Trials@uspto.gov
571-272-7822

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

KASHIV BIOSCIENCES, LLC,
Petitioner,

v.

AMGEN INC.,
Patent Owner.

Case IPR2019-00797
Patent 9,643,997 B2

Before ZHENYU YANG, CHRISTOPHER G. PAULRAJ, and KRISTI L. R. SAWERT, *Administrative Patent Judges.*

SAWERT, *Administrative Patent Judge.*

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

I. INTRODUCTION

Kashiv BioSciences, LLC ("Petitioner") filed a Petition (Paper 2, "Pet.") to institute an *inter partes* review of claims 9, 10, 13–15, 17–21, 23, and 26–30 of U.S. Patent No. 9,643,997 B2 ("the '997 patent"). Amgen Inc. ("Patent Owner") timely filed a Preliminary Response (Paper 7, "Prelim. Resp."). On our authorization (Paper 12), Petitioner filed a Reply (Paper 13, "Reply") and Patent Owner filed a Sur-reply (Paper 14, "Sur-reply").

We have authority under 35 U.S.C. § 314 to determine whether to institute an *inter partes* review. To institute an *inter partes* review, we must determine that the information presented in the Petition shows "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 Supreme Court has held that a decision to institute under 35 U.S.C. § 314(b) may not institute review on less than all claims challenged in the petition. *SAS Inst., Inc. v. Iancu,* 138 S. Ct. 1348, 1355–56 (2018). Moreover, in accordance with USPTO Guidance, "if the PTAB institutes a trial, the PTAB will institute on all challenges raised in the petition." *See Guidance on the Impact of SAS on AIA Trial Proceedings* (April 26, 2018) (available at https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial) ("USPTO Guidance"); *see also PGS Geophysical AS v. Iancu*, 891 F.3d 1354, 1360 (Fed. Cir. 2018) (interpreting the statute to require "a simple yes-or-no institution choice respecting a petition, embracing all challenges included in the petition").

Applying those standards, and upon consideration of the information presented in the Petition, the Preliminary Response, the Reply, and the Sur-reply, and for the reasons explained below, we determine that Petitioner has

demonstrated a reasonable likelihood of success in proving that at least one claim of the '997 patent is unpatentable. Accordingly, we institute an *inter partes* review of all challenged claims (9, 10, 13–15, 17–21, 23, and 26–30) of the '997 patent, based on the grounds raised in the Petition.

II. BACKGROUND

A. Related Proceedings

The parties identify the following district-court litigations as related matters under 37 C.F.R. § 42.8(b)(2): *Amgen Inc. v. Adello Biologics LLC*, No. 2:18-cv-03347-CCC/MF (D.N.J.); *Amgen Inc. v. Mylan Inc.*, No. 2:17-cv-01235-MRH (W.D. Pa.); *Amgen Inc. v. Hospira Inc.*, No. 1:18-cv-01064-CFC (D. Del.); and *Sandoz Inc. v. Amgen Inc.*, No. 3:19-cv-00977 (N.D. Cal.). Pet. 73; Paper 5, 2.

The '997 patent is related to U.S. Patent No. 8,940,878 ("the '878 patent"). Petitioner filed a petition seeking *inter partes* review of the '878 patent, and that proceeding has been designated IPR2019-00791. Pet. 74; Paper 5, 3. Pending U.S. Patent Application No. 15/476,691 claims priority to the '997 patent. *Id.*

B. The '997 patent (Ex. 1001)

The '997 patent, titled "Capture Purification Processes for Proteins Expressed in a Non-Mammalian System," relates to methods for purifying proteins of interest expressed in non-mammalian expression systems. Ex. 1001, (54), Abstract. The '997 patent states that the proteins of interest are commonly expressed in non-mammalian expression systems in non-native, limited-solubility forms, such as inclusion bodies. *Id.* at 1:21–55. Because they are in non-native form, these proteins must undergo

"refolding" into native form—which typically occurs in a refold mixture or solution. *Id.* at 1:41–46.

"Commonly, a refold solution contains a denaturant (e.g., urea or other chaotrope, organic solvent or strong detergent), an aggregation suppressor (e.g., a mild detergent, arginine or low concentrations of [polyethylene glycol (PEG)], a protein stabilizer (e.g., glycerol, sucrose or other osmolyte, salts) and/or a redox component (e.g., cysteine, cystine, cystamine, cysteamine, glutathione)." *Id.* at 4:45–51. The '997 patent states that, although "beneficial for refolding proteins, these components can inhibit purification" of the expressed proteins. *Id.* at 4:52–54. Thus, in the prior art, "it was believed that after a protein has been refolded[,] it was necessary to dilute or remove the components of the refold mixture in a wash step" before purification. *Id.* at 1:46–52. "This dilution step can consume time and resources which, when working at a manufacturing scale of thousands of liters of culture, can be costly." *Id.* at 1:52–55.

According to the '997 patent, the disclosed methods allow for the "direct capture" of proteins of interest from the refold mixture. *Id.* at 1:16–17. The '997 patent states that "[t]he advantages of the present invention over typical processes include the elimination of the need to dilute the protein out of a refold solution prior to capturing it on a separation matrix." *Id.* at 3:54–57. "In one embodiment of the disclosed method, purification is achieved by directly applying a protein of interest, which is present in a refold mixture, to a separation matrix." *Id.* at 4:58–60.

C. Illustrative Claim

Of the challenged claims, only claim 9 is independent. *See* Ex. 1001, 22:36–24:33. Claims 10, 13–15, 17–21, 23, and 26–30 depend directly or

indirectly from claim 7. *See id.* at 22:56–24:33. Claim 9 is reproduced below:

> 9. A method of purifying a protein expressed in a non-native limited solubility form in a non-mammalian expression system comprising:
>
> (a) solubilizing the expressed protein in a solubilization solution comprising one or more of the following:
> (i) a denaturant;
> (ii) a reductant; and
> (iii) a surfactant;
>
> (b) forming a refold solution comprising the solubilization solution and a refold buffer, the refold buffer comprising one or more of the following:
>
> (i) a denaturant;
> (ii) an aggregation suppressor;
> (iii) a protein stabilizer; and
> (iv) a redox component;
>
> (c) applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix;
>
> (d) washing the separation matrix; and
>
> (e) eluting the protein from the separation matrix.

Ex. 1001, 22:36–55.

