Trials@uspto.gov
571-272-7822

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PFIZER, INC.,
Petitioner,

v.

CHUGAI PHARMACEUTICAL CO. LTD.,
Patent Owner.

Case IPR2017-01357
Patent 7,332,289 B2

Before GRACE KARAFFA OBERMANN, RAMA G. ELLURU, and JACQUELINE T. HARLOW, *Administrative Patent Judges.*

HARLOW, *Administrative Patent Judge.*

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Pfizer, Inc. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–8 and 13 of U.S. Patent No. 7,332,289 B2 (Ex. 1001, "the '289 patent"). Paper 2 ("Pet."). Chugai Pharmaceutical Co. Ltd. ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp.") We have authority to determine whether to institute an *inter partes* review under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted unless 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."

For the reasons set forth below, we institute an *inter partes* review of claims 1–8 and 13 of the '289 patent.

A. Related Matters

The parties inform us of no related pending litigations. Pet. 3–4; Paper 5, 2–3. In addition to the instant proceeding, Petitioner has filed a petition for *inter partes* review of related U.S. Patent No. 7,927,815 B2 (IPR2017-01358). Pet. 3–4; Paper 5, 3.

B. The '289 Patent

The '289 patent, titled "Method of Purifying Protein," issued February 19, 2008, from U.S. Patent Application No. 10/471,374, which is the U.S. National Stage Application of International Application No. PCT/JP02/02248, filed on March 11, 2002. Ex. 1001, at [54], [45], [21], [22], [86]. The '289 patent claims priority to Japanese Patent Application No. 2001-067111, filed on March 9, 2001. *Id*. at [30].

The ’289 patent describes a “method for purifying proteins, more specifically [] a method for removing contaminant DNA from a sample containing a physiologically active protein such as antibody molecules.” Ex. 1001, 1:5–8.

The ’289 patent recognizes that methods for removing contaminant DNA from recombinant antibody drug formulations were known in the art. *See*, *e.g.*, *id.* at 1:35–43. The ’289 patent states, however, the chromatographic processes associated with known purification methods were “time-, labor- and cost-consuming, as well as being complicated. Moreover, they fail to provide stable results.” *Id*. at 1:44–47.

To address these shortcomings, the ’289 patent discloses the “surprising finding that contaminant DNA can be efficiently removed from a sample containing a physiologically active protein without using complicated chromatographic processes.” *Id.* at 1:59–62. In particular, the ’289 patent teaches that such a sample can be “converted into an acidic aqueous solution of low conductivity, neutralized by addition of a buffer to raise the pH to a neutral level, and then filtered through a filter to remove the resulting particles.” *Id.* at 1:59–66.

The ’289 patent explains that “[a]s used herein, ‘an acidic aqueous solution of low conductivity’ generally refers to an aqueous solution of pH 1.5 to pH 3.9, . . . which bas a molarity of 0 to 100 mM, . . . or has an ionic strength of 0 to 0.2, . . . or has a conductivity of 0 to 300 mS/m . . . .” *Id.* at 5:29–35. The ’289 patent further discloses that “[t]he acidic aqueous solution may be selected from aqueous solutions of hydrochloric acid, citric acid, acetic acid and other acids.” *Id.* at 5:35–37. The ’289 patent also

states that "[t]he type, conductivity and pH of acidic aqueous solution of low conductivity will vary depending on the type of physiologically active protein or antibody to be purified. Those skilled in the art will readily determine optimal conditions for these parameters in preliminary experiments as described herein." *Id.* at 5:37–42.

With regard to the neutralization and particle removal steps of the above-described purification procedure, the '289 patent teaches that neutralization of the solution containing a physiologically active protein to a "neutral pH level" "in turn, produces particles (i.e., becomes clouded). These particles may be removed by filtration through a filter to ensure efficient removal of contaminant DNA." *Id.* at 6:4–8. The '289 patent exemplifies a "1.0–0.2 μm Cellulose Acetate Filter System (Corning) or TFF" as filters available for particle filtration. *Id.* at 6:10–15.
The '289 patent goes on to state that "[w]ithout being bound by any particular theory, the inventors of the present invention estimate that each of these particles is a conjugate formed between physiologically active protein and DNA." *Id.* at 6:16–19.

C. Illustrative Claim

Claim 1, reproduced below, is the sole independent claim in the ’289 patent, and is illustrative of the claimed subject matter.

> 1. A method for removing contaminant DNA in an antibody-containing sample, which comprises the followings [sic] steps:
>
> 1) applying the antibody-containing sample to affinity chromatography on Protein A or Protein G;
>
> 2) eluting the antibody with an acidic aqueous solution of low conductivity having a molarity of 100 mM or less;
>
> 3) neutralizing the eluate from step (2) to form particles by addition of a buffer to raise the pH to 4 to 8, wherein the molarity of the neutralized eluate is 100 mM or less; and
>
> 4) removing the particles to thereby remove contaminant DNA from the antibody-containing sample.

Ex. 1001, 12:45–58.

D. Evidence Relied Upon

Petitioner relies upon the following as prior art reference (Pet. 5):

Shadle	WO 95/22389	Aug. 24, 1995	(Ex. 1003)

Petitioner also relies on the Declaration of Todd M. Przybycien, Ph.D. (Ex. 1002).

E. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–8 and 13 of the '289 patent on the following grounds (Pet. 5):

Claim(s)	Basis	References
1–8 and 13	§ 102(b)	Shadle
1–8 and 13	§ 103(a)	Shadle

II. ANALYSIS

A. Level of Ordinary Skill in the Art

The level of skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

According to Petitioner, a person of ordinary skill in the art at the time of the invention would have had "at least a graduate degree, such as a Ph.D., and several years of postgraduate training or practical experience in a relevant discipline such as biochemistry, process chemistry, protein chemistry, chemical engineering and/or biochemical engineering, among others." Pet. 6 (citing Ex. 1002 ¶¶ 28–29). Petitioner further contends that "[s]uch a person would also understand that protein purification is a multidisciplinary field, and could take advantage of the specialized skills of others using a collaborative approach." *Id*. (citing Ex. 1002 ¶¶ 28–29). Patent Owner does not address Petitioner's position on this matter and does

not propose its own description for a person of ordinary skill in the art at the time of the invention.

At this stage in the proceeding, we determine that Petitioner's description of the level of ordinary skill in the art is comparable to the level of skill reflected in the asserted prior art. On this record, we find that the applied prior art reflects the appropriate level of skill at the time of the claimed invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001). We have reviewed the credentials of Dr. Przybycien (Ex. 1002, Attachment A), and, at this stage in the proceeding, we consider him to be qualified to opine on the level of skill and the knowledge of a person of ordinary skill in the art at the time of the invention.

B. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2142 (2016) (affirming applicability of broadest reasonable construction standard to *inter partes* review proceedings). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention, in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

"acidic aqueous solution of low conductivity having a molarity of 100 mM or less"

Claim 1 of the '289 patent recites, in pertinent part, "eluting the antibody with an acidic aqueous solution of low conductivity having a molarity of 100 mM or less."

In conjunction with its anticipation argument, Petitioner asserts:

> The specification of the '289 patent defines "an acidic aqueous solution of low conductivity" as:
>
> [G]enerally refer[ing] to an aqueous solution of pH 1.5 to pH 3.9, preferably-of [sic] pH 2.0 to pH 3.9, more preferably of pH 2.0 to pH 3.0, which has a molarity of 0 to 100 mM, preferably 0 to 50 mM, more preferably 0 to 30 mM, or has an ionic strength of 0 to 0.2, preferably 0 to 0.12, or has a conductivity of 0 to 300 mS/m, preferably 0 to 200 mS/m, more preferably 0 to 150 mS/m.

Pet. at 30 (alterations in original) (quoting Ex. 1001, 5:29–35).

Petitioner additionally contends that the term "molarity" refers to "[a] measure of the concentration of a given solute within a solution in terms of the moles of that solute contained per liter of solution." *Id.* at 24. Petitioner appears to recognize, however, that "molarity" may take account of multiple solutes present in a solution. Specifically, Petitioner proposes that the term "molarity," as it is used in the greater claim phrase "an acidic aqueous solution of low conductivity having a molarity of 100 mM or less," should be understood to mean "that the molarity of the acidic aqueous solution is 100 mM or less, without considering any effects of the contaminant DNA or protein from the sample." *Id.* at 24–25.

Patent Owner responds that the meaning of "molarity" "is not limited to the concentration of a single solute, as the '289 specification and file

history make clear in addressing the contributions of multiple solutes to the solution's molarity." Prelim. Resp. 12. Patent Owner goes on to point out that Petitioner must recognize that the "molarity" of a solution takes account of the various solutes present in a solution, rather than just a single solute, because Petitioner "adds the concentrations of tris and citrate (*i.e.*, two solutes) in determining [the] molarity" of the neutralized eluate in Shadle. *Id.* Patent Owner does not address Petitioner's contention that the claim phrase "an acidic aqueous solution of low conductivity having a molarity of 100 mM or less" excludes the contributions of any protein or contaminant DNA. *See id.* at 10–12. Nor does Patent Owner address Petitioner's assertion that the specification of the '289 patent defines "an acidic aqueous solution of low conductivity," other than to say that "Petitioner fails to address the construction of the claim term 'low conductivity.'" *Id.* at 15–16.

We agree with Petitioner that the specification of the '289 patent explains that the claim phase "an acidic aqueous solution of low conductivity" generally refers to:

> an aqueous solution of pH 1.5 to pH 3.9, preferably-of [sic] pH 2.0 to pH 3.9, more preferably of pH 2.0 to pH 3.0, which has a molarity of 0 to 100 mM, preferably 0 to 50 mM, more preferably 0 to 30 mM, or has an ionic strength of 0 to 0.2, preferably 0 to 0.12, or has a conductivity of 0 to 300 mS/m, preferably 0 to 200 mS/m, more preferably 0 to 150 mS/m.

Ex. 1001, 5:27–35. We observe that this disclosure broadly provides that a solution of pH 1.5 to pH 3.9 as well as a molarity of 0 to 100 mM *or* an ionic strength of 0 to 0.2, *or* a conductivity of 0 to 300 mS/m qualifies as "an acidic aqueous solution of low conductivity." The greater phrase "an acidic aqueous solution of low conductivity having a molarity of 100 mM or less"

serves to narrow the scope of claim 1, however, by requiring that the recited solution both be of pH 1.5 to pH 3.9 and have a molarity of 0 to 100 mM. *See* Ex. 1005, 37–38 (Patent Owner representation during prosecution of the '289 patent that "a molarity of over 0.1 M" is of "higher conductivity" in order to distinguish prior art). Accordingly, we determine, for purposes of this decision, that the claim 1 phrase "an acidic aqueous solution of low conductivity having a molarity of 100 mM or less" encompasses an aqueous solution of pH 1.5 to pH 3.9, which has a molarity of 0 to 100 mM.

Turning to the meaning of the term "molarity," as it is used in claim 1, we determine that the plain language of the claims, as well as the specification of the '289 patent, indicates that the term "molarity" refers to the total concentration of solute present in the solution, rather than the concentration of one particular solute. Step (2) of claim 1 of the '289 patent requires "eluting the antibody with an acidic aqueous solution of low conductivity having a molarity of 100 mM or less." Ex. 1001, 12:50–51. By its plain language, this claim requirement refers to the overall molarity of the solution, and not of any particular solute in the solution.

Similarly, the specification of the '289 patent refers to the molarity of the complete solution, rather than one solute in that solution. *See, e.g., id.* at 4:61–66 ("As used herein, a 'neutral aqueous solution . . .' generally refers to an-aqueous [sic] solution . . . which has a molarity of 0 to 100mM"), 5:28–31 ("an 'acidic aqueous solution of low conductivity' generally refers to an aqueous solution . . . , which has a molarity of 0 to 100 mM"). The prosecution history of the '289 patent likewise references the molarity of the solution, rather than of a given solute in the solution. *See e.g.*, Ex.1005, 12

("an important feature of the present invention is to adjust pH value of the solution, the eluate, to from 4 to 8 while maintaining the molarity of the solution at 100mM or less."), 37 ("0.1 M buffer was used as an eluent, and 1 M Tris-HCl was used to adjust the pH of the eluted fraction, that is, the fact that 0.1 M and 1 M solutions were used means that the molarity of the eluted fration [sic] must be over 0.1 M (100 mM)").

With regard to Petitioner's further contention that the molarity of the acidic aqueous solution should be calculated without considering any effects of the contaminant DNA or protein from the sample (Pet. 24–25), we determine that, for purposes of institution, it is not necessary to decide this point. In this regard, we note that neither Patent Owner nor Petitioner affirmatively contends that contaminant DNA or protein is present in the recited solution *prior* to antibody elution. *See* Prelim. Resp. 17, n.3 ("Petitioner confusingly argues that contributions to molarity from protein or contaminant DNA, if considered, would be negligible to the buffer's molarity. . . . At best, Petitioner's expert purports to determine the contribution of protein and contaminant DNA in the eluate but not in the acidic aqueous solution, as claimed." (citations omitted)). Furthermore, Petitioner accounts for contaminant DNA and protein in the eluate produced by performing step (2) of claim 1. *See* Pet. 30, n.3 ("To the extent Chugai argues that molarity should be determined by considering contributions from the protein or contaminant DNA, Dr. Przybycien explains that such added contribution would be negligible (*i.e.*[,] less than 1 mM), and certainly not enough to raise the molarity of the ProSep A citrate elution buffer above the claimed 100 mM limit. Ex. 1002 ¶ 73."). Therefore, because there is no

controversy to resolve concerning the contribution of protein and contaminant DNA to the "acidic aqueous solution of low conductivity having a molarity of 100 mM or less," for purposes of this decision, we need not decide the issue. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("we need only construe terms 'that are in controversy, and only to the extent necessary to resolve the controversy'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

Accordingly, we determine, for purposes of this decision, that under the broadest reasonable interpretation, the claim phrase "an acidic aqueous solution of low conductivity having a molarity of 100 mM or less" encompasses an aqueous solution of pH 1.5 to pH 3.9, which has a molarity of 0 to 100 mM, and that molarity refers to the total concentration of solute present in the solution.

