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Paper 18
Date: March 31, 2020

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PROLLENIUM US INC.,
Petitioner,

v.

ALLERGAN INDUSTRIE, SAS,
Patent Owner.

IPR2019-01632
Patent 8,357,795 B2

Before GRACE KARAFFA OBERMANN, SHERIDAN K. SNEDDEN, and ROBERT A. POLLOCK, *Administrative Patent Judges.*

SNEDDEN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Prollenium US Inc. ("Petitioner") filed a Petition for *inter partes* review of claims 26–39 of U.S. Patent No. 8,357,795 ("the '795 patent," Ex. 1001). Paper 1 ("Pet."). Allergan Industrie, SAS ("Patent Owner") filed a Preliminary Response. Paper 7 ("Prelim. Resp."). On January 10, 2020, we issued an Order granting Petitioner's request for additional briefing regarding whether we should exercise our discretion to deny the Petition under §325(d) and/or §314(a). Paper 12. In response to our Order, Petitioner filed a Reply to the Patent Owner Preliminary Response (Paper 13, "Reply"), and Patent Owner filed a corresponding Sur-reply (Paper 17, "Sur-reply).

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) (2012). The Supreme Court has held that a decision to institute under 35 U.S.C. § 314 may not institute on fewer than all claims challenged in the petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018) ("SAS"). After considering the evidence and arguments presented in the Petition, we determine that Petitioner has demonstrated a reasonable likelihood of success in proving that at least claim 26 of the '795 patent is unpatentable. Accordingly, an *inter partes* review of all of the claims and all of the grounds presented in the Petition is hereby instituted.

In this Decision, we address all issues raised by the parties in the pre-trial briefing. Our factual findings and conclusions at this stage of the proceeding are based on the evidentiary record developed thus far. This is not a final decision as to the patentability of claims for which *inter partes*

review is instituted. Our final decision will be based on the record as fully developed during trial.

A. Real Parties in Interest

Petitioner identifies its real parties-in-interest as Prollenium US Inc. and Prollenium Medical Technologies Inc. Pet. 61. Patent Owner identifies its real parties-in-interest as Allergan Industrie, SAS; Allergan USA, Inc.; Allergan Sales, LLC; Allergan Holdings France SAS; Allergan Holdings Limited; Allergan Holdings, Inc.; Allergan Puerto Rico Holdings, Inc.; and Allergan, Inc. Paper 4, 2.

B. Related Matters

Petitioner has filed a separate Petition for *inter partes* review of claims 1–11, 22, 40, and 41 of the '795 patent as IPR2019-01506. The '795 patent is at issue in *Allergan USA, Inc. et al v. Prollenium US Inc., et al.*, Case No. 1:19-cv-00126 (D. Del. filed Jan. 22, 2019). Pet. 61; Paper 4, 2. The '795 patent was the subject of two previous *inter partes* reviews: IPR2014-01422 filed August 29, 2014 and terminated June 19, 2015 by way of joint motion to terminate, and IPR2017-01906 filed August 2, 2017 and denied on March 9, 2018. Paper 4, 2–3.

Petitioner has filed Petitions for *inter partes* review of related U.S. patents as follows: U.S. Patent No. 8,450,475 B2 ("the '475 patent") in IPR2019-01505; U.S. Patent No. 8,822,676 B2 ("the '676 patent") in IPR2019-01617; U.S. Patent No. 9,089,519 B2 ("the '519 patent") in IPR2020-00084; U.S. Patent No. 9,238,013 B2 ("the '013 patent") in IPR2019-01509; and U.S. Patent No. 9,358,322 B2 ("the '322 patent") in IPR2019-01509. Pet. 61–62; Paper 4, 3. The '475, '676, '519, '013, and '332 patents are also at issue in A*llergan USA, Inc. et al v. Prollenium US Inc., et al.*, Case No. 1:19-cv-00126 (D. Del. filed Jan. 22, 2019). *Id.*

C. The '795 Patent

1. Specification

The subject matter claimed in the '795 patent is directed to soft tissue filler compositions. Ex. 1001, 19:20–22:27. The compositions include a hyaluronic acid (HA) component and an anesthetic agent, e.g., lidocaine. *Id.* at 2:36–49. The hyaluronic acid component is crosslinked with a crosslinking agent, e.g., 1,4-butanediol diglycidyl ether (BDDE). *Id.* at 2:50–59. "The pH of the purified, substantially pH neutral, crosslinked HA gels are preferably adjusted to cause the gels to become slightly alkaline such that the gels have a pH of greater than about 7.2, for example, about 7.5 to about 8.0." *Id.* at 10:64–67.

The compositions are sterilized, for example by autoclaving, to form sterile compositions. *Id.* at 3:42–47. The compositions may be used as dermal fillers to help fill in facial lines and depressions and for restoring fat loss-related tissue volume. *Id.* at 1:30–34. Allergan markets dermal fillers containing crosslinked hyaluronic acid and lidocaine under the tradename Juvéderm®. Prelim. Resp. 1–2.

2. Illustrative Claims

Independent claims 26 and 29, reproduced below, are illustrative of the challenged claims.

> 26. A composition comprising a crosslinked hyaluronic acid (HA) at a concentration of about 20 mg/mL to about 30 mg/mL and lidocaine at a concentration of about 0.1% to about 5% by weight, wherein the composition has a pH above about 7.5.
>
> 29. A sterile composition comprising a crosslinked hyaluronic acid (HA) at a concentration of about 22 mg/mL and lidocaine at a concentration of about 0.2% to about 1% by weight, wherein the composition is stable during storage under ambient conditions for at least 3 months.

Ex. 1001, 21:10–14, 19–23.