D. The Prior Art

Petitioner advances the following references as the prior art upon which it relies for the asserted grounds challenging the claims of the '997 patent:

1. Henrik Ferré et al., *A novel system for continuous protein refolding and on-line capture by expanded bed adsorption*, 14 PROTEIN SCIENCE 2141–53 (2005) (Ex. 1004, "Ferré");

2. Uma Komath et al., *Process for preparing G-CSF*, WO 2004/001056 A1 (published Dec. 31, 2003) (Ex. 1005, "Komath");

3. Moon Sun Hahm and Bong Hyun Chung, *Refolding and Purification of Yeast Carboxypeptidase Y Expressed as Inclusion Bodies in* Escherichia coli, 22 PROTEIN EXPR. PURIF. 101–107 (2001) (Ex. 1009, "Hahm");

4. Arndt Dietrich et al., *Method for the Purification of G-CSF*, US 2008/0260684 A1 (published Oct. 23, 2008) (Ex. 1008, "Dietrich"); and

5. Mary S. Rosendahl et al., *Method for Refolding Proteins Containing Free Cysteine Residues*, US 2004/0018586 A1 (published Jan. 29, 2004) (Ex. 1006, "Rosendahl").

E. Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 9, 10, 13–15, 17–21, 23, and 26–30 of the '997 patent on the following grounds:

Reference(s)	**Basis**	**Claims challenged**
Ferré	35 U.S.C. § 102	9, 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30
Komath	35 U.S.C. § 102	9, 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30
Komath	35 U.S.C. § 103	9, 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30
Hahm	35 U.S.C. § 102	9, 10, 13–15, 17, 18, 21, 23, 26, and 29
Dietrich	35 U.S.C. § 102	9, 10, 13–15, 17–21, 23, and 26–30
Ferré or Komath or Dietrich in view of Rosendahl	35 U.S.C. § 103	15, 19, 23, 27, and 28

Petitioner further relies upon the declaration of Anne S. Robinson, Ph.D., to support its grounds of unpatentability. *See* Ex. 1002.

III. PATENTABILITY ANALYSIS

We organize our patentability analysis into five sections. First, we address the level of ordinary skill in the art. Second, we address claim construction. Third, we provide an overview of the asserted references. Fourth, we consider the printed publication status of several references. And fifth, taking account of the information presented, we consider whether the Petition satisfies the threshold requirement for instituting an *inter partes* review under 35 U.S.C. § 314(a).

A. Level of Ordinary Skill in the Art

Relying on Dr. Robinson's declaration, Petitioner contends that a person of ordinary skill in the art for the '997 patent "would have had at least a Bachelor's degree (or the equivalent) in Biochemistry or Chemical Engineering with several years' experience in biochemical manufacturing, protein purification, and protein refolding, or, alternatively, an advanced degree (Masters or Ph.D.) in Biochemistry or Chemical Engineering with emphasis in these same areas." Pet. 23 (citing Ex. 1002 ¶¶ 19, 110). Petitioner further contends that an ordinarily skilled artisan "may also work in collaboration with other scientists and/or clinicians who have experience in protein purification, protein refolding, or related disciplines." *Id.*

Patent Owner does not propose a definition for the level of ordinary skill in the art in its Preliminary Response, or otherwise dispute Petitioner's definition. *See generally* Prelim. Resp. Petitioner's definition appears consistent with the level of ordinary skill in the art reflected in the prior art, and we apply it for this Decision. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate

level and a need for testimony is not shown" (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp*., 755 F.2d 158, 163 (Fed. Cir. 1985))).

B. Claim Construction

Because the Petition was filed after November 13, 2018, we interpret the claims "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b)." 37 C.F.R. § 42.100(b) (as amended Oct. 11, 2018). Under this standard, we construe a claim "in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.* Furthermore, at this stage in the proceeding, we need only construe the claims to the extent necessary to determine whether to institute *inter partes* review. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("[W]e need only construe terms 'that are in controversy, and only to the extent necessary to resolve the controversy.'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999))).

Petitioner proposes constructions for the terms "non-native limited solubility form," "aggregation suppressor," "protein stabilizer," "applying the refold solution to a separation matrix," and "refold buffer." Pet. 25–33. Patent Owner responds with constructions for "aggregation suppressor," "protein stabilizer," "applying the refold solution to a separation matrix," and "refold buffer." Prelim. Resp. 15–26. For this Decision, we determine that we need only construe the claim terms "aggregation suppressor" and "protein stabilizer."

Claim 9 recites a refold buffer comprising "one or more of" a denaturant, an aggregation suppressor, a protein stabilizer, and a redox

component. Ex. 1001, 22:44–50. Petitioner contends that "aggregation suppressor" means "'any compound having the ability to disrupt and decrease or eliminate interactions between two or more proteins.'" Pet. 25 (quoting Ex. 1001, 5:45–47). Petitioner also contends that "protein stabilizer" means "'any compound having the ability to change a protein's reaction equilibrium state, such that the native state of the protein is improved or favored.'" *Id.* at 26 (quoting Ex. 1001, 5:54–57).

Patent Owner contends that an aggregation suppressor "must actually disrupt or decrease or eliminate interactions between two or more proteins at the concentration used," such that "[i]f it does not 'disrupt and decrease or eliminate interactions between two or more proteins' when in the presence of proteins, then it is not an 'aggregation suppressor.'" Prelim. Resp. 16 (quoting Ex. 1001, 5:45–47). Similarly, for protein stabilizer, Patent Owner contends that "a protein stabilizer must actually stabilize protein in the refold solution at the concentration used," such that "[i]f it does not 'change a protein's reaction equilibrium state, such that the native state of the protein is improved or favored,' it is not a protein stabilizer." *Id.* (quoting Ex. 1001, 5:54–57) (emphasis omitted).

We discern the dispute between the parties to be whether claim 9 requires the aggregation suppressor and protein stabilizer to be present in the refold buffer at concentrations necessary for the aggregation suppressor to suppress aggregation and for the protein stabilizer to stabilize protein interactions. *Compare* Pet. 25 (stating that "[n]either the claims nor the specification requires that the aggregation suppressor have a particular concentration") and Pet. 26 (same as to protein stabilizer), *with* Prelim. Resp. 15–16 (stating that Petitioner's use of the term "ability" in its

proposed constructions "is misleading"). Although we acknowledge Patent Owner's argument, we decline to impose a concentration requirement on the constructions of "aggregation suppressor" and "protein stabilizer" at this stage of the proceeding.

The '997 patent expressly sets forth the definitions of these terms in the written description. Specifically, the '997 patent states that, "[a]s used herein, the term 'aggregation suppressor' means any compound having the ability to disrupt and decrease or eliminate interactions between two or more proteins." Ex. 1001, 5:45–47. And as to "protein stabilizer," the '997 patent similarly states that, "[a]s used herein, the term 'protein stabilizer' means any compound having the ability to change a protein's reaction equilibrium state, such that the native state of the protein is improved or favored." *Id.* at 5:54–56. Because the written description expressly defines these terms, we find those definitions to govern, at least for this Decision. *See Inventio AG v. ThyssenKrupp Elevator Americas Corp.*, 649 F.3d 1350, 1356–57 (Fed. Cir. 2011) (stating that express definitions of claim terms in the written description "govern the construction of the claims" (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005))), overruled on other grounds by *Williamson v. Citrix Online, LLC*, 792 F.3d 1339 (Fed. Cir. 2015).