C. Prior Art Relied Upon: Overview of Shadle

Petitioner relies on the teachings of Shadle (Ex. 1003) as the basis for its patentability challenges in this proceeding.

Shadle discloses methods for the "purification of antibody molecule proteins" that employ "sequential steps of Protein A affinity chromatography, ion exchange chromatography, and hydrophobic interaction chromatography." Ex. 1003, Abstract. In this regard, Shadle teaches that a "purification protocol should not only provide a protein product that is essentially free of other proteins, . . . but also eliminate or

reduce to acceptable levels other host cell contaminants, DNA, RNA, potential pyrogens and the like." *Id.* at 9:12–16. In particular, Shadle discloses:

> The purified antibodies obtained by practicing the process of this invention have the following properties: 1) greater than 97% antibody protein by weight; 2) stable to proteolytic degradation at 4°C for at least three months; 3) low (< 0.1 E.U./mg protein) endotoxin; 4) low (< 1 pg/mg protein) DNA; 5) non-antibody protein < 5% by weight; and 6) virally inactive.

Id. at 14:21–27.

Shadle exemplifies the disclosed protein purification method by describing a procedure "for the isolation and purification of a monoclonal antibody against Respiratory Syncytial Virus (RSV)," identified as "RSHZ 19." *Id.* at 15:3–7. Shadle explains that this "process is designed to prepare RSHZ-19 of >95% purity while removing contaminants derived from the host cell, cell culture medium, or other raw materials." *Id.* at 15:7–9.

In Example IA, Shadle teaches the application of 100 liters of conditioned culture medium containing 0.8 grams per liter of RSHZ-19 monoclonal antibody to a previously equilibrated ProSep A affinity column. *Id*. at 21:4–8. Subsequent to washing with 15 liters of PBS/glycine, the "IgG was eluted by applying 15–20 liters of ProSep A elution buffer. Fractions of the non-bound peak and the elution peak were collected and assayed for IgG content using an HPLC assay. The eluate was approximately 15 liters in volume, and contained approximately 5 milligrams protein per milliliter." *Id.* at 21:9–13. Shadle identifies the

"ProSep Elution Buffer" as being composed of 25 mM citrate, and having pH 3.5. *Id.* at 20:10. Shadle additionally explains that "[t]he eluate fractions from the Protein A capture . . . are pooled based on the UV tracing on the chromatogram, and the entire peak is collected." *Id.* at 19:3–5.

Shadle further discloses that

> [i]mmediately after elution, the sample was adjusted to pH 3.5 by the addition of 2.5 M hydrochloric acid, held for approximately 30 minutes, and adjusted to pH 5.5 by the addition of approximately 350 milliliters of 1 M Tris base. After neutralizing to pH 5.5, the sample was filtered through a 0.1 micron Polygard CR filter in tandem with a sterile 0.2 micron Millipak 200, into a sterile container.

Id. at 21:15–19. Subsequently, the filtered sample was subject to cation exchange chromatography and hydrophobic interaction chromatography. *Id.* at 21:26–22:29.

D. Anticipation Ground of Unpatentability Based on Shadle

Petitioner asserts that claims 1–8 and 13 are anticipated under § 102(b) by Shadle. Pet. 26–43. In support of its assertion, Petitioner provides detailed explanations as to how Shadle discloses each claim limitation (*id.*) and relies upon the Przybycien Declaration (Ex. 1002) to support its positions. Patent Owner disagrees that Shadle anticipates the challenged claims. Prelim. Resp. 13–31.

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either expressly or inherently. *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1341 (Fed. Cir. 2016). Where a reference is silent regarding a given claim requirement, "such gap

in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Cont'l Can Co. USA 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. [Citations omitted.] If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

Id. at 1269 (alteration in original) (quoting *In re Oelrich*, 666 F.2d 578, 581 (C.C.P.A. 1981)).

Petitioner asserts that Shadle discloses methods for purifying monoclonal antibody samples that remove "contaminants derived from the host cell, cell culture medium, or other raw materials" (Ex. 1003, 15:7–9) and teaches in particular that the purified antibodies obtained have "low (< 1 pg/mg protein) DNA" (*id.* at 14:21–24). Pet. 27. Petitioner reasons, therefore, that Shadle "discloses that DNA is among the derived contaminants that are removed because the purified antibody product obtained by practicing the disclosed process has a reduced DNA concentration." *Id.* at 27–28 (citing Ex. 1002 ¶¶ 66–67).

Petitioner also contends that Shadle discloses "applying the antibody-containing sample to affinity chromatography on Protein A or

Protein G" (Ex. 1001, 12:48–49), as required by claim 1 of the '289 patent. Pet. 28. In particular, Petitioner points to Shadle's disclosure that

> [a] 5.0 liter (20 cm diameter by 16 cm length) *ProSep A affinity column* was equilibrated with PBS (see Table 1) at 5.2 liter/min. 100 liters of conditioned *culture medium containing* 0.8 grams per liter of RSHZ-19 *monoclonal antibody* was clarified by microfiltration as described above, and *applied to the column* at a flow rate of 5.2 liter/min.

Id. (quoting Ex. 1003, 21:4–8). Petitioner explains that the purification process disclosed by Shadle "is exactly the same as what is required in step 1 of claim 1: the antibody-containing sample (*i.e.* the medium containing the monoclonal antibody) is applied to a ProSep A Protein A affinity chromatography column." *Id.* at 29 (citing Ex. 1002 ¶ 70).

Petitioner asserts further, relying on Dr. Przybycien's declaration testimony, that the disclosure by Shadle that the antibody is subsequently eluted from the ProSep A column using ProSep A Elution Buffer (Ex. 1003, 21:9–10) satisfies the claim 1 requirement of "eluting the antibody with an acidic aqueous solution of low conductivity having a molarity of 100 mM or less" (Ex. 1001, 12:50–51). Pet. 29; *see also* Ex. 1002 ¶¶ 71–73. Petitioner explains that Shadle discloses that "the conditions of the ProSep A Elution Buffer are '25 mM citrate, pH 3.5.'" *Id.* (quoting Ex. 1003, 20:10). Petitioner contends that the ProSep A Elution Buffer disclosed in Shadle, thus, constitutes "an acidic aqueous solution of low conductivity," consistent with the scope that term set forth in the '289 patent specification (*id.* at 30 (citing Ex. 1002 ¶¶ 71–73)); Ex. 1001, 5:27–35.

