. 2007, 5, 11, 13, Figs. 2, 12).

We also are persuaded by Petitioner’s argument and evidence that “[l]ater publications citing to Ex. 2007 . . . reiterat[e] that SDS kills pathogens by lysing cells and releasing vital cellular components, just as Birnboim discloses.” *Id.* at 3. For example, Exhibit 1044, citing Exhibit 2007, states that “SDS has been shown more than 40 years ago to cause **significant bacterial membrane damage** with subsequent **release of DNA, RNA and protein.**” *Id.* at 3–4 (quoting Ex. 1044¹³). Thus, on this

¹² Woldringh et al., Effects of treatment with sodium dodecyl sulfate on the ultrastructure of *Escherichia coli*, J. BACTERIOL. 111:801–13 (1972) (Ex. 2007). Petitioner cites to the exhibit page number Patent Owner provides. For consistency, we do the same.

¹³ McDaniel et al., A Putative ABC Transporter Permease is Necessary for Resistance to Acidified Nitrite and EDTA in *Pseudomonas aeruginosa*

record, we find it reasonably established that the SDS in Birnboim's Example 3 would "kill pathogens," as required in challenged claim 1.

Patent Owner also argues that "Birnboim is focused on collection and preservation of nucleic acids from native human cells, not pathogens." Prelim. Resp. 12–13.¹⁴ According to Patent Owner, "[t]he amount of extracted nucleic acid needed for analysis [in Birnboim] is small and does not require lysing all or even most of the cells in the sample." *Id.* at 12. Acknowledging Birnboim's express teaching to isolate nucleic acid "from a bacterium or a virus," Patent Owner argues this "off-hand reference . . . fails to expressly teach killing pathogens because extracting the small amount of DNA necessary for testing does not 'kill pathogens' in the meaning of the '240 Patent—to prevent 'dissemination of live infections pathogens.'" *Id.* at 15–16. Patent Owner's argument, again, is unavailing.

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

Patent Owner equates the claim language "kill pathogens" with complete sterilization of a sample "to prevent 'dissemination of live infections pathogens.'" Prelim. Resp. 15–16 (citing Ex. 1001, 2:21–22,

under Aerobic and Anaerobic Planktonic and Biofilm Conditions, *FRONTIERS IN MICROBIOL.* 7:1–14 (2016) (Ex. 1044).

¹⁴ In this context, we understand Patent Owner's reference to "human nuclease material" and "human cell nucleases" as indicating "nucleases" or, more commonly, "nuclei," as opposed to enzymes capable of cleaving the phosphodiester bonds between nucleotides of nucleic acids. The reference to "denaturing nucleases" on page 13 is ambiguous given the error in referring to "nuclei" by the term "nucleases."

6:42–45; Ex. 2001 ¶ 7). 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 similar arguments fail because “they are not based on limitations appearing in the claims”). Birnboim expressly discloses isolating nucleic acid from bacteria and viruses. Ex. 1003 ¶¶ 18, 22, 27. It does not suggest such isolation is non-destructive, and we presume that at least some pathogens are “killed” in the extraction process according to the plain and ordinary meaning of the term.

Dr. DeFilippi testifies that Birnboim fails to kill pathogens because it only references “bacteriostatic” and “bactericidal,” and does not teach killing “yeast or other fungi or viruses.”¹⁵ Ex. 2001 ¶ 18. On this record, we do not read the challenged claims as requiring the claimed composition to clear every sample of every type of pathogenic agent. *See* Ex. 1001, 27:35–29:46 (the ’240 patent itself disclosing killing bacteria only in Example 8).

To the extent Patent Owner implies that the term “kill pathogens” has a special meaning in the ’240 patent, Patent Owner has not proposed a specific construction of the term. Patent Owner argues “one of the major objectives of the ’240 Patent is to render the sample sufficiently or entirely non-pathogenic to allow safe handling and transport of the sample.” Prelim. Resp. 17–18 (citing Ex. 1001, 2:20–29, 3:39–46, 6:42–45, 9:27–36, 14:61–

¹⁵ Petitioner contends Dr. DeFilippi admitted that “[Birnboim] does not teach killing of anything but bacteria.” Reply 1 (citing Ex. 2001 ¶ 22). Patent Owner reasonably argues that Dr. DeFilippi merely stated that “the word ‘bactericidal’ itself (not Birnboim’s composition) ‘does not teach the killing of anything but bacteria.’” Sur-Reply 1 (citing Ex. 2001 ¶ 22). Birnboim, nevertheless, expressly teaches compositions comprising antimicrobial agents that “can be bacteriostatic, bactericidal or both.” Ex. 1003 ¶ 21.