C. The Prior Art

Before turning to Petitioner's asserted grounds of unpatentability, we provide a brief summary of the asserted references.

1. Ferré (Ex. 1004)

Ferré relates to a "novel two-step protein refolding strategy" "where continuous renaturation-by-dilution is followed by direct capture on an

expanded bed adsorption (EBA) column." Ex. 1004, 1[1] (Abstract). Ferré states that experiments were performed using "extracted and denatured inclusion body proteins from *Escherichia coli*." *Id.* The proteins were "continuously diluted into refolding buffer . . . and then fed directly to an EBA column, where the protein was captured, washed, and finally eluted as soluble folded protein." *Id.* Ferré identifies the "refolding buffer" as "20 mM Tris-Hcl [pH 8.0]." *Id.* at 10. Ferré states that the eluted proteins were "in a correctly folded state," and exhibited increased purity and concentration. *Id.* at 1 (Abstract). Ferré states that the disclosed protein-refolding strategy "represents a novel approach to small and preparative scale protein refolding, which should be applicable to many other proteins." *Id.*

2. Komath (Ex. 1005)

Komath relates to "[a] simple, economic and scalable process for the purification of recombinant human G-CSF expressed in *E.coli*." Ex. 1005, 1 [57]. According to Komath, hG-CSF was purified "by a simple three step procedure involving lysis of the cells, washing of inclusion bodies and ion exchange chromatography." *Id.* at 9. As to the washing step, Komath states that "[t]he final washed [inclusion body] pellet . . . is essentially free of endotoxins, host cell proteins and host DNA," and "ready to be solubilized, refolded into native form and concentrated by ion exchange chromatography." *Id.* Komath states that the washed inclusion-body pellet "is solubilized using a combination of a denaturant and high alkaline pH."

[1] For this and other references, we use the pagination provided by Petitioner in the exhibits to be consistent with the parties and to avoid confusion.

Id. at 10. In one example, the washed inclusion body pellet "is solubilized with urea at concentrations ranging from 2M to 6M." *Id.* at 12. Table 1 of Komath presents the "percentage recovery of the protein with various sodium chloride concentrations." *Id.* Table 1 shows that, at 25 mM and 50 mM of NaCl, no elution was observed, and at 100 mM, 250 mM, and 500 mM, less than 1% recovery of the protein was observed. *Id.* at 13 (Table 1).

3. Hahm (Ex. 1009)

Hahm relates to a method for the refolding and purification of the protein carboxypeptidase Y ("CPY") expressed as inclusion bodies in *E. coli*. Ex. 1009, 1 (Abstract). In Hahm's method, the genes encoding CPY from yeast were cloned and expressed in *E. coli* cells "in the form of inclusion bodies in the bacterial cytoplasm." *Id.* For purification, Hahm states that the *E. coli* cells were harvested by centrifugation and then lysed by sonication. *Id.* at 2. The recovered inclusion bodies were then solubilized in a buffer of 50 mM Tris-HCl/3 mM EDTA (pH 8.0) ("Buffer A"), containing 6 M guanidinium chloride (GdmCl). *Id.* Hahm states that, for refolding, the denatured CPY was "rapidly diluted into Buffer A containing 0.5 M NaCl to give a final GdmCl concentration of 0.1 M." *Id.*; *see also id.* at 4 ("The inclusion bodies harvested were solubilized in Buffer A containing 6 M GdmCl and refolded by dilution 1:60 into Buffer A to give a final CPY concentration of 20 μg/mL."). A CPY propeptide ("CPYPR-His_6") was added to the refolding buffer to promote the *in vitro* refolding of CPY. *Id.* at 2, 4–5. Hahm states that "[t]he refolded CPY was purified by *p*-aminobenzylsuccinic acid affinity chromatography." *Id.* at 2–3.

4. Dietrich (Ex. 1008)

Dietrich relates to methods for purifying recombinant G-CSF using cation exchange chromatography and hydrophobic interaction chromatography, "wherein [the] two chromatographic steps are immediately consecutive in optional order." Ex. 1008, (57).

Dietrich states that "a frequently occurring problem in the production of recombinant proteins" such as G-CSF in *E. coli* is "the formation of hardly soluble intracellular aggregates of denatured forms of the protein expressed, the so-called inclusion bodies." *Id.* ¶ 5. According to Dietrich, the disclosed method provides for the purification of G-CSF "with satisfactory purity and yield," but "with as few chromatographic steps as possible in order to keep technical complexity and costs on a low level." *Id.* ¶ 13.

In the examples, Dietrich teaches a solubilization step wherein the inclusion bodies containing G-CSF were solubilized in solubilization buffer containing 30 mM Tris, 1 mM EDTA, 6.0 M guanidine-HCl, 100 mM GSH (glutathione), pH 8.0. *Id.* ¶ 68. Next, Dietrich teaches forming a refolding solution comprising the solubilization buffer and a refolding buffer, the refolding buffer containing 30 mM Tris, 2 mM GSSG (glutathione disulfide), 2 mM GSH, and 3 M urea at pH 7.5. *Id.* ¶ 69. Dietrich teaches filtering the refolding solution after refolding and "before the first chromatographic step." *Id.* ¶ 70. Dietrich teaches, in a first chromatographic step, applying the filtered solution to a cation exchange chromatography column SP Sepharose XL matrix, washing the column with sodium acetate, and subsequently eluting G-CSF with an elution buffer of 20 mM sodium acetate and 200 mM NaCl, pH 5.0). *Id.* ¶¶ 71–72.

Dietrich teaches that second and third chromatography steps provide for the further purification of G-CSF. Specifically, the second step involves hydrophobic interaction chromatography, *id.* ¶¶ 73–76, and the third step involves a second cation exchange chromatography, *id.* ¶¶ 77–81.

5. Rosendahl (Ex. 1006)

Rosendahl relates to a method "for making and refolding insoluble or aggregated proteins having free cysteines" from a host cell. Ex. 1006, (57). Rosendahl's method includes a solubilization step that exposes the insoluble or aggregated proteins "to a denaturing agent, and a disulfide reducing agent." *Id.* ¶ 38. Rosendahl states that "[u]seful disulfide reducing agents that also are cysteine blocking agents include, but are not limited to, thiols such as cysteine, thioglycolic acid, reduced glutathione and cysteamine." *Id.* Rosendahl's method also includes a refolding step "to obtain the protein's native conformation and native disulfide bonds." *Id.* ¶ 39. Rosendahl states that refolding may be achieved through "immobilization [of the protein] on a resin followed by buffer washes" by a refold mixture. *Id.* The refold mixture may include "an oxidizing agent" such as "cysteine, oxidized glutathione, and cystamine," or "a redox mixture of an oxidizing agent and a reducing agent," such as "cysteine/cystine, cysteine/cystamine, cysteamine/cystamine, reduced glutathione/oxidized glutathione, and the like." *Id.*

D. Printed Publication Status of Certain References

As an initial matter, Patent Owner argues that the Petition should be denied because it fails to establish that Ferré, Hahm, and several other references (i.e., Exs. 1007, 1010–1012, 1016–1033, 1050–1062, 1064, 1065,

1068, and 1071–1073) qualify as prior-art printed publications. Prelim. Resp. 30, 48–51.