3. Relevant Prosecution History

The '795 patent issued from U.S. Application Serial No. 12/393,884 ("the '884 application," Ex. 1023). During the prosecution of the '884 application, the Examiner rejected the claims as obvious over Lebreton, disclosing BDDE-crosslinked hyaluronic dermal fillers, and secondary references disclosing adding lidocaine to hyaluronic acid dermal fillers. Ex. 1023, 43–46, 78–80. For example, the Examiner rejected the claims as obvious over Lebreton and Wang[1] (teaching crosslinked hyaluronic acid that further comprises preferably an anesthetic such as lidocaine) or Calias[2] (teaching hyaluronic acid crosslinked with DVS and further comprising a drug such as lidocaine). *Id.* at 45, 80. After a final rejection over Lebreton and Calias, the Applicant argued that "the heat stable property of the claimed dermal filler compositions, as shown in the Declaration and as supported by the data of record, is evidence that the claimed compositions comprising hyaluronic acid and lidocaine, are nonobvious." *Id.* at 24–25.

To support this argument, the Applicant submitted a Declaration by the inventor, Pierre F. Lebreton, Ph.D. (Ex. 1024). Ex. 1023, 11–29. Dr. Lebreton attested as follows:

> It was believed that adding lidocaine to hyaluronic acid gel compositions during manufacturing caused degradation of the hyaluronic acid prior to injection of the HA as a dermal filler.
>
> It was believed that lidocaine caused degradation of HA gel compositions during high temperature sterilization.

[1] Ex. 1047, W. Wang, U.S. Patent Application Publication No. 2005/0271729 A1, published Dec. 8, 2005 ("Wang").
[2] Ex. 1048, P. Calias et al., U.S. Patent No. 6,521,223 B1, issued Feb. 18, 2003 ("Calias").

> It was not known whether HA compositions comprising lidocaine were stable or not after high temperature sterilization when placed in storage for any significant length of time.
>
> It was also believed that the instability of HA described above would have caused a viscosity reduction of the HA that would make it unsuitable for soft tissue filling applications.
>
> Based upon the facts set forth above, a person of ordinary skill in the art would have expected that a dermal filler comprising hyaluronic acid and lidocaine would not have remained sufficiently stable to be useful as soft tissue filler.
>
> It was not appreciated that a dermal filler comprising a cohesive gel of hyaluronic acid makes it possible for lidocaine to be combined with hyaluronic acid in a gel that is sufficiently stable to be useful as a soft tissue filler.
>
> The enhanced stability properties of the inventive dermal fillers was evidenced by certain experiments performed under my direction by my research team prior to the application filing date.
>
> To my knowledge, it was a surprising and unexpected discovery, not appreciated prior to the present invention, that certain cohesive HA gels, as defined in the application, when mixed with lidocaine, could be made to be heat and shelf stable.

See Pet. 14; Prelim. Resp. 10–12. The Applicant further submitted Cui[3] as evidence "that HA gels are known to be sensitive to heat sterilization, and that even more particularly, that HA gels crosslinked with BDDE are known to be especially sensitive to heat sterilization relative to HA gels cross linked with other, i.e. non-BDDE, crosslinkers." Ex. 1023, 28.

D. Evidence

Petitioner relies upon the following prior art references.

[3] Cui et al., *The comparison of physicochemical properties of four Cross-linked sodium hyaluronate gels with different cross-linking agents*, 396–398 ADV. MATS. RES. 1506–1512 (2012) (Ex. 1025).

Ex. 1050, *Cosmetic Tissue Augmentation Product, Summary of Safety and Effectiveness*, Premarket Approval (PMA) Application No. P050033 (FDA Dec. 20, 2006) ("CTA Summary").[4]

Ex. 1051, Letter from Mark N. Melkerson, Director, Division of General, Restorative and Neurological Devices, FDA, to Constance Garrison, Vice President, Regulatory, Clinical and Quality Systems, Anika Therapeutics, Inc. (Dec. 20, 2006) ("PMA Letter").

Ex. 1054, FDA Medical Devices; Availability of Safety and Effectiveness Summaries for Premarket Approval Applications, 72 Fed. Reg. 15885, 15886 (Apr. 3, 2007).

Ex. 1029, P. Lebreton, U.S. Patent Application Publication No. 2006/0194758 A1 (published Aug. 31, 2006) ("Lebreton").

Ex. 1030, K. K. Sadozai et al., U.S. Patent Application Publication No. 2005/0136122 A1 (published Jun. 23, 2005) ("Sadozai").

Petitioner also relies upon the Declaration of Dr. Dale P. DeVore (Ex. 1002) to support its contentions.

E. Asserted Grounds of Unpatentability

Petitioner asserts that claims 26–39 would have been unpatentable on the following grounds.

Ground	Claim(s)	35 U.S.C. §[5]	References/Basis
1	26–39	103(a)	CTA Summary
2	26–39	103(a)	Lebreton, Sadozai

[4] We address the status of the CTA Summary as prior art below.
[5] The Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) ("AIA"), amended 35 U.S.C. §§ 102 and 103. Because the challenged claims of the '795 patent have an effective filing date before the effective date of the applicable AIA amendments, we refer to the pre-AIA versions of 35 U.S.C. § 103 throughout this Decision.