64, 26:44–46; Ex. 2001 ¶ 36). Patent Owner, however, has not provided sufficient reasoned argument why we should import such description in the Specification into the challenged claims. Accordingly, on this record, we decline to do so. *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.”).

Considering the record as a whole, Petitioner persuades us that the exemplary composition in Birnboim’s Example 3 kills at least some bacteria and/or viruses. Thus, we find 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,” under its plain and ordinary meaning. *See* Ex. 1003 ¶ 27.

Patent Owner further contends that “nothing in Birnboim teaches using the ***claimed composition***, as opposed to utilizing additional unclaimed substances, to kill pathogens.” Prelim. Resp. 20. According to Patent Owner, Birnboim suggests that the unclaimed reagents LiCl and NaOAc “were important for one or more of the functions of denaturing one or more proteins, inactivating one or more nucleases, and preventing degradation of one or more nucleic acids,” as recited in challenged claim 1. *Id.* at 24 (citing Ex. 2001 ¶ 39). Thus, Patent Owner argues Birnboim does not teach “the combination of only two denaturing agents in Birnboim’s Example 3, without the unclaimed ethanol and without other unexplained components of Birnboim’s Example 3 composition that likewise are not claimed in the composition of claim 1, including LiCl and NaOAc, would be sufficient to

perform the claimed functions.” *Id.* at 11. Patent Owner’s argument is unavailing.

At the time of the ’240 patent, ordinarily skilled artisans were well versed in the methods and reagents used in isolating nucleic acids. See Ex. 1002 ¶¶ 49–63; *see also, e.g.*, Ex. 1004, 192–193 (use of NaOAc to wash/precipitate nucleic acids); Ex. 1009, 1:66–68 (the same); Ex. 1013, 4.3.1, 4.5.2 (use of LiCl for selective precipitation of RNA and as buffer component); Ex. 1018, 15:55–67 (commercial RNA extraction kits comprising LiCl in combination with chaotrope); Ex. 1016, 8:26–9:2 (“Typically, the nucleic acid releasing composition will further include salt . . . The type of salt included in the nucleic acid releasing composition is not critical . . . however, optimum results are obtained with . . . [NaOAc].”). Given the extensive background knowledge in the field, we reject Patent Owner’s implication that an ordinarily skilled artisan at the time of the invention would not have understood the role of LiCl or NaOAc in Birnboim’s Example 3.

Furthermore, we note that Petitioner’s argument and Dr. DeFilippi’s testimony at paragraph 39—directed to the functions of denaturing proteins, inactivating nucleases, and preventing degradation of nucleic acids—does not implicate LiCl and NaOAc in the lysis of cells, and we are not directed to any evidence contrary to the reasonable determination that the composition without these components would kill bacteria. Additionally, with respect to ethanol, Petitioner elsewhere relies on Dr. DeFilippi’s testimony at paragraph 21 that “[E]thanol is not sufficient to kill pathogens except in very high concentrations. 30% ethanol (by any measure of percent) is not sufficient to have a bactericidal effect, much less to kill viruses or vegetative bacteria or fungi.” Prelim. Resp. 14 (citing Ex. 2001

¶ 21). Yet, as detailed above, it is reasonably apparent that the relied on composition lyses cells. Accordingly, on this record, the fact that Birnboim's exemplary composition includes additional unclaimed substances—LiCl, NaOAc, and ethanol—does not undercut that the urea (chaotrope), SDS (detergent), sodium ascorbate (reducing agent), CDTA (chelator), and TRIS-HCl (buffer) are present in amounts sufficient to “kill one or more pathogens,” thereby meeting the functional requirement of the claim.

Patent Owner refers to Birnboim for “stat[ing] in Example 4 that the enzyme proteinase K is added to the solution of Example 3 to prepare the solution for precipitating DNA.” Prelim. Resp. 23 (citing Ex. 1003 ¶ 117). This, according to Patent Owner, 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.* (citing Ex. 2001 ¶¶ 40–45, 47). We disagree.