At the institution stage, the Board has required the petitioner to make a "threshold showing" that any reference relied upon was publicly accessible before the effective filing date of the challenged patent. *See, e.g., Frontier Therapeutics, LLC v. Medac Gesellschaft Für Klinische Spezialpräparate mbH*, IPR2016-00649, Paper 10 at 22 (PTAB Sept. 1, 2016) (denying institution upon finding that petitioner failed to make a threshold showing that an alleged "printed package insert" was a printed publication); *Instradent USA, Inc. v. Nobel Biocare Servs. AG*, IPR2015-01786, Paper 14 at 16–17 (PTAB Feb. 19, 2016) (finding that deposition testimony from the challenged patent's co-inventor stating that hundreds of copies of a catalog may have been printed and distributed to customers was sufficient to make a threshold showing of public accessibility). Upon review of the evidence and arguments in the current record, we are persuaded that Petitioner has made the requisite threshold showing.

Ferré, on its face, appears to be a scientific article published in the journal *Protein Science.* Ex. 1004, 1. As with most scientific articles, the publication year is included as part of the citation itself: "*Protein Science* (**2005**), 14:2141–2153." *Id.* (emphasis added). Moreover, the face of the journal article indicates that the authors submitted the article for review on February 4, 2005, and submitted a final version on May 19, 2005. *Id.* The face of the journal article also indicates that the final form of the article was accepted on May 23, 2005, and published by Cold Spring Harbor Laboratory Press. *Id.* These indicia are conventional markers that, in this case, signal

that Ferré was published in 2005, years before the earliest-possible priority date of June 25, 2009 for the '997 patent *See* Ex. 1001, (60).

Similarly, Hahm, on its face, appears to be a scientific article published in the journal *Protein Expression and Purification.* Ex. 1009, 101. The publication year is included as part of the citation itself: "*Protein Expression and Purification* **22**, 101–107 (2001)," and the face of the journal article exhibits a copyright date of 2001 by Academic Press. *Id.* The face of the journal article also indicates that the authors submitted a first version of the article on December 11, 2000 and a revised version on February 5, 2001, and that the scientific article was published online on May 7, 2001. *Id.* As with Ferré, these indicia are conventional markers signaling that Hahm was published in 2001.

Because we find that Petitioner has made a sufficient threshold showing that Ferré and Hahm qualify as prior-art printed publications for institution, and institution is an all-or-nothing decision, we will make our determination as to whether Petitioner has satisfied its burden of proving public accessibility of the relevant challenged references in our final written decision based on the entire record. Thus, to the extent Patent Owner continues to challenge the printed-publication status of these references after institution, the parties are requested to further develop the record on this issue.

E. Asserted Anticipation by Ferré

Petitioner contends that Ferré anticipates claims 9, 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30 of the '997 patent. Pet. 34–41. A claim is anticipated, and therefore unpatentable under 35 U.S.C. § 102, if all its limitations are disclosed either explicitly or inherently in a single prior art reference. *In re*

Schreiber, 128 F.3d 1473, 1477 (Fed. Cir. 1997). That single prior art reference must disclose all the limitations of the claim "arranged or combined in the same way as in the claim." *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1370 (Fed. Cir. 2008).

Petitioner contends that Ferré teaches the preamble of claim 9, because Ferré "discloses a method of purifying a protein, tagged human β_2-microglobulin (HAT-hβ_2m), expressed in a non-native limited solubility form in a non-mammalian expression system, *E. coli*." Pet. 34 (citing Ex. 1004, 1 (Abstract), 2). Petitioner also contends that Ferré teaches the method steps of claim 9, because Ferré discloses solubilizing inclusion bodies with a denaturant, forming a refold solution comprising a refold buffer of 20 mM Tris-HCl, applying the refold solution to a separation matrix (EBA), and washing the separating matrix to elute the protein. *Id.* at 35–39 (citing Ex. 1004, 1–4, 9–11; Ex. 1002 ¶¶ 128–140).

Having considered the arguments and evidence before us, we find that the record establishes a reasonable likelihood that Petitioner would prevail on its asserted ground of anticipation by Ferré. Specifically, we are satisfied on this record that Ferré teaches each and every limitation of claim 9.

As to the preamble ("method of purifying a protein expressed in a non-native limited solubility form in a non-mammalian expression system"), Ferré discloses purifying a protein—N-terminally tagged human β_2-microglobulin (HAT-hβ_2m)—that is expressed as "insoluble inclusion bodies" in *E. coli*. Ex. 1004, 1 (Abstract), 2, 10. *E. coli* is a well-known bacterial (or non-mammalian) expression system. *See id.* at 1 (stating that "[h]eterologous protein production in bacteria has the potential to supply virtually unlimited amounts of high-value products").

As to the first method step ("solubilizing the expressed protein in a solubilization solution comprising one or more of the following: (i) a denaturant; (ii) a reductant; and (iii) a surfactant"), Ferré discloses that "[t]he released inclusion bodies were washed and solubilized in 8 M urea under nonreducing conditions, yielding denatured and oxidized HAT-hβ_2m." *Id.* at 2. The present record shows that urea is well known in the art as a denaturant. *See e.g.*, Ex. 1001, 2:38–39, 4:35–37, 5:29–30, 13:49–51, 22:38–41; Ex. 1002 ¶ 124.

Turning to the second method step ("forming a refold solution comprising the solubilization solution and a refold buffer, the refold buffer comprising one or more of the following: (i) a denaturant; (ii) an aggregation suppressor; (iii) a protein stabilizer; and (iv) a redox component"), we agree with Petitioner—on this record and for institution—that an ordinarily skilled artisan would have understood that Ferré discloses forming a refold solution by diluting the solubilizing solution containing the "denatured protein suspension" with a refolding buffer, "by pumping the denatured protein suspension and the aqueous buffer through a very small flowthrough mixing chamber." Ex. 1004, 3–4, 9; *see also* Pet. 35–36.