Petitioner additionally argues that to the extent Patent Owner contends the molarity of the "acidic aqueous solution of low conductivity" should

account for protein or DNA present in the eluate, any contribution from protein or DNA "would be negligible (*i.e.* less than 1 mM), and certainly not enough to raise the molarity of the ProSep A citrate elution buffer above the claimed 100 mM limit." Pet. 30, n.3 (citing Ex. 1002 ¶ 73).

With regard to the claim 1 requirement of "neutralizing the eluate from step (2) to form particles by addition of a buffer to raise the pH to 4 to 8, wherein the molarity of the neutralized eluate is 100 mM or less" (Ex. 1001, 12:52–54), Petitioner asserts that Shadle expressly describes neutralizing the eluate by addition of a buffer to raise the pH to 4 to 8, and inherently teaches particle formation and that the molarity of the neutralized eluate is 100 mM or less. Pet. 31–37 (citing Ex. 1002 ¶¶ 74–85).

Petitioner identifies the following excerpt of Shadle as disclosing "neutralizing the eluate from step (2) . . . by addition of a buffer to raise the pH to 4 to 8" (Ex. 1001, 12:52–54):

> The eluate was approximately 15 liters in volume, and contained approximately 5 milligrams protein per milliliter.
>
> Immediately *after elution, the sample* was adjusted to pH 3.5 by the addition of 2.5 M hydrochloric acid, held for approximately 30 minutes, and *adjusted to pH 5.5 by the addition of approximately 350 milliliters of l M Tris base*. After *neutralizing to pH 5.5*, the sample was filtered through a 0.1 micron Polygard CR filter in tandem with a sterile 0.2 micron Millipak 200, into a sterile container.

Pet. 31 (quoting Ex. 1003, 21:11–19).

Petitioner acknowledges that Shadle does not expressly describe the formation of particles upon eluate neutralization, or identify the molarity of the neutralized eluate, but contends that these claim requirements are

inherently disclosed. With respect to the claim 1 requirement that the molarity of the neutralized eluate be 100 mM or less, Petitioner explains, relying on Dr. Przybycien's declaration testimony, that the molarity of the neutralized eluate in Shadle can be calculated based on other disclosures in Shadle. Pet. 33 (citing Ex. 1002 ¶ 77). In particular, Petitioner asserts that the molarity of citrate and Tris base in the neutralized elute of Shadle is 47.2 mM. *Id.* (citing Ex. 1002 ¶ 79).

Concerning the contribution of HCl to the molarity of the neutralized eluate, again relying on the testimony of Dr. Przybycien, Petitioner explains:

> Example IA discloses that eluate of 15 L in volume is produced using 15–20 liters of the 25mM Citrate elution buffer with a pH of 3.5. Ex. 1003, 21. As such, the volume of 2.5 M HCl needed to adjust the pH of the eluate to 3.5 is minimal. Ex. 1002 ¶¶ 78-82; Ex. 1007, 1–3. In fact, WO '389 [Shadle] explicitly states that the HCl addition step can be omitted. Ex. 1003, 17 ("The pH 3.5 treatment can be omitted if desired.").

Id. Petitioner, therefore, contends that "even if the minimal effect of the HCl solution on the molarity of the neutralized eluate were included, the overall effect would be insignificant and the molarity of the neutralized eluate in Example IA would still be well below the required [limit of] 100 mM." *Id.* at 34–35 (citing Ex. 1002 ¶ 82). Furthermore, Dr. Przybycien provides a molarity calculation that expressly accounts for the contribution of HCl to the molarity of the neutralized eluate, and determines that "the total molarity of the neutralized eluate" would be "50.8 mM." Ex. 1002 ¶ 82.

In support of this conclusion, Petitioner and Dr. Przybycien point out that during prosecution of the '289 patent, in order to secure allowance,

Patent Owner represented to the examiner that because the amount of buffer used to adjust the pH of the solution "is very small compared with that of the solution to which the buffer is added, *the effect of the molarity of the buffer to the molarity of the whole solution is extremely small*" (Ex. 1005, 13), and further that "use of a small amount of a buffer solution to modulate a pH value of a solution of a relatively large volume is well known in this technical field" (*id.*). Pet. 34; Ex. 1002 ¶ 80. Petitioner and Dr. Przybycien additionally identify Patent Owner's representation during prosecution of a European counterpart to the '289 patent that the molarity of the neutralized eluate in Shadle "can be calculated to at least: (375 + 350)/15.35 = 47.2 mM" (Ex. 1006, 27–28) as consistent with Petitioner's understanding of Shadle. Pet. 34; Ex. 1002 ¶ 81.

As for the contribution of protein and contaminant DNA to the molarity of the eluate, Petitioner asserts that such contributions should not be considered. *See* Pet. 34, n.4; Ex. 1002 ¶ 79. Nevertheless, relying on Dr. Przybycien's testimony, Petitioner asserts that to the extent protein and contaminant DNA are included in the molarity determination, "such added contribution would be negligible (*i.e.* less than 1 mM), and certainly not enough to raise the molarity of the adjusted ProSep A citrate elution buffer above the claimed 100 mM limit." Pet. 34 n.4 (citing Ex. 1002 ¶ 79). Specifically, Dr. Przybycien calculates that the contribution of the RSHZ-19 antibody, the purification of which is the subject of Shadle, to the molarity of the neutralized eluate is 0.03 mM. Ex. 1002 ¶ 79; Ex. 1007, 1.

With respect to the particle formation requirement of claim 1, Petitioner contends, relying on D. Przybycien's declaration testimony, that

neutralization of the eluate under the conditions described in Shadle would inherently result in the recited particle formation, and further, that the particles so formed would necessarily contain contaminant DNA. Pet. 35 (citing Ex. 1002 ¶¶ 83–85).

In particular, Petitioner asserts that "[t]he conditions from [Shadle's] Example IA fall within the same range of conditions (pH of 4–8 and molarity less than 100 mM) recited in step 3 of the claimed process that the '289 patent claims is sufficient to form particles." *Id.* at 36 (citing Ex. 1002 ¶ 83). Petitioner also identifies the disclosure in the '289 patent specification stating "[a]ccording to the present invention, the solution neutralized to a neutral pH level in the above stage, in turn, produces particles (i.e., becomes clouded)" (Ex. 1001, 6:4–6) as indicating that particle formation necessarily follows from eluate neutralization under the conditions set forth in claim 1. Pet. 36 (citing Ex. 1002 ¶ 83); *see also id.* (explaining that the '289 patent specification discloses after neutralization, the solution is "then filtered through a filter to remove the resulting particles" (quoting Ex. 1001, 1:62–67)).