Birnboim discloses that

[l]ow specificity proteases such as proteinase K are frequently used in the purification of nucleic acids. Since proteases are themselves proteins, their action can be inhibited by denaturing agents. Thus, 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.

Ex. 1003 ¶ 69 (emphasis added). Thus, Birnboim as a whole shows the exemplary composition in Example 3 contains denaturing agents at concentrations sufficient to denature proteins in the saliva sample without rendering the later added proteinase K inoperable. *See also* Ex. 1016, 7:19–25 (teaching chaotropic agent, such as urea used in the exemplary

composition in Birnboim's Example 3, "is both an effective protein denaturant and a strong inhibitor of nucleases").

Patent Owner further asserts that "Birnboim does not necessarily prevent degradation of nucleic acids." Prelim. Resp. 31–32 (citing Ex. 2001 ¶¶ 13, 46–50). As support, Patent Owner points out that Birnboim states DNA is stable for "desirably more than 60 days" when ascorbic acid, a reducing agent preferred in Birnboim, is present and "desirably more than 360 days" when "the composition does not contain ascorbic acid." *Id.* at 31 (citing Ex. 1003 ¶¶ 13, 25). Patent Owner also points out that Birnboim defines "stable" when referring to nucleic acid as retention of at least about 50% of the initial amount. *Id.* (citing Ex. 1003 ¶ 45). Thus, according to Patent Owner, it is inaccurate to equate "stabilizing nucleic acid" in Birnboim with "'prevent[ing] one or more nucleic acids from degrading' as required in claim 1." *Id.* at 31–32; Ex. 1001, 32:16–17. Patent Owner's argument, again, is unavailing.

Dr. DeFilippi contrasts the disclosure of Birnboim ("at least about 50%" retention) with that of the '240 patent ("desirable" to have "at least about 70%" to "at least about 98% of the polynucleotides contained within the stored sample will not be degraded upon prolonged storage," such as "several days to several weeks," or "several weeks to even several months or more"). See Ex. 2001 ¶¶ 9–10 (citing Ex. 1001, 9:52–57, 10:30–46). These disclosures in the '240 patent Specification, however, are not the limitations of challenged claim 1; and Patent Owner does not provide sufficient reasoned argument why we should import them into the claim. In fact, Patent Owner has not proposed a construction of the phrase "prevent one or more nucleic acids from degrading" that is recited in claim 1.

Absent importing Patent Owner's narrower meaning for the phrase "prevent one or more nucleic acids from degrading," Birnboim's teaching that its chelating agents, reducing agents, and buffers prevent nucleic acid degradation are sufficient, with its Example 3, because it is reasonably established these components of the exemplary composition reduce nucleic acid degradation. Pet. 18–19; Ex. 1003 ¶¶ 13, 14, 19, 64, 66–68, 70–73.

Thus, on this record, and for purposes of this Decision, we find Petitioner has met its burden in showing that Birnboim discloses "prevent[ing] one or more nucleic acids from degrading" under the plain and ordinary meaning of this phrase.

Moreover, Patent Owner's position in the parallel district court case undercuts its various arguments on the functional limitations of claim 1 here. In the district court, Patent Owner argued 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 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 this statement constitutes a prior admission that "Birnboim's compositions having these five reagents perform the functions recited in claim 1 of the '240 patent." Pet. 23 n.3; *see also* Reply 4–5 (asserting Patent Owner's arguments in the Preliminary Response are inconsistent with its district court complaint). Patent Owner responds that it "does not admit anything regarding what was known in the art at the

time of the invention,” but refers to “what is known in the art **today** because of PO’s disclosures.” Sur-Reply 4.

On this record, particularly in light of Birnboim’s disclosure of compositions comprising all the claimed reagents and the general skill in the art at the time of the alleged invention regarding methods and reagents for isolating nucleic acids, we provisionally find that the “common knowledge [of] one skilled in the art” referred to in the district court complaint encompasses the knowledge as of the priority date of the ’240 patent. Thus, Patent Owner’s statement in the district court complaint demonstrates the exemplary composition in Birnboim’s Example 3, having the five reagents recited in challenged claim 1, performs the functions recited therein.