We also agree with Petitioner—on this record and for institution—that an ordinarily skilled artisan would have understood that Ferré discloses that the refold buffer comprises Tris-HCl, and thus meets the claim language of "the refold buffer comprising one or more" of the selected ingredients. Pet. 36. Specifically, Ferré identifies the "refolding buffer" as "20 mM Tris-Hcl [pH 8.0]." Ex. 1004, 10. And, as Petitioner points out, the '997 patent lists Tris-HCl as an example of a protein stabilizer and as an example of an aggregation suppressor. Ex. 1001, 2:43–50, 5:44–49, 14:21–25, 14:27–30,

22:47–51, 22:23–56; Pet. 36. Further, on this record, we are persuaded by Dr. Robinson's currently unrebutted testimony that "skilled artisans were well-versed in using Tris-HCl to protect proteins, for example, from changes in pH of a solution or heat, which may otherwise lead to protein denaturation and/or aggregation," and that "Tris-HCl was well known to be useful for promoting stable native protein structure and suppressing protein aggregation." Ex. 1002 ¶ 132 (citing Ex. 1075, 2, 6, 7, 11; Ex. 1076, 5, 7, Fig. 4 (A, B)).

We are not persuaded—on this record and for institution—by Patent Owner's arguments to the contrary. Prelim. Resp. 29–33. First, we do not read a concentration requirement into the claims, as Patent Owner suggests, for the reasons explained above in our claim construction analysis. *See supra* § III.B; *see also* Prelim. Resp. 31 (arguing that "Petitioner did not provide any analysis of Ferré under the proper construction of 'protein stabilizer' or 'aggregation suppressor'"). Second, having considered the arguments and evidence before us, we are of the opinion that Patent Owner's arguments demonstrate that there are disputed genuine issues of material fact about whether an ordinarily skilled artisan would have understood 20mM Tris-HCl to be a protein stabilizer and/or an aggregation suppressor as recited in the claims. Again, Dr. Robinson's testimony that skilled artisans would have understood 20mM Tris-HCl as such is currently unrebutted. *See* 37 C.F.R. § 42.108(c) (requiring certain "genuine issue[s] of material fact" to "be viewed in the light most favorable to the petitioner . . . for purposes of deciding whether to institute an *inter partes* review").

In addition, Patent Owner's argument that "Petitioner's own reference from its simultaneously filed '878 Petition teaches that *severe protein*

aggregation was detected in a solution containing 20mM Tris," Prelim. Resp. 32, lacks support in the record and/or adequate explanation. Specifically, Patent Owner points to Exhibit 1071 (as filed in IPR2019-00791) at page 5 as support for its argument, but page 5 of that Exhibit lists only the references cited in the article, and says nothing about protein aggregation or Tris solutions. Ex. 1071 (IPR2019-00791), 5.[2] Our own review of the remainder of the article finds a reference to 200mM, but not 20mM, Tris-Cl, and nothing to suggest undesirable protein aggregation at that concentration. *See* Ex. 1071 at 2 ("Pellets were resuspended in a minimal quantity (20 ml) of cold 200 mM Tris-Cl, pH 8.0 . . . ."). For these reasons, we conclude that this issue is best resolved following trial with the benefit of a full record, keeping in mind that Petitioner bears the burden of proving that the claims are unpatentable for anticipation.

Turning to method steps three ("applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix"), four ("washing the separation matrix"), and five ("eluting the protein from the separation matrix"), we are satisfied on this record that Ferré teaches these limitations by disclosing that its "novel . . . protein refolding strategy" comprises the steps of: (a) continuously diluting the denatured inclusion body proteins "into refolding buffer, using a short pipe

[2] In IPR2019-00791, Petitioner entered into the record as Exhibit 1071 the article David N. Garboczi et al., *Mitochondrial ATP Synthase: Overexpression in* Escherichia Coli *of a Rat Liver p Subunit Peptide and its Interaction with Adenine Nucleotides*, 263(30) J. BIOL. CHEM. 15694–98 (1988). Petitioner, however, did not enter that exhibit into the record of this proceeding. To the extent that Patent Owner wishes to cite to this article, Patent Owner should enter it into the record as an exhibit. 37 C.F.R. § 42.6(c).

reactor, [which] allow[s] for a defined retention and refolding time," and (b) then feeding the proteins "directly to an EBA column, where the protein was captured, washed, and finally eluted as soluble folded protein." Ex. 1004, 1; *see also id.* at 2 (stating that "the nascently folded protein is directly captured by expanded bed adsorption (EBA)—a special type of fluidized bed chromatography"); *id.* at 4 (Fig. 3) (providing a "[s]chematic representation of the system for continuous protein refolding and on-line EBA capture"); Pet. 39–41.

In summary, based on the record before us and the application of the reasonable likelihood standard, we are satisfied that Petitioner has shown sufficiently for instituting trial that it would prevail in showing claim 9 unpatentable for anticipation by Ferré. Patent Owner does not raise additional arguments specific to dependent claims 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30 at this stage of the proceeding. *See generally* Prelim. Resp. We have reviewed Petitioner's contentions and supporting evidence regarding these claims, and find them sufficient based on the current record. *See* Pet. 39–41 (citing Ex. 1004, 2, 4, 5, 10, 11; Ex. 1002 ¶¶ 127–146).

F. Asserted Anticipation by, or Obviousness Over, Komath

Petitioner contends that Komath anticipates, or renders obvious, claims 9, 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30 of the '997 patent. Pet. 41–57. A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007).

For anticipation, Petitioner contends that Komath teaches each and every limitation of claims 9, 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30. *See* Pet. 41–48 (citing Ex. 1005, 1, 3, 5–7, 9–12; Ex. 1002 ¶¶ 147–165). For obviousness, Petitioner contends that, "to the extent the Board disagrees that Komath anticipates these claims, the claims remain unpatentable as obvious," because an ordinarily skilled artisan "would have been motivated to purify a target protein using the steps of Komath and would have understood that these steps could be practiced together as arranged in claim 9 with a reasonable expectation of success." *Id.* at 48–49 (citing Ex. 1005, Abstract; Ex. 1002 ¶¶ 181–196).

Having determined that Petitioner has met its burden under § 314(a) as to its challenge of claim 9 for anticipation by Ferré, we also conclude that it is appropriate to institute *inter partes* review as to all claims challenged in the Petition, and on all grounds presented, pursuant to *SAS* and the USPTO Guidance. Thus, we institute *inter partes* review of claims 9, 10, 13, 14, 17, 18, 20, 21, 26, 29, and 30 based on anticipation by, or obviousness over, Komath.

As to the limitations of claim 9, for example, Komath "provides a simple and cost effective process for purifying large quantities of recombinant human G-CSF from *E. coli* and other cells in which inclusion bodies of G-CSF are formed." Ex. 1005, 5. Komath states that the process comprises "culturing hG-CSF producing recombinant cells in which over-expressed hG-CSF accumulates as inclusion bodies," "lysing said cells" and "isolating the inclusion bodies," "solubilizing and denaturing hG-CSF . . . with a combination of solubilizing agent and high alkaline pH," "refolding

hG-CSF by a two step method," "subjecting the hG-CSF to ion exchange chromatography," and "recovering purified hG-CSF." Ex. 1005, 6.