Petitioner further contends, relying on the declaration testimony of Dr. Przybycien, that "[t]he '289 patent specification further describes that the formed particles will contain contaminant DNA." Pet. 36 (citing Ex. 1002 ¶ 83). Specifically, Petitioner points to disclosure by the '289 patent that

> [w]ithout being bound by any particular theory, the inventors of the present invention estimate that *each of these particles is a conjugate formed between physiologically active protein and DNA*. Particle removal by filtration results in a small loss of

> physiologically active protein because it is removed in the form of *DNA-physiologically active protein conjugates*.

Pet. 36 (quoting Ex. 1001, 6:16–19); Ex. 1002 ¶ 83.

Petitioner additionally explains that "[t]he inherent formation of particles under the recited eluate solution conditions and containing contaminant DNA is also consistent with the teachings in the prior art," as evidenced by Scopes (Ex. 1009).[1] Pet. 37 (citing Ex. 1002 ¶ 84). Specifically, Petitioner contends, relying on Dr. Przybycien's testimony, that an ordinarily skilled artisan would have understood from Scopes "[i]n many cases isoelectric precipitates can be formed in a tissue extract by lowering the pH to between 6.0 and 5.0" (Ex. 1009, 28), and further that "[m]ost isoelectric precipitates are aggregates of many different proteins and may include particulate fragments and *protein-nucleic acid complexes*" (*id.* at 29 (emphasis added)). Pet. 37 (citing Ex. 1002 ¶ 85).

Turning to the final step of claim 1, which requires "removing the particles to thereby remove contaminant DNA from the antibody-containing sample" (Ex. 1001, 12:56–57), Petitioner contends that this claim step is taught, either expressly or inherently, by Shadle. Pet. 38 (citing Ex. 1002 ¶¶ 86–91). In particular, Petitioner asserts that "[a]fter neutralizing the eluate to pH 5.5, the next step of Example IA discloses that 'the sample was filtered through a 0.1 micron Polygard CR filter in tandem with a sterile 0.2 micron Millipak 200, into a sterile container.'" *Id.* (quoting Ex. 1003, 21:17–19). Petitioner argues, relying on Dr. Przybycien's testimony, that

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[1] Robert K. Scopes, *Protein Purification: Principles and Practice* (Charles R. Cantor ed., 2nd ed. 1987) (Ex. 1009).

"the particles that formed according to the steps of Example IA, including those containing contaminant DNA, would inevitably and necessarily be removed by the disclosed filters, because the purpose of such filters is to remove all particles above a certain size through filtration." *Id.* (citing Ex. 1002 ¶¶ 86–88; Ex. 1010, 27, 30). Petitioner, therefore, asserts that Shadle "expressly disclosed using its two filters to remove particles, including those formed in step 3 and containing contaminant DNA." *Id.* (citing Ex. 1002 ¶ 88).

Petitioner further argues, relying on Dr. Przybycien's declaration testimony, that "the particles that formed according to the steps of Example IA, including those containing contaminant DNA, would inevitably and necessarily be removed by the disclosed filters, because the purpose of such filters is to remove all particles above a certain size through filtration." Pet. 38 (citing Ex. 1002 ¶¶ 86–88). In this regard, Dr. Przybycien testifies that "[a]lthough Example IA does not describe what is removed using these two filters, a POSA would understand that the purpose of such filters is to remove all particles above a certain size through filtration." Ex. 1002 ¶ 88. Dr. Przybycien explains that an ordinarily skilled artisan would have understood, as disclosed by Martin,[2] that "[a]bsolute removal of particulate solids from the process stream, including sterile filtration, serves as an essential prefiltration/protection step for downstream chromatography and

[2] Jerry M. Martin et al., "Cartridge Filtration for Biotechnology," in *Bioprocessing Engineering: Systems, Equipment and Facilities*, 317–370 (Bjorn K. Lydersen et al., eds. 1994) (Ex. 1010).

ultrafiltration systems" (Ex. 1010, 27). Ex. 1002 ¶ 89; *see also* Pet. 39. Dr. Przybycien also opines that such an artisan would have further understood that "[i]n most cases, a 0.2-μm-rated sterilizing-grade membrane filter is employed as the fluid filter" (Ex. 1010, 30). Ex. 1002 ¶ 89; *see also* Pet. 39.

Based upon our review of the current record, and in light of our preliminary claim construction, we discern no deficiency in Petitioner's characterization of Shadle and the knowledge in the art, or in Petitioner's assertions as to the reasonable inferences an ordinary artisan would make from that reference. In addition, for purposes of this decision only, we accept Dr. Przybycien's testimony concerning the express and inherent teachings of Shadle.

Patent Owner contends that Petitioner fails to explain where, in the portions of Shadle asserted as disclosing the steps of claim 1, that reference teaches a method for removing contaminant DNA, as recited in the preamble. Prelim. Resp. 14. Specifically, Patent Owner argues that the Petition fails to establish a link between Shadle's disclosure of "the pH adjustment and filtration step using Polygard and Millipak filters" and the removal of contaminant DNA. *Id.* In this regard, Patent Owner observes that Shadle identifies the Protein A and hydrophobic interaction chromatography as removing DNA from the sample, but does not expressly describe the filtration step as so doing. *Id.* Patent Owner additionally contends that the cation exchange and hydrophobic interaction chromatography steps taught by Shadle are "precisely of the sort criticized

and rendered unnecessary by the ’289—a step that Shadle would have no reason to perform if DNA were removed earlier." *Id.* at 15.

As an initial matter, even assuming, for purposes of this decision, that the preamble of claim 1 is limiting,[3] we determine that Petitioner has established a reasonable likelihood of showing that Shadle discloses "[a] method for removing contaminant DNA in an antibody-containing sample, which comprises the followings [sic] steps . . . ." (Ex. 1001, 12:45–47). Specifically, because claim 1 recites a method "comprising" the recited steps, we determine, for purposes of institution, the fact that Shadle discloses additional chromatography steps beyond those expressly recited in claim 1 does not preclude that reference from anticipating claim 1. Moreover, at this juncture, the identification of the purported drawbacks of prior art antibody purification methods in description of the "Background Art" in the specification of the ’289 patent does not persuade us otherwise, because claim 1 is not commensurate in scope with that description in the specification. Rather, because claim 1 is a "comprising" claim, "the named [claim] elements are essential, but other elements may be added and still form a construct within the scope of the claim." *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997).