In sum, based on the current record and for purposes of this Decision, Petitioner has met its burden in showing that Birnboim discloses each limitation of claim 1. Pet. 13–23. Because there is a reasonable likelihood that Petitioner would prevail in its challenge of claim 1 as anticipated by Birnboim, we institute an *inter partes* review as to all challenges raised in the Petition. See Patent Trial and Appeal Board Consolidated Trial Practice Guide 64 (Nov. 2019)¹⁶ (“The Board will not institute on fewer than all claims or all challenges in a petition.”). We nevertheless offer the following observations on Petitioner’s challenge of the other independent claim, claim 35.

Independent claim 35 differs from claim 1 in that it is a method claim, but also in that provides no limit to the composition except that it is a “one-step aqueous formulation” that, when contacting a biological sample

¹⁶ Available at <https://www.uspto.gov/sites/default/files/documents/tpgnov.pdf>

suspected of containing nucleic acids, is “effective to” perform the recited functions. These recited functions are similar to recited functions of claim 1, which required the composition to meet at least one. Specifically, claim 35 requires the “one-step aqueous formulation” to “at least substantially kill or inactivate potentially-infectious pathogens,” “lyse a portion of cells to release RNAs and/or DNAs,” and “substantially inhibit or prevent the released polynucleotides . . . from further hydrolysis or enzymatic degradation, modification, or inactivation” in order “to obtain the population of polynucleotides from the sample.”

Petitioner again provides an analysis where each element of the claim is found in Birnboim, albeit with frequent reference back to the ground as applied to claim 1. Pet. 33–35. Petitioner again relies on Birnboim’s Example 3 as disclosing an aqueous composition meeting each limitation of the claim. *Id.*

Patent Owner argues that Petitioner has failed to establish that Birnboim’s composition functions to “substantially kill or inactivate potentially-infectious pathogens in the sample.” Prelim. Resp. 33–34. Patent Owner further argues that even if Birnboim were “found to teach killing some pathogens, discussion of an antimicrobial agent in Birnboim . . . is limited to inhibiting bacteria (bacteriostatic) agents, at most, not to agents that would kill other pathogens besides bacteria.” *Id.* at 34 (citing Ex. 2001 ¶ 22). Patent Owner further argues, “[t]hus Birnboim cannot disclose ‘substantially kill[ing] or inactivat[ing]’ the entire set of potentially-infectious pathogens in a sample, which may include viruses, yeast, or fungi, in addition to bacteria.” *Id.*

As discussed in regard to claim 1, it is reasonably established that the relied on composition kills at least some pathogens in the process of

extracting nucleic acids. It is less clear, on this record, whether the composition is effective to “substantially kill or inactivate” because it is neither apparent what fraction of potential infectious pathogens must be disrupted in Birnboim’s method to detect the released nucleic acids nor what fraction is required for “substantially kill[ing] or inactivat[ing]” a pathogen. We further note that Patent Owner’s position that the claim requires this effect across “the entire set of potentially-infectious pathogens in a sample, which may include viruses, yeast, or fungi, in addition to bacteria” does not appear to be well founded.

Patent Owner argues that Petitioner has failed to establish that Birnboim’s composition “functions to ‘substantially inhibit or prevent the released polynucleotides in the sample from further hydrolysis or enzymatic degradation, modification, or inactivation.’” Prelim. Resp. 34.

As discussed in regard to claim 1, it is reasonably established that the relied on composition inhibits the released polynucleotides from further hydrolysis or enzymatic degradation. Less clear, however, is what is required by “substantially inhibit or prevent,” and whether that is met by Birnboim’s Example 3.

Patent Owner argues that Birnboim’s Example 3 composition “does not perform the claimed functional limitations in one step” because “Birnboim requires additional steps (adding a protein digester, then purifying the sample, and then precipitating the DNA) before the nucleic acids of the sample are detectable by a nucleic acid test.” Prelim. Resp. 35 (citing Ex. 1003 ¶¶ 83, 117, 119; Ex. 2001 ¶¶ 51–52). Patent Owner relies on claim 35 reciting that the “one step” formulation is effective to carry out the recited “substantially killing or inhibiting,” “lys[ing],” and “substantially inhibit[ing] or prevent[ing]” steps “so as to obtain [a] population of

polynucleotides from the sample” as requiring the polynucleotides to be sufficiently purified to be detectable by a nucleic acid test. *Id.* at 35–36.