We offer the following observations on Patent Owner's arguments that Petitioner has failed to show a reasonable likelihood of prevailing on either ground of unpatentability based on Komath. *See* Prelim. Resp. 33–58. Patent Owner first appears to suggest that Komath is not enabled, and faults Petitioner for failing to address this issue in its Petition. Prelim. Resp. 33–34. Patent Owner, however, does not direct us to any Board decision or Federal Circuit case law squarely addressing whether a petitioner must prove enablement of a non-patent reference (such as a foreign patent application) in its petition.[3] *See id.* Thus, we decline to deny institution on this basis. *See Samsung Elecs Co. v. Affinity Labs of Tx., LLC*, Case IPR2014-01181, Paper 36 at 63 (PTAB Jan. 28, 2016) (stating that "Petitioner cannot anticipate or seek to refute every possible argument that will be made by Patent Owner in its Petition").

Patent Owner also argues that Komath "fails to disclose every element of the asserted claims *arranged as in the claim*, and thus cannot anticipate." Prelim. Resp. 40–41 (citing Ex. 2002, 68; *SynQor, Inc. v. Artesyn Techs., Inc.*, 709 F.3d 1365, 1375 (Fed. Cir. 2013)). Similarly, Patent Owner argues that, because "Komath provides *different choices* for various steps, and the

[3] We note that, in the context of patent examination, the Federal Circuit has held that "a prior art printed publication cited by an examiner is presumptively enabling barring any showing to the contrary by a patent applicant or patentee." *In re Antor Media Corp.*, 689 F.3d 1282, 1288 (Fed. Cir. 2012). The Federal Circuit also has found that a similar presumption as to enablement of unclaimed materials in a patent applies in contested district court proceedings as well as during patent examination. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1355 (Fed. Cir. 2003).

Petition does not explain *which* options [an ordinarily skilled artisan] would have chosen and *why* or *how* such selection of certain options would impact reasonable expectation of success," Komath cannot render the claims unpatentable for obviousness. *Id.* at 43–44. In this regard, Patent Owner argues that "the techniques disclosed in Komath are separately discussed in different discrete sections addressing distinct processes (e.g., 'Source of rHG-CSF Gene,' 'Fermentation,' 'Purification,' and 'Ion Exchange Chromatography') and different examples." *Id.* at 41.

On this record, however, it is not clear to us that Komath's examples address, in fact, distinct processes as Patent Owner asserts. Instead, it appears that Komath's examples describe different, but sequential, steps of Komath's process for the purification of hG-CSF. *See* Ex. 1005, 9 (stating that "[p]urification of rhG-CSF from the harvested *E.coli* cells is done by a simple three step procedure involving lysis of the cells, washing of inclusion bodies and ion exchange chromatography"). In accordance with the order of those steps, Example 1 describes the lysis of cells to obtain the inclusion bodies containing protein, *id.* at 10–11, Example 2 describes "a repeated wash procedure" to purify the inclusion bodies, *id.* at 11–12, and Examples 3 and 4 describe the solubilization of protein from the inclusion bodies and ion-exchange chromatography "as a final polishing step for the protein," *id* at 12.

Finally, we acknowledge that, under the heading "Ion Exchange Chromatography," Komath describes eluting protein from an ion-exchange column with 0.1 M Tris-HCl (pH 8.0), *see* Ex. 1005, 10, but in "Example 4," Komath describes eluting protein from an ion-exchange column with various concentrations of NaCl, *see id.* at 12–13. We are not persuaded on this

record, however, that Komath's use of two different elution buffers is necessarily inconsistent. Komath expressly teaches that recovery of hG-CSF after elution with 0.1 M Tris-HCl buffer at pH 8.0 is "maximal," because it yields "3 to 5 times more than with NaCl at pH 4.5." Ex. 1005, 10. Consistent with that statement, Komath shows that, when hG-CSF protein is eluted from an ion-exchange column with "various concentrations of sodium chloride," either no protein or less than 1% of protein was recovered. *Id.* at 12–13. Thus, we do not find—at least on this record—that Patent Owner's arguments undermine Petitioner's showing of a reasonable likelihood of success.

We also observe that Patent Owner has yet to submit expert testimony supporting its attorney arguments as to the ordinarily skilled artisan's understanding of Komath's teachings. *See* Prelim. Resp. 34–40. Again, we determine that these issues are best resolved following trial with the benefit of a full record. *See* 37 C.F.R. § 42.65(a) (opinion testimony that does not disclose underlying facts "is entitled to little or no weight").

G. Asserted Anticipation by Hahm and Dietrich

Petitioner contends that Hahm anticipates claims 9, 10, 13, 14, 15, 17–21, 23, 26, and 29 of the '997 patent, Pet. at 57–62, and that Dietrich anticipates 9, 10, 13–15, 17–21, 23, and 26–30, *id.* at 62–67. In light of *SAS* and USPTO Guidance, we institute an *inter partes* review on the ground of anticipation by Hahm and on the ground of anticipation by Dietrich, for all challenged claims.

Before leaving these grounds, however, we briefly address Patent Owner's arguments that neither Hahm nor Dietrich discloses the claimed limitation of "applying the refold solution to a separation matrix under

conditions suitable for the protein to associate with the matrix." Prelim. Resp. 50–55. Petitioner asserts that Hahm satisfies this claim limitation because "Hahm does not disclose any intermediate steps before applying the refold solution to the separation matrix." Pet. 59 (citing Pet. 1009; Ex. 1002 ¶ 211). Petitioner also asserts that an ordinarily skilled artisan would not have had a reason to remove the EDTA present in the refold buffer (such as by centrifugation, precipitation, or dialysis), because the skilled artisan would have understood that 3 mM EDTA "would not significantly affect the performance of p-aminobenzylsuccinic acid affinity chromatography." *Id.* at 59–60 (citing Ex. 1002 ¶ 211). In response, Patent Owner argues that "Hahm *does not actually state there are no intermediate steps*," and that the Petitioner's own reference, Exhibit 1031, "states '[i]t is *highly recommended* to *centrifuge and filter* any sample *immediately before chromatographic purification*.'" Prelim. Resp. 50–51 (quoting Ex. 1031, 131).

As to Patent Owner's argument that the method of Hahm may require intermediate steps, including the removal of EDTA, between forming the refold solution and applying it to a separation matrix, we observe that claim 9 states only that the refold solution is applied to the separation matrix. This is in contrast to independent claim 7 in the '878 patent (at issue in IPR2019-00791), which states that the refold solution is applied "directly" to the separation matrix. *Compare* Ex. 1001, 22:51–53 (reciting "applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix"), *with* Ex. 3002, 22:21–23 (reciting "*directly* applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix"). Moreover, the method of claim 9 recites the transitional term "comprising," indicating that

additional method steps are encompassed within its scope. *See Solvay S.A. v. Honeywell Int'l Inc.*, 742 F.3d 998, 1005 (Fed. Cir. 2014) ("The well-established meaning of 'comprising' in a method claim indicates that the claim is open-ended and allows for additional steps." (quotation omitted)). Thus, at this stage of the proceeding, even if the method of Hahm utilizes intermediate steps, we do not read claim 9 so narrowly as to exclude them.