Nor do we agree with Patent Owner’s assertion that Petitioner has not adequately shown how the neutralization and filtration steps of Shadle

[3] We note that Petitioner does not assert that the preamble of claim 1 is non-limiting, but rather states that "[t]o the extent that the preamble is a limitation—a matter that the Board need not reach—WO ’389 [Shadle] discloses it." Pet. 27.

remove contaminant DNA. As discussed in greater detail below, we determine, for purposes of this decision, that Petitioner has established a reasonable likelihood of showing that neutralization of the eluate of Shadle to pH 5.5 with Tris base, and subsequent filtration of that eluate, as expressly disclosed by Shadle (Ex. 1003, 21:15–19), would necessarily remove DNA containing particles from the eluate (*see* Pet. 35–40; Ex. 1002 ¶¶ 82–91).

Patent Owner also asserts that the Petition fails to show that Shadle discloses step (2) of claim 1, which recites, "eluting the antibody with an acidic aqueous solution of low conductivity having a molarity of 100 mM or less" (Ex. 1001, 12:51–52). Prelim. Resp. 15. Specifically, Patent Owner contends that Petitioner has not established that the elution buffer of Shadle is of "low conductivity," or that it has a "molarity of 100 mM or less." *Id.* at 15–18.

Turning first to Patent Owner's contention that the Petition fails to demonstrate sufficiently that the elution buffer employed by Shadle is of "low conductivity," we do not agree at this point in the proceeding. Rather, as discussed above with regard to claim interpretation, Petitioner argues that the '289 patent specification describes "an aqueous solution of low conductivity" as encompassing a solution of "pH 1.5 to pH 3.9, . . . which has a molarity of 0 to 100 mM" (Ex. 1001, 5:29–30). Pet. 30. Petitioner further asserts that "the citrate elution buffer solution used in Example IA of WO '389 [Shadle] has a pH of 3.5, which is an acidic pH, and has a molarity of 25 mM, which is significantly lower than the required 100 mM." *Id.* Accordingly, because we determine that Petitioner has established a

reasonable likelihood of demonstrating that Shadle discloses eluting the antibody with an aqueous solution of pH 1.5 to pH 3.9, which has a molarity of 0 to 100 mM, we do not find Patent Owner's position sufficiently persuasive.

We are likewise unpersuaded by Patent Owner's arguments that "Petitioner does not address whether there are other solutes in the 'ProSep Elution Buffer'" (Prelim. Resp. 17), and that "Petitioner never asserts, let alone explains, where, how, or why Shadle teaches that the eluting solution of Example IA (*i.e.*, '*ProSep A* elution buffer') is the same as the buffer listed in Table 1 (*i.e.*, '*ProSep* Elution Buffer')" (*id.* at 18). As an initial matter, we note that Patent Owner does not contend in its Preliminary Response that additional solutes are present in the elution buffer disclosed by Shadle, or that ProSep Elution Buffer and ProSep A elution buffer are distinct solutions. Moreover, solely for purposes of this decision, we credit the unrebutted testimony by Dr. Przybycien that "Table 1 of WO '389 further discloses that the conditions of the ProSep A Elution Buffer are '25 mM citrate, pH 3.5'" (Ex. 1002 ¶ 72). We similarly credit, for purposes of this decision, Dr. Przybycien's unchallenged testimony that "the citrate elution buffer solution used in Example IA of WO '389 has a pH of 3.5, which a POSA would understand is an acidic pH. The citrate elution buffer solution also has a molarity of 25 mM, which is significantly lower than the required 100 mM" (*id.* ¶ 73).

Patent Owner argues that "[t]he Petition fails to establish that the molarity of the neutralized eluate in Example IA is 100 mM or less" (Prelim. Resp. 18), as required by step (3) of claim 1. In this respect, Patent Owner

asserts that the molarity calculation proffered by Petitioner accounts for the contributions of citrate and Tris base, while "arbitrarily excluding other solutes." *Id.* at 19. Specifically, Patent Owner contends that Petitioner should have accounted for the wash buffer employed prior to elution in its molarity calculation (*id.* at 20–21), as well as "the molarity contribution from the undisclosed solution that raised the pH of the elution buffer in the eluate" (*id.* at 21 (emphasis omitted)). Patent Owner additionally asserts that its representation to the European Patent Office that the molarity of the eluate described in Example IA of Shadle was "at least" 47.2 mM (Ex. 1006, 27–28) does not "imply that the molarity of the neutralized eluate in Example IA was less than 100mM" (Prelim. Resp. 21).

We do not find Patent Owner's arguments persuasive based on the record presented at this preliminary stage of the proceeding. Dr. Przybycien testifies that in addition to protein and DNA, the neutralized eluate of Shadle would include citrate, HCl, and Tris base. Ex. 1002, ¶¶ 77–79, 82; Ex. 1007, 1–3. This testimony is consistent with Shadle's disclosure that "Protein A chromatography removes a large proportion of cell and media derived impurities (particularly protein and DNA in the flow-through and wash fractions), and concentrates RSHZ-19 in the elution buffer for further processing" (Ex. 1003, 16:25–27), which suggests that the wash and eluate fractions are distinct. *See also id.* at 21:9–13 ("IgG was eluted by applying 15–20 liters of ProSep A elution buffer. Fractions of the non-bound peak and the elution peak were collected and assayed for IgG content using an HPLC assay. The eluate was approximately 15 liters in volume, and contained approximately 5 milligrams protein per milliliter."), 19:3–5 ("The

eluate fractions from the Protein A capture and cation exchange steps are pooled based on the UV tracing on the chromatogram, and the entire peak is collected.").

With regard to the purported contribution to eluate molarity of an "undisclosed solution," we note that this assertion by Patent Owner is attorney argument, which, at this stage of the proceeding, is unsupported by objective evidence suggesting the presence of an "undisclosed solution" in the neutralized eluate of Shadle. For purposes of determining whether to institute a trial, we are sufficiently persuaded by Shadle's indication that, in addition to antibody and DNA, the neutralized eluate includes citrate, Tris base, and optionally, HCl. Ex. 1003, 20:10, 21:9–19; Ex. 1002 ¶ 75.

This determination is consistent with Patent Owner's representation, below, to the European Patent Office during prosecution of claims similar to those presently challenged that Shadle's eluent includes citrate, HCl, and Tris base and has a molarity of "at least" 47.2 mM:

> Thus, the eluent before the filtration has:
>
> 375 mmol (25 mM • 15 l) of citrate
>
> "x" mmol (2.5 M • "Y" l (unknown)) of HCl
>
> 350 mmol (1 M • 0.35 l) of Tris base
>
> at least 15.35 1(15 l + "Y" l +0.351) in total volume.
>
> Based thereon, the molarity of the eluent can be calculated to at least: (375 + 350)/15.35 = 47.2 mM.

Ex. 1006, 28. Accordingly, at this stage in the proceeding, and solely for purposes of this decision, we accept Dr. Przybycien's testimony that the neutralized eluate of Shadle includes citrate, HCl, and Tris base, but not wash buffer constituents, such as PBS and glycine.