F. Abbreviations

HA	Hyaluronic Acid
CTA	Cosmetic Tissue Augmentation
FDA	Food & Drug Administration
PMA	Premarketing Approval
BDDE	butanediol diglycidyl ether
BCDI[6]	p-phenylene-bis(ethylcarbodiimide)
DVS	1,4-divinylsulfone
DEO	Diepoxyoctane

II. ANALYSIS

A. Level of Ordinary Skill in the Art

The person having ordinary skill in the art is a hypothetical person who is presumed to be aware of all the relevant prior art. *Custom Accessories, Inc. v. Jeffrey-Allan Indust., Inc.*, 807 F.2d 955, 962 (Fed. Cir. 1986); *Kimberly-Clarke Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1453 (Fed. Cir. 1984). Moreover, the prior art itself is generally sufficient to demonstrate the level of skill in the art at the time of the invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001) (explaining that specific findings regarding ordinary skill level are not required "where the prior art itself reflects an appropriate level and a need for testimony is not shown") (quoting *Litton Indus. Prods., Inc. v. Solid State Sys. Corp*., 755 F.2d 158, 163 (Fed. Cir. 1985)).

Petitioner asserts that a person of ordinary skill in the art would have been "a scientist involved in the development of dermal fillers, who would

[6] Ex. 1030 ¶ 85.

have an advanced degree, such as a Ph.D., M.S., or M.D., and several years of experience developing dermal fillers for cosmetic use, including HA-based dermal fillers." Pet. 16 (citing Ex. 1002 ¶¶ 69–72). Petitioner asserts that the person of ordinary skill "would be aware of commercially sold dermal fillers, in the United States and abroad, as well as those products for which approvals were being publicly sought." *Id.* Petitioner asserts that the person of ordinary skill "would also be aware of the process by which FDA reviews dermal filler products, and how FDA communicates the results of such reviews to the public." *Id.* (citing Ex. 1002 ¶¶ 73–75; Ex. 1032, 227).

Patent Owner contends that the Board should adopt the same definition for the person of ordinary skill as previously adopted in IPR2017-01906, which also involved the '795 patent.[7] Prelim. Resp. 13–15. In IPR2017-01906, the Board determined that a person of ordinary skill in the art would have had "a B.S. or M.S. in biochemistry, polymer chemistry, medicinal chemistry, pharmaceutical chemistry, or a related field with 'several years' of practical experience. Alternatively . . . the ordinary artisan would have had less practical experience but a Ph.D. in one of those fields, or an M.D. in dermatology, plastic surgery, or a specialty related to the clinical use of dermal fillers." *Id.* at 13 (citing IPR2017-01906, Paper 15 at 8–9).

On the present record, we find Petitioner's definition reasonable. Consistent with Petitioner's argument, the proposed definition is not clearly inconsistent with our prior determination and is supported by Dr. DeVore's presently uncontested testimony. *See* Ex. 1002 ¶¶ 69–72. Further, the art of

[7] *Teoxane S.A. v. Allergan, PLC*, IPR2017-01906, Paper 15 (PTAB Mar. 9, 2018)

record abundantly supports Petitioner's proposition that one of ordinary skill in the art would have been aware of commercially sold dermal fillers and publically available information regarding their FDA approval.

Monheit[8], for example, discusses clinical trials and approval dates of "five FDA-approved HA skin fillers available in the United States: Hylaform, Hylaform Plus, Captique (Inamed Corporation), Restylane (Medicis Aesthetics Inc.), and, most recently, Juvéderm (Allergen Aesthetics)," noting, for example, that "Hylaform has been available worldwide since 1998 and in the United States since 2004." Ex. 1022, 79–80. And in summarizing an FDA clinical study comparing Hylaform to Zyplast, Monheit cites data from a 2003 FDA publication "Available at: http://www.fda.gov/ohrms/dockets/ac/03/slides/4004s1_01_lerner_files/frame.htm." *Id.* at 80, Box 1.

Moreover, in reviewing the state of the art of injectable skin fillers for soft tissue augmentation, Narins[9] notes the FDA approval status for commercially available products Zyderm I and II, CosmoDerm, CosmoPlast, Restylane, Hylaform, Radiance FN, Sculptra, and Silikon 1000. Ex. 1007, 152, 153, 156–157, 158, 159. Kinney[10] similarly notes the FDA approval

[8] Ex. 1014, Gary D. Monheit & Chad L. Prather, *Juvéderm: A Hyaluronic Acid Dermal Filler*, Journal of Drugs in Dermatology, Vol. 6, Issue 11, 1091-1095 (Nov. 2007) ("Monheit"). *See also*, Ex. 1002 ¶¶ 39, 105 (Dr. DeVore's reliance on Monheit); Prelim. Resp. 31 (same).

[9] Ex. 1007, R. S. Narins and P. H. Bowman, *Injectable Skin Fillers*, 32 CLIN. PLAST. SURG. 151–162 (2005) ("Narins").

[10] Ex. 1012, B. M. Kinney, *Injecting Puragen Plus into the Nasolabial Folds: Preliminary Observations of FDA Trial*, 26 AESTHETIC SURG. J. 741–748 (2006) ("Kinney").

dates of Restylane and Juvaderm (Ex. 1012, 741), and Smith[11] discusses the "FDA status and Approved Uses" of Juvéderm 30, 24HV, and 30HV injectable gels," further noting that the FDA "recently announced a label extension for Juvéderm Ultra and Juvéderm Ultra plus" (Ex. 1009, 67S–68S).

Thus, as a whole, the evidence of record strongly suggests that skilled artisans were aware of and monitored the commercial and approval status of dermal filler compositions. In light of these teachings and the testimony of Dr. DeVore, we expand upon the Board's earlier definition of one of ordinary skill in the art as indicated by Petitioner's arguments. Thus, for the purpose of institution, a person of ordinary skill in the art as of the filing date of the '795 patent would have a B.S. or M.S. in biochemistry, polymer chemistry, medicinal chemistry, pharmaceutical chemistry, or a related field with several years of practical experience or have had less practical experience but a Ph.D. in one of those fields, or an M.D. in dermatology, plastic surgery, or a specialty related to the clinical use of dermal fillers. Such a person would have been aware of commercially sold dermal fillers in the United States and abroad, as well as those products for which approvals were being publicly sought.