Turning to Dietrich, Petitioner contends that this reference discloses "applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix," because Dietrich does not disclose any intervening steps of "dilution, centrifugation, dialysis, or precipitation," and because Dietrich teaches adjusting the pH of the refold solution to pH 3.2 before applying the refold solution to the ion-exchange column. Pet. 64–65 (citing Ex. 1008 ¶¶ 32–36, 70–72). Relying on the Declaration of Dr. Robinson, Petitioner contends that, by adjusting the pH, Dietrich's method satisfies the requirement of claim 9 that "conditions [are] suitable for the protein to associate with the matrix." *Id.* (citing Ex. 2002 ¶ 224). In response, Patent Owner argues that the pH adjustment would cause "*precipitation* of components out of solution." Prelim. Resp. 53–54.

We understand Patent Owner's argument to be that, because the pH adjustment would precipitate components out of solution, Dietrich does not apply the claimed "refold solution"—which comprises at least "one or more of" a denaturant, an aggregation suppressor, a protein stabilizer, and a redox component—to the separation matrix. At this state of the proceeding, however, Patent Owner points to no evidentiary support for that argument. We again view this issue as one best resolved following trial with the benefit of a full evidentiary record.

H. Asserted Obviousness over Ferré, Komath, or Dietrich in view of Rosendahl

Petitioner contends that dependent claims 15, 19, 23, 27, and 28 of the '997 patent are unpatentable as obvious over Ferré, Komath, or Dietrich in view of Rosendahl. Pet. 67–71. Claims 15 and 23 depend from claims 9 and 14, respectively, and specify that the "reductant comprises one or more of cysteine, dithiothreitol (DTT), betamercaptoethanol and glutathione." Ex. 1001, 23:3–5 (claim 15), 24:1–3 (claim 23). Claims 19 and 27 depend from claims 9 and 18, respectively, and specify that the "redox component comprises one or more of glutathione-reduced, glutathione-oxidized, cysteine, cystine, cysteamine, cystamine and betamercaptoethanol." *Id.* at 23:19–22 (claim 19), 24:18–21 (claim 27). Claim 28 depends from claim 19, and specifies that the separation matrix is either an affinity resin or a non-affinity resin, with each type of resin limited to a specific Markush group. *Id.* at 24:22–29 (claim 28).

Upon review of the record, we are satisfied that Petitioner establishes sufficiently for institution that the combination of any of Ferré, Komath, or Dietrich with Rosendahl teaches the limitations of claims 15, 19, 23, 27, and 28. As to claims 15 and 23, Rosendahl teaches that "disulfide reducing agents" include "cysteine, thioglycolic acid, reduced glutathione and cysteamine," Ex. 1006 ¶ 38, thus satisfying the plain language of those claims. As to claims 19 and 27, Rosendahl teaches a refold mixture comprising "a redox mixture of an oxidizing agent and a reducing agent," such as "cysteine/cystine, cysteine/cystamine, cysteamine/cystamine, reduced glutathione/oxidized glutathione, and the like," *id.* ¶ 39, thus satisfying the plain language of those claims. Finally, as to claim 28, each of Ferré, Komath, and Dietrich disclose the use of a non-affinity separation

matrix in protein purification. For example, Ferré discloses use of the "STREAMLINE DEAE medium" for protein adsorption. Ex. 1004, 4. On this record, we are persuaded by Dr. Robinson's currently unrebutted testimony that ordinarily skilled artisans would have understood that STREAMLINE DEAE is an ion (i.e., anion)-exchange resin. Ex. 1002 ¶ 136 (citing Ex. 1019, 53); Pet. 42.

We are also satisfied on this record that Petitioner shows sufficiently for institution that an ordinarily skilled artisan would have had a reason to combine the disclosure of Rosendahl with Ferré, Komath, or Dietrich, with a reasonable expectation of success, at least for claims 15, 19, 23, 27. Pet. 68–71.

Specifically, we agree with Petitioner—on this record and for institution—that Rosendahl teaches a method for refolding proteins that are expressed in an insoluble or aggregated form by non-mammalian host cells, preferably *E. coli*. Pet. 68 (citing Ex. 1006 ¶¶ 14, 15, 21). We also agree that, like Ferré, Komath, and Dietrich, Rosendahl teaches that the method includes a solubilization step and a refolding step. *Id.* (citing Ex. 1006 ¶¶ 38–39; Ex. 1002 ¶¶ 237, 240). Thus, an ordinarily skilled artisan seeking to solubilize and refold proteins expressed in, for example, *E. coli*, in a limited solubility form would have been prompted to look to Rosendahl for its teachings of specific reductant/redox components that successfully solubilized and refolded aggregated proteins expressed in *E. coli*. *Id.* at 68–69 (citing Ex. 1002 ¶¶ 238–239, 241–242); *see also* Ex. 1006 ¶ 38 (stating that "[u]se of a disulfide-reducing agent that also is a cysteine blocking agent during the solubilization step reduces the number of compounds and

steps required in the overall process for refolding the insoluble or aggregated protein to a soluble, active form").

We have considered Patent Owner's arguments to the contrary, but again are not persuaded on this record. *See* Prelim. Resp. 56–61. In the main, these arguments raise disputed issues of fact about whether an ordinarily skilled artisan would have been led away from using Rosendahl's specific reductant/redox components, when the methods of Ferré and Komath are already allegedly optimized. Again, we conclude that these issues are best resolved following trial with the benefit of a full record.

Finally, we acknowledge Patent Owner's argument that Petitioner's obviousness analysis of claim 28 is incomplete because it consists of only two sentences, and does not specifically address reasonable expectation of success. *Id.* at 61 (citing Pet. 71). But, because we institute an *inter partes* review of all challenged claims on all grounds set forth in the Petition in accordance with USPTO Guidance and *SAS*, we leave this issue for trial.

IV. 35 U.S.C. § 314(a) ANALYSIS

Patent Owner argues that we should exercise our discretion under 35 U.S.C. § 314(a) to deny the Petition. Prelim. Resp. 8–15; *see also* Sur-reply. Petitioner disagrees. *See generally* Reply. Section 314(a) does not require the Director to institute an *inter partes* review. *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) ("[T]he PTO is permitted, but never compelled, to institute an IPR proceeding."). Rather, a decision whether to institute is within the Director's discretion, and that discretion has been delegated to the Board. *See* 37 C.F.R. § 42.4(a); *Cuozzo Speed Techs., LLC v. Lee,* 136 S. Ct. 2131, 2140 (2016) ("[T]he agency's

decision to deny a petition is a matter committed to the Patent Office's discretion.").