With respect to the requirement in step (3) of claim 1 of "neutralizing the eluate from step (2) to form particles . . . ," Patent Owner contends that "the disclosures in the '289 and its prosecution history do not support Petitioner's contention that particles *necessarily* formed *in Example IA of Shadle*." Prelim. Resp. 24. In particular, Patent Owner argues that Petitioner has not established that the conditions described in Example IA of Shadle fall within the same range of conditions required by claim 1. *Id.* Patent Owner asserts that Petitioner fails to account for statements in the '289 patent specification that the type, conductivity, and neutral pH level of the acidic aqueous solution of low conductivity "will vary depending on the type of physiologically active protein or antibody to be purified" (Ex. 1001, 5:37–40, 5:54–6:3). Prelim. Resp. 24–25. In addition, Patent Owner argues that its representations to the Patent Office during prosecution of the '289 patent that "it is recognized that no DNA particle was precipitated in this [prior art] example because of its higher conductivity, i.e. of a molarity of over 0.1M" (Ex. 1005, 37) and that "no such particles are formed during the procedure of [that reference] because the conditions described in the disclosure and carried out in the examples are fundamentally different from those stipulated in applicants' claims" (*id.* at 38) do not support Petitioner's position. Prelim. Resp. 25–26.

Patent Owner further asserts that Petitioner's reliance on teachings by Scopes as evidencing that an ordinarily skilled artisan would have understood "that proteins will aggregate by isoelectric precipitation under the conditions recited in the claims of the '289 patent" (Ex. 1002 ¶ 84) is misplaced. Prelim. Resp. 23. Patent Owner reasons that Scopes' discussion

of mere possibilities is insufficient to establish inherency. *Id*. Patent Owner additionally points out that Scopes describes lowering pH to obtain a pH of between 5.0 and 6.0, rather than raising it, as described by Shadle. *Id.* at 24.

We are mindful of the high bar for proving inherency; however, on the record before us, and solely for purposes of this decision, we determine that Petitioner has demonstrated a reasonable likelihood of establishing that the process of Shadle necessarily results in the formation of particles that contain contaminant DNA. As an initial matter we determine that Petitioner has established a reasonable likelihood of showing that Shadle discloses neutralizing the eluate by addition of a buffer to raise the pH to 5.5. *See* Ex. 1003, 21:15–19 ("Immediately after elution, the sample was adjusted to pH 3.5 by the addition of 2.5 M hydrochloric acid, held for approximately 30 minutes, and adjusted to pH 5.5 by the addition of approximately 350 milliliters of 1 M Tris base. After neutralizing to pH 5.5, the sample was filtered through a 0.1 micron Polygard CR filter in tandem with a sterile 0.2 micron Millipak 200, into a sterile container"). Likewise, for the reasons set forth above, and solely for purposes of this decision, we determine that Petitioner has demonstrated a reasonable likelihood of establishing that the molarity of the eluate taught by Shadle is 100 mM or less.

Moreover, based on the current record, and the particular facts and circumstances of this case, we discern no meaningful difference between the conditions sufficient for particle formation set forth in claim 1 and the specification of the '289 patent, and the conditions disclosed by Shadle in conjunction with the eluate neutralization step. In particular, we observe that step (3) of claim 1 recites "neutralizing the eluate from step (2) *to form*

particles by addition of a buffer to raise the pH to 4 to 8, wherein the molarity of the neutralized eluate is 100 mM or less." Ex. 1001, 12:53–55 (emphasis added). The specification likewise states that "[a]ccording to the present invention, *the solution neutralized to a neutral pH level in the above stage, in turn, produces particles* (i.e., becomes clouded). These particles may be removed by filtration through a filter *to ensure efficient removal of contaminant DNA*." *Id.* at 6:4–8 (emphasis added); *see also id.* at 1:62–66 ("[T]he sample is converted into an acidic aqueous solution of low conductivity, neutralized by addition of a buffer to raise the pH to a neutral level, and then filtered through a filter to remove the resulting particles."). On the current record, we discern no meaningful difference between the conditions set forth in the '289 patent, and Shadle's disclosure of neutralization of the eluate to pH 5.5 with Tris base (Ex. 1003, 21:15–19).

We further observe that the disclosures of Scopes that "isoelectric precipitates can be formed in a tissue extract by lowering the pH to between 6.0 and 5.0" (Ex. 1009, 28), and that "[m]ost isoelectric precipitates are aggregates of many different proteins and may include particulate fragments and protein-nucleic acid complexes" (*id.* at 29) are consistent with Dr. Przybycien's testimony that an ordinarily skilled artisan would have understood from Scopes "that proteins will aggregate by isoelectric precipitation under the conditions recited in the claims of the '289 patent" (Ex. 1002 ¶ 84).

Accordingly, for the limited purposes of this decision, in view of the record before us, we credit Dr. Przybycien's testimony for the sole purpose of deciding whether to institute trial, and conclude that Petitioner has

established a reasonable likelihood of showing that Shadle discloses "neutralizing the eluate from step (2) to form particles by addition of a buffer to raise the pH to 4 to 8, wherein the molarity of the neutralized eluate is 100 mM or less" (Ex. 1001, 12:53–55).

Lastly, Patent Owner contends "[e]ven if Example IA of Shadle inherently disclosed the formation of particles—and it does not—Petitioner fails to explain how Shadle discloses, explicitly or inherently, that (1) those particles were removed; and (2) removing those particles removed contaminant DNA." Prelim. Resp. 26. Patent Owner asserts that Dr. Przybycien's testimony that a 0.1 μm filter would necessarily remove contaminant DNA from the neutralized eluate described by Shadle is conclusory, and argues that the Petition does not address the size of the particles purportedly formed in Shadle, including whether they would be the same size as those disclosed in the '289 patent, or whether such particles would include contaminant DNA. *Id.* at 27–28.

Patent Owner further asserts that Petitioner does not reconcile Shadle's description of the filtration step that Petitioner contends removes contaminant DNA as relating to viral inactivation, with Shadle's subsequent discussion of hydrophobic interaction chromatography as removing "host DNA" (Ex. 1003, 18:18–19). *Id.*at 28. Patent Owner also argues that Petitioner's reliance on Martin as indicating that an ordinarily skilled artisan would have recognized that Shadle's filtration step necessarily would have removed contaminant DNA-containing particles is misplaced. Patent Owner reasons that Martin merely states that "[i]n *most* cases, a 0.2-μm-rate sterilizing grade membrane filter is employed as the fluid filter." *Id.* at 28–

29 (quoting Ex. 1010, 30). Similarly, Patent Owner asserts that the '289 patent specification identifies "a 1.0–0.2 μm Cellulose Acetate Filter System (Corning) or TFF" as an exemplary filter (Ex. 1001, 6:5–11), and not one that would necessarily remove the particles of Shadle. Prelim. Resp. 29.