The above definition is provisional and the parties are welcome to present further argument on this topic at trial.

B. Claim Construction

We interpret a claim "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C.

[11] Ex. 1009, Smith, *Practical Use of Juvéderm: Early Experience*, 120 PLASTIC AND RECONSTRUCTIVE SURG. 67S–73S (2007) ("Smith").

282(b)." 37 C.F.R. § 42.100(b) (2019). Under this standard, we construe the 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 construction for several claimed terms, which we address below. *See* Pet. 16–20. Patent Owner contends it is not necessary to construe any of the claimed terms. Prelim. Resp. 13.

Petitioner proposes construction for the following claimed terms: "sterile" (claim 29), "stable" (claim 29–31), "stable to autoclaving" (claim 28), "freely released in vivo" (claim 37), and "unbound to the HA" (claim 38–39). Pet. 16–20. Patent Owner contends it is not necessary to construe any of the claimed terms. Prelim. Resp. 11. For the purpose of this Decision, we find it helpful to address the term "sterile."

1. Sterile

Petitioner proposes "sterile" to mean a composition that is "substantially free of detectable viable organisms." Pet. 17 (citing *Allergan USA, Inc. et al. v. Medicis Aesthetics, Inc. et al.*, No. 13-1436 (C.D. Cal. Aug. 12, 2014) (claim construction order)) (Ex. 1027, 7). Petitioner further cites to the '795 patent's Specification which states "[s]terilization, as used herein comprises any method known in the art to effectively kill or eliminate transmissible agents." *Id.* (citing Ex. 1001, 12:4–7).

In IPR2017-01906, the panel adopted a more detailed definition of this term as:

> a sterile composition that maintains one or more of the following aspects: transparent appearance, pH, extrusion force and/or rheological characteristics, hyaluronic acid (HA) concentration, sterility, osmolarity, and lidocaine concentration, after being stored at a temperature of at least about 25˚ C for a specified period of time.

Teoxane, Paper 15 at 9–10 (quoting Pet. 11). The Board's prior construction does not appear inconsistent with Petitioner's broader proposed construction. Absent any persuasive argument for an alternative construction, we adopt the reasoning and definition of "sterile" as set forth in IPR2017-01906. *Id.* The parties are, nevertheless, welcome to present further arguments regarding claim construction at trial.

C. Petitioner's Patentability Challenges

1. Ground 1: Obviousness in view of CTA Summary

a) Summary of the Reference Relied Upon

(1) CTA Summary (Ex. 1050)

Petitioner asserts CTA Summary qualifies as prior art under 35 U.S.C. § 102(b) because a person of ordinary skill in the art "exercising reasonable diligence would have been able to locate the CTA Summary before August 4, 2007." Pet. 6. Petitioner asserts Anika Therapeutics Inc. (Anika) received premarket approval from FDA on December 20, 2006 for the dermal product initially designated CTA.[12] *Id.* at 3. Petitioner asserts the CTA Summary was made available on the FDA's website by December 31, 2006, as shown by the FDA Notice in the Federal Register. *Id.* (citing Ex. 1054, 15886). Petitioner asserts that the FDA would have expected the

[12] The product was later renamed "Elevess." Pet. 3. (citing Ex. 1002 ¶ 115).

interested public, including those of ordinary skill in the art, "to be aware of and locate such PMA approval orders." *Id.* (citing Ex. 1054, 15,886; Ex. 1002 ¶¶ 70–71). Petitioner asserts that those of ordinary skill in the art at the time would have reviewed such PMA notices and would have been aware of and recognized Anika's CTA product as a relevant HA-based dermal filler. *See id.* 4–5 (citing Ex. 1002 ¶¶ 70–75, 115–116, 118).

CTA Summary discloses an injectable dermal filler including crosslinked hyaluronic acid and 0.3% lidocaine HCl in a buffer solution. Ex. 1050, 1. The CTA Summary discloses the product was provided in a pre-filled syringe at a volume of 1 mL. *Id.* All lots of the CTA product were sterile and met the pH specification of 6.2–7.6. *Id.* at 6.

CTA Summary discloses that "[*i*]*n vitro* testing demonstrated that over 90% of the lidocaine elutes from CTA within 2 minutes." *Id.* Stability studies for shelf-life characteristics including: sterility, visual appearance, viscoelastic properties, HA concentration, extrusion force, HA fragments and lidocaine concentration, "support an expiration date of 15 months." *Id.*

b) Petitioner's Contentions

Petitioner asserts that claims 26–39 are unpatentable under 35 U.S.C. § 103(a) as obvious over CTA Summary. Pet. 23–30. Petitioner provides a detailed claim analysis for claims 26 and 29. *Id.* at 24–30. We address Petitioner's arguments as to claims 26 and 29.

(1) Claim 26

(a) "A composition comprising a crosslinked [HA] at a concentration of about 20 mg/mL to about 30 mg/mL"

Petitioner asserts CTA is a sterile gel containing crosslinked hyaluronic acid at a concentration of 28 mg/mL. Pet. 24 (citing Ex. 1050, 1).

(b) "and lidocaine at a concentration of about 0.1% to about 5% by weight,"

Petitioner asserts CTA contains 0.3% lidocaine. *Id.*

(c) "wherein the composition has a pH above about 7.5."

Petitioner asserts CTA Summary discloses a pH specification of 6.2–7.6, which overlaps the claimed range. *Id.* (citing Ex. 1050, 60). Petitioner asserts a person of ordinary skill would have selected any pH within the range, including 7.5 and 7.6. *Id.* (citing Ex. 1002 ¶ 144).