In *General Plastic Indus. Co. v. Canon Kabushiki Kaisha*, Case IPR2016-01357, Paper 19 (PTAB Sept. 6, 2017) (precedential as to Section II.B.4.i) ("*General Plastic*"), the Board articulated a non-exhaustive list of factors to consider in evaluating whether to exercise discretion under § 314(a) to deny a petition that challenges a patent that was previously challenged before the Board. *See also* Office Patent Trial Practice Guide Update (available at https://www.uspto.gov/sites/default/files/documents/2018_Revised_Trial_Practice_Guide.pdf) ("TPGU") at 9–11 (stating that the Board will consider the *General Plastic* factors when determining whether to institute a trial). These factors are:

1. whether the same petitioner previously filed a petition directed to the same claims of the same patent;

2. whether at the time of filing of the first petition the petitioner knew of the prior art asserted in the second petition or should have known of it;

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

4. the length of time that elapsed between the time the petitioner learned of the prior art asserted in the second petition and the filing of the second petition;

5. whether the petitioner provides adequate explanation for the time elapsed between the filings of multiple petitions directed to the same claims of the same patent;

6. the finite resources of the Board; and

7. the requirement under 35 U.S.C. § 316(a)(11) to issue a final determination not later than 1 year after the date on which the Director notices institution of review.

Gen. Plastic, Paper 19 at 9–10; *see also* TPGU at 9–10.

These factors, however, are "a non-exhaustive list" and "additional factors may arise in other cases for consideration, where appropriate." *Gen. Plastic*, Paper 19 at 16, 18; *see also* TPGU at 10 (stating that "[t]he *General Plastic* factors are also not exclusive" and that "[t]here may be other reasons" that "favor[] denying a petition"). Patent Owner acknowledges that, in this case, "the *General Plastic* factors themselves are not all directly applicable," because Petitioner's Petition is the first filed in the PTAB challenging the patentability of the claims of the '997 patent. Sur-reply 4. Nevertheless, Patent Owner argues that the rationale underlying *General Plastic* applies because the Petition is a "follow on *from litigation*, where Petitioner *asserts the same art and combinations*, adjusting some positions to account for [Patent Owner's] validity contentions while ignoring other deficiencies identified in those contentions." *Id.*

Specifically, Patent Owner points out that the parties are engaged in a district-court litigation in which validity contentions have been exchanged. Prelim. Resp. 9; *see also* Ex. 2001 (Petitioner's invalidity contentions); Ex. 2002 (Patent Owner's validity contentions). Patent Owner argues that Petitioner "has unfairly used [Patent Owner's] litigation validity contentions as a roadmap" for crafting its Petition. *Id.* at 8. For example, Patent Owner argues that Petitioner used Patent Owner's validity contentions to create "revised theories" of unpatentability. *Id.* at 10–11. Patent Owner argues that we should deny institution because Petitioner's access to Patent

Owner's validity contentions gave Petitioner an unfair advantage. *Id.* at 11–15. Having considered the respective arguments and evidence of the parties, we decline to exercise our discretion under 35 U.S.C. § 314(a) to deny the Petition.

As an initial matter, we agree with Patent Owner that the *General Plastic* factors *per se* are not directly applicable, but the parties do not point us to any Board decision directly addressing the effect of exchanging validity contentions in an underlying district-court litigation on a PTAB proceeding. Nevertheless, the TPGU explains that "events in other proceedings related to the same patent, either at the Office, in district courts, or the ITC" may constitute a reason to deny a petition under § 314(a). TPGU 10. In *NHK Spring Co. v. Intri-Plex Techs. Inc.*, IPR2018-00752, Paper 8 at 2 (PTAB Sept. 12, 2018) (precedential), for example, the Board exercised its discretion under both § 314(a) and 35 U.S.C. § 325(d) to deny institution of an *inter partes* review. As to its discretion under § 314(a), the Board considered "the status of the district court proceeding between the parties," and concluded that "the advanced state of the district court proceeding is an additional factor that weighs in favor of denying the Petition under § 314(a)." *Id.* at 19–20.

Unlike in *NHK*, however, we have no evidence here that the underlying district-court litigation is in an advanced state or that a trial will occur before the Board likely will be able to rule on patentability. *See NetApp, Inc. v. Realtime Data LLC*, Case IPR2017-01195, Paper 9 at 12–13 (PTAB Oct. 12, 2017) (denying institution under § 314(a) of a follow-on petition filed by a different petitioner where, due to petitioner's delay, the Board likely would not have been able to rule on patentability until after the

district court trial date). Indeed, Petitioner represents—and Patent Owner does not contest—that the exchanged contentions were preliminary, and that no trial date has been set in the district-court litigation. Reply 3, 5; *see generally* Sur-reply. Thus, we are not persuaded by Patent Owner's argument about delay in filing the Petition, which was filed within the one-year time period set by statute, 35 U.S.C. § 315(b).

Turning to Patent Owner's main argument, we are not persuaded, on the particular circumstances of this case, that Petitioner has used Patent Owner's validity contentions as a "roadmap" in a manner unfair to Patent Owner. Here, as Petitioner points out, the parties have *exchanged* validity contentions, and thus both parties have had access to the other's litigation positions. Reply 3. Petitioner also points out that Patent Owner appears to have tailored its claim-construction arguments in this case to respond to Petitioner's claim-construction positions taken in district court *after* the Petition's filing date. *See* Prelim. Resp. 23 (citing Ex. 2009); *see also* Reply 3. Thus, we agree with Petitioner that, on these facts, any unfairness appears to be borne by both parties.

For the reasons discussed above, we determine that the factors in this particular case do not weigh in favor of exercising our discretion under 35 U.S.C. § 314(a). Therefore, we decline Patent Owner's request to deny the Petition under 35 U.S.C. § 314(a).

V. CONCLUSION

After considering the arguments presented in the Petition, the Preliminary Response, the Reply, and Sur-reply, as well as the evidence of record, we determine that Petitioner has demonstrated a reasonable likelihood of success in proving that at least one claim of the '997 patent is

unpatentable. Thus, in accordance with *SAS* and USPTO Guidance, we institute an *inter partes* review of all challenged claims on all grounds set forth in the Petition. Our determinations at this stage of the proceeding are based on the evidentiary record currently before us. This decision to institute trial is not a final decision as to patentability of any claim for which we have instituted an *inter partes* review. We will base any final decision on the full record developed during trial.

VI. ORDER

Accordingly, it is:

ORDERED that pursuant to 35 U.S.C. § 314(a), an *inter partes* review of claims 9, 10, 13–15, 17–21, 23, and 26–30 of U.S. Patent No. 9,643,997 B2 is instituted with respect to all grounds set forth in the Petition;

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, an *inter partes* review of the '997 patent shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

For PETITIONER:

Rolando Medina
Eric Marandett
CHOATE, HALL, & STEWART LLP
rmedina@choate.com
emarandett@choate.com

For PATENT OWNER:

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