Patent Owner also reiterates its argument, described above in the discussion of step (3) of claim 1, that "Petitioner does not explain why any formed particles in Example IA would necessarily comprise contaminant DNA." Prelim. Resp. 29. In addition to its previously addressed arguments concerning the insufficiency of Petitioner's reliance on Scopes and the '289 patent as supporting its contention that Shadle necessarily discloses contaminant DNA-containing particles, Patent Owner asserts that Petitioner fails to explain how Shadle itself discloses the formation and removal of particles including contaminant DNA. *Id.* at 30. Patent Owner also reasserts its contention that the Petition fails to explain why hydrophobic interaction chromatography, which is identified by Shadle as removing host DNA, would be performed if Shadle's filtration step removes contaminant DNA. *Id.* at 31. Patent Owner also reiterates its contention that Shadle does not anticipate claim 1 because it discloses precisely the additional chromatography steps that the '289 patent specification criticizes. *Id.*

In view of the current record, we do not find Patent Owner's position sufficiently persuasive. Based on the record as it exists before us, as well as the particular facts and circumstances of this case, we discern no meaningful difference between the conditions set forth in claim 1 and the specification of the '289 patent, and the eluate filtration step disclosed by Shadle. Shadle teaches the use of a "0.1 micron Polygard CR filter in tandem with a sterile

0.2 micron Millipak 200" for eluate filtration. Ex. 1003, 21:18–19. Step (4) of claim 1 of the '289 patent recites "removing the particles *to thereby remove contaminant DNA*" (Ex. 1001, 12:57–58 (emphasis added)), indicating that removal of the particles formed upon eluate neutralization in accordance with step (3) necessarily removes contaminant DNA. In addition, the '289 patent specification expressly identifies filtration of the neutralized eluate through 1.0–0.2 μm filters as sufficient to remove contaminant DNA:

> According to the present invention, the solution neutralized to a neutral pH level in the above stage, in turn, produces particles (i.e., becomes clouded). These particles may be removed by filtration through a filter to ensure efficient removal of contaminant DNA. Examples of a filter available for filtration include, but are not limited to, a 1.0–0.2 μm Cellulose Acetate Filter System (Corning) or TFF.

Ex. 1001, 6:4–11. The disclosures of Martin on which Petitioner and Dr. Przybycien's declaration testimony rely are consistent with these teachings of the '289 patent. Pet. 38; Ex. 1002 ¶ 88; Ex. 1010, 27, 30.

In view of the above determination, we do not find persuasive, for purposes of this decision, the argument that Shadle does not expressly or inherently disclose the removal of contaminant DNA. Similarly, the fact that Shadle describes a method for viral inactivation subsequent to cation exchange chromatography, and identifies hydrophobic interaction chromatography as removing "additional protein and non-protein impurities, most notably residual Protein A, IgG aggregates, and host DNA" (Ex. 1003, 18:18–19), does not overcome Petitioner's demonstration of a reasonable likelihood of showing that the neutralization and filtration steps of Shadle

would necessarily remove contaminant DNA. In this respect, we note that Patent Owner does not contend that claim 1 specifies the extent to which contaminant DNA must be removed through the performance of step (4) (*See* Ex. 1001, 12:57–58), or precludes the performance of additional chromatography steps beyond the Protein A chromatography recited in the claim (*see id.* 12:45–47 "[a] method for removing contaminant DNA in an antibody-containing sample, which comprises the followings steps"). With regard to Shadle's hydrophobic interaction chromatography step, in particular, we observe that the '289 patent specification distinguishes between "host DNA"—*i.e.*, the DNA Shadle purports to remove through hydrophobic interaction chromatography (Ex. 1003, 18:18–19)—and "contaminant DNA associated with viral contamination" (Ex. 1001, 1:20–21), further suggesting that the removal of "host DNA" by hydrophobic interaction chromatography is immaterial to the instant analysis.

In sum, based on the current record, Petitioner has demonstrated a reasonable likelihood that at least claim 1 of the '289 patent is anticipated by Shadle. Having decided that Shadle supports a reasonable likelihood that at least one of the challenged claims is unpatentable, we exercise our discretion under 37 C.F.R. § 42.108 to have the review proceed on all of the claims on which Shadle is the basis for anticipation. In doing so, we seek to achieve finality of review at the Board and avoid parallel or serial review in the district court, at least with respect to the petitioner in this proceeding and the Fast reference. *See Synopsys, Inc. v. Mentor Graphics Corp.*, 814 F.3d 1309, 1316 (Fed. Cir. 2016) (stating that "[t]he validity of claims for which

the Board did not institute *inter partes* review can still be litigated in district court").

E. Obviousness Ground of Unpatentability Based on Shadle

Petitioner's second ground challenges the same set of claims over the same reference as challenged in the first ground, except on obviousness under 35 U.S.C. § 103(a). Pet. 44. We are "cognizant of the ramifications of partial institution where the grounds are in different statutory classes." *Amendments to the Rules of Practice for Trials Before the Patent Trial and Appeal Board*, 80 Fed. Reg. 50720, 50739 (Aug. 20, 2015) (Response to Comment 12). Concerns of fairness and efficiency in this case, therefore, persuade us to institute on the ground of anticipation by Shadle, as well as on the ground of obviousness over Shadle. *See HP Inc. v. MPHJ Tech. Inv., LLC*, 817 F.3d 1339, 1347 (Fed. Cir. 2016) (holding that petitioner was "not estopped from raising the obviousness of claim 13 in a subsequent court or Board proceeding" where Board instituted only on grounds of anticipation of claim 13). Thus, we exercise our discretion to institute *inter partes* review on Petitioner's second ground, namely, that claims 1–8 and 13 would have been obvious over Shadle.

III. CONCLUSION

After considering the evidence and arguments of record, we conclude that Petitioner has demonstrated a reasonable likelihood of succeeding in challenging the patentability of at least independent claim 1 of the '289 patent. And, in keeping with our mission of "the just, speedy, and

inexpensive resolution" of patentability disputes, we exercise our discretion to institute *inter partes* review of all of the claims and grounds specified in the Petition. 37 C.F.R. §§ 42.1(b), 42.108.

At this stage in 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.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review is instituted as to claims 1–8 and 13 of the '289 patent on the following grounds of unpatentability:

A. Claims 1–8 and 13 under 35 U.S.C. § 102(b) as anticipated by Shadle;

B. Claims 1–8 and 13 under 35 U.S.C. § 103(a) as obvious over Shadle; and

FURTHER ORDERED that no other ground of unpatentability asserted in the Petition is authorized for this *inter partes* review; 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.

PETITIONERS:

Jovial Wong
WINSTON & STRAWN LLP
jwong@winston.com

PATENT OWNER:

J. Steven Baughman
Megan Raymond
PAUL, WEISS, RIFKIND, WHARTON & GARRISON LLP
sbaughman@paulweiss.com
mraymond@paulweiss.com