(2) Claim 29

(a) "A sterile composition comprising a crosslinked [HA]"

Petitioner asserts CTA is a sterile gel containing crosslinked hyaluronic acid." Pet. 27 (citing Ex. 1050, 1).

(b) "at a concentration of about 22 mg/mL and"

Petitioner asserts CTA has a concentration of 28 mg/mL. *Id.* Petitioner contends the "concentration of crosslinked HA is a result-effective variable," subject to routine optimization. *Id.* at 26. Petitioner contends that other "commercially successful HA fillers (e.g., Perlane and Restylane) were known to possess HA concentrations of 20 mg/mL," establishing a reasonable expectation of success. *Id.* (citing Ex. 1008, 29S; Ex. 1039, 266; Ex. 1002 ¶ 153).

(c) "lidocaine at a concentration of about 0.2% to about 1% by weight,"

Petitioner asserts CTA contains 0.3% lidocaine. *Id.* at 27 (citing Ex. 1050, 1).

(d) "wherein the composition is stable during storage under ambient conditions for at least 3 months."

Petitioner asserts CTA summary discloses stability studies supported an expiration date of 15 months. *Id.* (citing Ex. 1050, 6).

(3) Objective Evidence of Non-obviousness

Petitioner contends "the Examiner allowed the claims of the challenged patent (and its related applications) based on Allergan's arguments and proffered evidence pointing to supposed 'unexpected results' of the invention." Pet. 43. Petitioner challenges the Inventor's Declaration, the comparative data in the specification, and the extrinsic evidence cited by the Applicant during prosecution. *Id.* at 43–44.

First, Petitioner asserts that the Inventor's Declaration is unsubstantiated and contradicted by the prior art. *Id.* at 44–47. Petitioner asserts that "contrary to Lebreton's statements, the totality of the prior art instead gave the POSITA the expectation lidocaine could be successfully combined with various crosslinked HA dermal fillers, including a BDDE-crosslinked HA dermal filler." *Id.* at 45. To show that sterile and stable lidocaine-hyaluronic acid combinations were previously known, Petitioner cites dermal fillers commercially available as of the filing date, e.g., Elevess, Prevelle Silk, Puragen Plus, in addition to Sadozai and Kinney. *Id.* at 45–46 (citing Ex. 1002 ¶¶ 209–210). Moreover, Dr. DeVore states his opinion that "the POSITA would not have believed that lidocaine caused degradation of HA gels compositions during high temperature sterilization and would have believed that HA compositions comprising lidocaine were stable after high temperature sterilization when placed in storage for any significant length of time." Ex. 1002 ¶ 210. Dr. DeVore attests that "during the development of Elevess, it was observed that the autoclave-sterilized [BCDI]-crosslinked HA composition with lidocaine was sufficiently stable to support a product shelf life of 15 months, which is reflected in the Elevess label." *Id.* (citing Ex. 1050, 6).

Second, Petitioner asserts that the comparative data relied on by the Inventor's Declaration does not support nonobviousness. Pet. 56. The comparative data appears as Example 4 of the '795 patent's Specification. Ex. 1001, 15:20–17:2. Dr. DeVore attests that "Example 4 describes experiments in which six samples were evaluated. . . . Allergan argued that the results of Samples 1–3 were consistent with the expectations of the POSITA, and that it was unexpected that Samples 4–6 did not exhibit the same viscosity reduction." Ex. 1002 ¶ 216. Dr. DeVore states "[i]n my opinion, Sample 1 is completely irrelevant—it is a mixture of uncrosslinked HA and a completely different polymer (hydroxypropyl methylcellulose). I am not aware of a mixture of uncrosslinked HA and HPMC being used as a dermal filler, either in 2008 or now." *Id.* ¶ 217. Dr. DeVore states that the viscosity differences are not indicative of instability as "[t]he final viscosity for Samples 2 and 3 in each test (~75–375 Pa*s) is substantially the same as the final viscosities of Samples 4–6 (~50–90 Pa*s), all of which are within the range of marketed dermal fillers (50–1,200 Pa*s)." *Id.* ¶ 219(citing Ex. 1039, 267). Dr. DeVore states that there is no meaningful difference in viscosity reduction between Sample 3 (35% reduction when combined with lidocaine without pH adjustment) and Sample 4 (30% reduction in viscosity in the same test) and that the difference was not "much lower" as alleged by Allergan. *Id.* ¶¶ 223–224.

Third, Petitioner asserts that the extrinsic evidence cited in the Application during prosecution, i.e., Cui, "is irrelevant to the question of whether Allergan's BDDE-crosslinked HA composition showed unexpected results compared to the other crosslinkers known to POSITAs at the time." Pet. 61 (citing Ex. 1002 ¶ 243). Petitioner argues that "Cui was published in 2012, well after the claimed priority date of the patent. The reasonable

expectation of success (and expected results) is evaluated at the time the invention was made—a later published reference that might have taught away from the claimed invention is irrelevant." *Id.* at 60 (citing *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc*. 752 F.3d 967, 976 (Fed. Cir. 2014)). Dr. DeVore states that Cui compares the stability of BDDE-crosslinked hyaluronic acid with three crosslinkers that had not "been seriously investigated for use in dermal fillers as of August 2008," as opposed to the known non-BDDE crosslinkers for dermal fillers. Ex. 1002 ¶ 213. Dr. DeVore states his opinion that "the Cui reference in no way supports Allergan's assertion that BDDE crosslinked HA was 'especially sensitive' to heat sterilization relative to 'non-BDDE' crosslinkers. At the very least, Cui is irrelevant . . . because Cui's comparisons do not relate to any of the crosslinkers relied upon here." *Id.* ¶ 214.

c) Patent Owner's Contentions

In its Preliminary Response, Patent Owner directs substantially all of its argument to whether the Board should exercise discretion to deny the Petition under 35 U.S.C § 325(d). *See* Prelim. Resp. 1–2, 26–39. We address Patent Owner's arguments under 35 U.S.C § 325(d) below.

d) Conclusion

Having considered the parties positions and evidence of record, summarized above, we determine that Petitioner has established a reasonable likelihood of prevailing in demonstrating the unpatentability of claims 26–39 with respect to Ground 1.