Patent Owner’s “one step” argument falls short because it not apparent that the plain language of “obtain[ing] [a] population of polynucleotides from the sample” requires anything more than “lys[ing] . . . cells to release RNAs and/or DNAs” and preserving the “released polynucleotide” by “substantially inhibit[ing] . . . further hydrolysis or enzymatic degradation, modification, or inactivation.”

The Parties are invited to explore these issues relating to claim 35 at trial.

Patent Owner provides no additional argument with respect to the challenge to claims 2, 5–11, 16, 21–30, 32, and 33, all of which depend, directly or indirectly, from independent claim 1. The Parties are encouraged to further address these claims, and issues raised, as necessary to fully develop the record during trial.

E. Asserted Obviousness over Birnboim Alone and in View of Additional References

Petitioner challenges claims 1, 2, 4–14, 16, 21–30, 32, 33, and 35 as unpatentable for having been obvious over Birnboim. Pet. 35–52. Patent Owner only addresses the challenge as applied to independent claim 1 and independent claim 35. Prelim. Resp. 36–42. 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 do not address this challenge as applied to claim 1.

We offer the following observations on Petitioner’s challenge of claim 35 as obvious over Birnboim. As discussed above, claim 35 requires

the “one-step aqueous formulation” to “at least substantially kill or inactivate potentially-infectious pathogens,” “lyse a portion of cells to release RNAs and/or DNAs,” and “substantially inhibit or prevent the released polynucleotides . . . from further hydrolysis or enzymatic degradation, modification, or inactivation” in order “to obtain the population of polynucleotides from the sample.”

Petitioner contends that a person of ordinary skill in the art “would have understood that Birnboim’s successful preservation of nucleic acids involves using an amount of Birnboim’s composition effective to kill or inactivate the pathogens and lyse the sample of cells to release polynucleotides without hydrolyzing, enzymatically degrading, or modifying the released polynucleotides.” Pet. 50 (citing Ex. 1003 ¶ 84; Ex. 1002 ¶ 239). Petitioner also contends that a person of ordinary skill in the art would have found it obvious to “apply[] Birnboim’s methods and compositions to yield the predictable results of stabilizing and preserving nucleic acids so as to obtain a population of polynucleotides.” *Id.* (citing Ex. 1003 ¶¶ 27, 84, 115–121; Ex. 1002 ¶¶ 239–240).

Patent Owner argues that “Petitioner fails to make any argument as to how a [person of ordinary skill in the art] would supposedly modify any example of Birnboim to fill the gaps in Birnboim’s disclosure and to perform the [recited] functions . . . in particular the requirements of killing pathogens and of achieving the other functions of claim 35.” Prelim. Resp. 42.

The obviousness challenge to claim 35 relying on Birnboim appears stronger than that for anticipation because, on this record, there is an apparent reasonable basis set forth for a skilled artisan to use an effective amount of Birnboim’s compositions to kill or inactivate any pathogens that

may be present, to lyse cells to release polynucleotides, and to preserve the released polynucleotides from being hydrolyzed, enzymatically degraded, with a reasonable expectation of success.

Petitioner also challenges other claims as obvious over combinations of Birnboim and other prior art references. Pet. 50–69. Patent Owner does not address these challenges on the merits. Prelim. Resp. 42–43. Because we institute an *inter partes* review as to all challenges raised in the Petition, the Parties are encouraged to further address the relevant issues to fully develop the record during trial.

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 even if asserted in the Preliminary Response. In addition, nothing in this Decision authorizes Petitioner to supplement information advanced in the Petition in a manner not permitted by the Board’s Rules.

III. CONCLUSION

Based on the current record, we find Petitioner has demonstrated a reasonable likelihood that it would prevail with respect to at least one claim challenged in the Petition.

At this stage of the proceeding, the Board has not made a final determination as to the construction of any claim term or the patentability of any challenged claim. Our view with regard to any conclusion reached in the foregoing could change upon further development of the record during trial.

IV. ORDER

It is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on all challenged claims of the '240 patent based on all the asserted 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 commencing on the entry date of this decision.

IPR2021-00854
Patent 8,669,240 B2

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