2. Ground 2: Obviousness in view of Lebreton and Sadozai

a) Summary of the References Relied Upon

(1) Lebreton

Lebreton is directed to crosslinking low and high molecular weight polymers to form injectable monophase hydrogels. Ex. 1029, code (57). The hydrogels may be used as filling materials in plastic surgery. *Id.* ¶ 5. Lebreton discloses buffering the crosslinked product to a pH compatible with the human body, being between 6.5 and 7.5, preferably between 7 and 7.4, and even more preferably between 7.1 and 7.3. *Id.* ¶¶ 48–49. Particularly, Lebreton discloses hydrogels prepared by crosslinking sodium hyaluronate (sodium salt of hyaluronic acid) with 1,4-butanediol diglycidyl ether (BDDE). *Id.* ¶¶ 68–76.

Lebreton discloses two examples of mixtures of low and high molecular weight hyaluronic acid crosslinked with BDDE in the presence of sodium hydroxide. *Id.* ¶¶ 74, 80–92 (Examples 3 and 4). "The crosslinked product is neutralized to a pH of 7.2 in a phosphate solution and then dialyzed." *Id.* ¶¶ 76. The resulting monophase hydrogel "is mechanically homogenized before being packed into syringes and sterilized in an autoclave." *Id.* ¶¶ 76, 85, 91.

(2) Sadozai

Sadozai is directed to a crosslinked hyaluronic acid composition effective for tissue augmentation or drug delivery. Ex. 1030 ¶¶ 7, 8. "[T]he storage modulus G′ is increased, e.g., composition is stabilized, by the inclusion of a local anesthetic, e.g., lidocaine, compared to a non-stabilized composition, e.g., an identical composition except that the local anesthetic is not included." *Id.* ¶ 68. Particularly, Sadozai discloses compositions including hyaluronic acid crosslinked with p-phenylene-

bis(ethylcarbodiimide) (BCDI). *Id.* ¶ 85. The crosslinked hyaluronic acid compositions are combined with phosphate buffer containing 0.30% lidocaine (Phosphate Buffer 4) to form a suspension. *Id.* ¶¶ 84, 90, 100, 102. The suspensions are loaded into syringes and autoclaved for sterilization. *Id.* ¶¶ 90 (Example 12), 100 (Example 17). Sterilization/hydration may be performed in an autoclave at temperatures between 100° C to 150° C. *Id.* ¶¶ 54–55.

Sadozai discloses that compositions processed according to Example 12 "with lidocaine have significantly higher modulus G′ over the time of the test. Thus, crosslinked hyaluronic acid with lidocaine can have good biostability, and can in some cases have a synergistic effect, increasing G′." *Id.* ¶ 107.

b) Petitioner's Contentions

Petitioner asserts that claims 26–39 are unpatentable under 35 U.S.C. § 103(a) as obvious over Lebreton and Sadozai. Pet. 30–43. Petitioner provides a detailed claim analysis for claims 26 and 29. *Id.* at 33–43. We address Petitioner's arguments as to claims 26 and 29.

(1) Claim 26

(a) "A composition comprising a crosslinked [HA] at a concentration of about 20 mg/mL to about 30 mg/mL"

Petitioner asserts Lebreton discloses a composition comprising crosslinked hyaluronic acid at a concentration of from 10–40 mg/mL, preferably 20–30 mg/mL. Pet. 33 (citing Ex. 1029 ¶ 49).

(b) "and lidocaine at a concentration of about 0.1% to about 5% by weight,"

Petitioner asserts Sadozai discloses 0.3% lidocaine in a dermal filler. *Id.* at 34 (citing Ex. 1030 ¶ 107).

(c) "wherein the composition has a pH above about 7.5."

Petitioner contends the claim term "pH above *about* 7.5 encompasses "a range above and below 7.5." *Id.* Petitioner asserts Lebreton discloses a pH of between 6.5–7.5. *Id.* (citing Ex. 1029 ¶ 49). Petitioner asserts Lebreton's pH range overlaps the pH range of claims 26 (above about 7.5) and 27 (about 7.5 to about 8). *Id.*

(2) Claim 29

(a) "A sterile composition comprising a crosslinked [HA] at a concentration of about 22 mg/mL and"

Petitioner asserts Lebreton discloses a composition comprising crosslinked hyaluronic acid at a concentration of from 10–40 mg/mL, preferably 20–30 mg/mL. *Id.* at 38 (citing Ex. 1029 ¶ 49).

(b) "lidocaine at a concentration of about 0.2% to about 1% by weight,"

Petitioner asserts Sadozai discloses 0.3% lidocaine in a dermal filler. *Id.* (citing Ex. 1030 ¶ 107).

(c) "wherein the composition is stable during storage under ambient conditions for at least 3 months."

Petitioner asserts "the term stable includes compositions that maintain sterility over a length of time," and both Lebreton and Sadozai disclose gels packed into syringes and sterilized in an autoclave. *Id.* at 39 (citing Ex. 1029 ¶ 70; Ex. 1030 ¶ 54).

c) Patent Owner's Contentions

In its Preliminary Response, Patent Owner directs substantially all of its argument to whether the Board should exercise discretion to deny the Petition under 35 U.S.C § 325(d). *See* Prelim. Resp. 1–2, 26–39. We address Patent Owner's arguments under 35 U.S.C § 325(d) below.

Although Patent Owner does not directly address the merits of Petitioner's grounds, Patent Owner does address the relevance of Cui in the context of its § 325(d) arguments. *See* Prelim. Resp. 33–34; Sur-Reply 3–4. In sum, Patent Owner argues that Cui is relevant because it "discusses divinyl sulfone (DVS) crosslinked HA gels, which Petitioner admits were known and approved before August 2008." Prelim. Resp. 33. We accord this argument little weight at this juncture because Cui provides no comparative information about the stability of HA gels crosslinked with either DVS or BDDE. Rather, and as Patent Owner admits, "Cui focused on gels crosslinked with four new agents of 'lower toxicity'" as compared to DVS." *Id.* (citing Ex. 1025, 1506); *see* Reply 3 (noting that "Cui does not *test or compare* BDDE to *any* of the three crosslinkers discussed in the Petition[] or the Examiner's art").

Patent Owner responds that we should discount Dr. DeVore's testimony because it is "conclusory and fails to provide a well-reasoned rationale or objective support for the proposed grounds." Prelim. Resp. 36. As an initial matter, at this stage of the proceeding, we give at least some weight to an expert's unopposed testimony. Moreover, we accord little weight to Patent Owner's argument about the lack of support in Dr. DeVore's testimony as Patent Owner appears to rely on summary statements from Dr. DeVore's declaration that are further explained, with specific support, elsewhere in the Declaration. Patent Owner argues, for example, that a sentence fragment from paragraph 193 of Dr. DeVore's declaration ("the POSITA could have easily modified the Lebreton process to incorporate lidocaine") is "without evidentiary support." Prelim. Resp. 37. The passage, read in full, however, expressly cites to Exhibits 1029 and 1030 as support for the proposition that "[t]he POSITA would have

recognized that merely including lidocaine hydrochloride in the buffer solution . . . would be sufficient to obtain the lidocaine-containing gel." Ex. 1002 ¶ 170. Accordingly, we do not find persuasive Patent Owner's argument that we should discount Dr. DeVore's testimony as unduly conclusory. Patent Owner will have the opportunity to rebut and challenge Dr. DeVore's testimony at trial.

d) Conclusion

Having considered the parties' positions and evidence of record, summarized above, we determine that Petitioner has established a reasonable likelihood of prevailing in demonstrating the unpatentability of claims 26–39 with respect to Ground 2.

III. DISCRETION TO DENY INSTITUTION

Patent Owner argues the Board should exercise its discretion and deny the Petition under 35 U.S.C. §§ 325(d) and 314(a). Prelim. Resp. 17–40. With regard to Ground 1, Patent Owner contends that Petitioner "used the institution decision in IPR2017-01906 as a roadmap for its attempt to prove that the CTA Summary is a printed publication." *Id.* at 17. With regard to Ground 2, Patent Owner contends Petitioner presents substantially the same art or arguments previously presented to the Office. *Id.* at 26. We address each of these arguments below.

A. Discretion under 35 U.S.C. § 314(a)

Patent Owner argues that the Board should exercise its discretion under 35 U.S.C. § 314(a) and deny Petitioner's request for institution of *inter partes* review. Prelim. Resp. 17–26. In urging the Board to deny institution under § 314(a), Patent Owner points to criteria set forth by the Board in *General Plastic Industrial Co., Ltd. v. Canon Kabushiki Kaisha*,

No. IPR2016-01357 (PTAB Sept. 6, 2017). Prelim. Resp. 33–34. These factors include:

> (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.

Id. (citing *General Plastic*, Paper 11 at 2, 9–10).

Patent Owner contends that "[t]he Board denied the petition [in IPR2017-01906] because the petitioner failed to prove the CTA Summary qualified as a printed publication." Prelim. Resp. 16.[13] Patent Owner urges that we deny this Petition because

[13] As noted by the parties, the Board declined to institute trial on an earlier Petition by a third unrelated Petitioner for failure to timely identify all real parties in interest. Pet. 54 (citing *Galderma S.A. v. Allergan Industrie, SAS*,

> Petitioner now uses the institution decision in IPR2017-01906 as a roadmap to remedy that defect, albeit unsuccessfully, by crafting an artificial definition of a POSITA that requires the POSITA to be "aware of the process by which FDA reviews dermal filler products, and how FDA communicates the results of the reviews to the public."

Id. (footnotes omitted). According to Patent Owner, "Petitioner relied on the prior institution decision to prove the CTA Summary is a printed publication" (*id.* at 18), which raises fairness concerns (*Id.* at 24). We do not agree.

1. General Plastic Factors 1 and 3

Relevant to *General Plastic* factors 1 and 3, Patent Owner argues that

> Petitioner had access to the Board's institution decision in IPR2017-01906 before filing this Petition. [Pet. 54–55] Petitioner acknowledges its awareness of the Teoxane petition and institution decision, and states it "overcomes the deficiencies of the Teoxane petition." [*Id.* at 61.]

Prelim. Resp. 21. Patent Owner further contends that the issue of whether the CTA Summary was available to a person of ordinary skill in the art was addressed by the Board in IPR2017-01906 where "[t]he Board held that Teoxane failed to meet its burden to demonstrate that a POSITA exercising reasonable diligence would have located the CTA Summary before the critical date." *Id.* at 19. Patent Owner contends that "Petitioner used the institution decision from IPR2017-01906 as a guide to address[] the deficiencies related to the CTA Summary's status as a printed publication" and "now offers testimony from Dr. DeVore regarding what a

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No. IPR2014-01422, Paper 14 (PTAB Mar. 5, 2015) (case terminated after additional proceedings); Paper 3, 2.

POSITA allegedly would have been aware of and would have done with respect to the CTA Summary." *Id.* at 21 (citing Pet. 3–6; Ex. 1002 ¶¶ 70–75, 115–118). Patent Owner contends that Petitioner offers a "new definition of a POSITA, which adds additional requirements to the definition the Board adopted earlier in IPR2017-01906 as consistent with the prior art." *Id.*; Pet. 16.

Relevant to *General Plastic* factor 1, Petitioner avers that, "[b]ecause this is Prollenium's first challenge to the '795 patent, and Prollenium has no connection to the prior petitioner, General Plastic Factor 1 weighs heavily in favor of institution. And only Prollenium has been sued in the pending lawsuit." Pet. 55–56; *see also* Reply 8 ("Allergan makes no effort to show why *Prollenium*, which has *no relationship* to Teoxane and was sued years later, should be barred."). Relevant to *General Plastic* factor 3, Petitioner concedes reviewing the preliminary response and the Board's decision denying institution in IPR2017-01906, but contends that, "to the extent there is overlap between the two petitions, Prollenium has addressed Teoxane's evidentiary failings." Pet. 56. Petitioner further contends that its obviousness grounds raise different evidentiary issues and challenges the claims in different ways. *Id.*

On the present record, we agree that Prollenium has no significant relationship to the Petitioner of IPR2017-01906. *See Valve Corp. v. Electronic Scripting Prods., Inc.* IPR2019-00062, Paper 11, 9 (Apr. 2, 2019) (precedential) ("[W]e consider any relationship between those petitioners when weighing the General Plastic factors."). Accordingly, *General Plastic* factor 1 weighs against exercising our discretion under § 314(a).

As to *General Plastic* factor 3, even if we were to accept Patent Owner's position that the issue before the Board in IPR2017-01906 was

"whether the CTA Summary itself was available to a person of ordinary skill in the art exercising reasonable diligence before the critical date" (Prelim. Resp. 34), that issue was not fully adjudicated on the merits. IPR2017-01906, Paper 15. Rather, we agree with Petitioner that the panel in IPR2017-01906 merely determined that the record lacked the evidentiary support necessary to establish that CTA Summary was public accessible before the critical date. *See* IPR2017-01906, Paper 15, 11–12 ("the Petition advances bare attorney argument that the '[CTA] Summary was published online at least by January 10, 2007.'"). Furthermore, we note in particular that the weight the Board should accord the Lebreton Declaration—a cornerstone of Petitioner's argument in this case—is not mentioned, let alone addressed on the merits, in the IPR2017-01906 decision. *See e.g.*, Ex. 1002 ¶¶ 70–75, 115–116, 118. As such, in this instance, we do not find determinative that Petitioner was in possession of the Board's decision denying IPR2017-01906 prior to filing this Petition. Under the particular circumstances presented, General Plastic factor 3 carries less weight, for example, than factor 1 (namely, that the earlier proceeding was filed by a different petitioner).

2. General Plastic factors 2, 4, and 5

With respect to *General Plastic* factors 2 and 4, we agree with Petitioner that these factors relate to prior art *withheld* from the first Petition and, because there is no evidence that Petitioner was involved with any earlier petition challenging the '795 patent, and because there is no evidence that Petitioner was aware of any infringement assertions against it at the time of the earlier petition filings, these factors are inapplicable here.

Likewise, factor 5, ("[w]hether the petitioner provides adequate explanation for the time elapsed between the filings of multiple petitions

directed to the same claims of the same patent"), also fails to weigh in favor of denying institution because, as there is no evidence that Petitioner was involved in any such earlier petition or that Petitioner was even aware of the infringement assertions against it at the time of the earlier petition filings, there is no elapsed time to explain.

3. General Plastic factors 6 and 7

Finally, because Patent Owner has not shown, nor do we discern, that this Petition raises unusual issues challenging the finite resources of the Board or our capacity to issue a final determination within the statutory limits of 35 U.S.C. § 316(a)(11), *General Plastic* factors 6 and 7 do not weigh in favor of denying institution under § 314(a).

4. Conclusion

Having weighed each of the *General Plastic* factors, and for the reasons explained above, we decline to exercise our discretion under 35 U.S.C. § 314(a) to deny institution of the Petition.

B. Discretion under 35 U.S.C. §§ 325(d)

Institution of an *inter partes* review is discretionary. *See Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016) (explaining that under 35 U.S.C. § 314(a), "the PTO is permitted, but never compelled, to institute an IPR proceeding"). Our discretionary determination of whether to institute review is guided, in part, by 35 U.S.C. § 325(d), which states, in relevant part:

> In determining whether to institute or order a proceeding under this chapter, chapter 30, or chapter 31, the Director may take into account whether, and reject the petition or request because, the same or substantially the same prior art or arguments previously were presented to the Office.

See also 157 CONG. REC. S1360, S1376 (daily ed. Mar. 8, 2011) (statement of Sen. Kyl) ("[T]he second sentence of section 325(d) . . . authorizes the Director to reject any . . . petition . . . on the basis that the same or substantially the same prior art or arguments previously were presented to the Office. This will prevent parties from mounting attacks on patents that raise issues that are substantially the same as issues that were already before the Office with respect to the patent. The Patent Office has indicated that it currently is forced to accept many requests . . . that are cumulative to or substantially overlap with issues previously considered by the Office with respect to the patent.").

In evaluating whether the same or substantially the same prior art or arguments were previously presented to the Office under § 325(d), the Board has considered a number of non-exclusive factors, including, for example:

> (a) the similarities and material differences between the asserted art and the prior art involved during examination;
>
> (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
>
> (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
>
> (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguished the prior art;
>
> (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
>
> (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the asserted prior art or arguments.

Becton, Dickinson and Co. v. B. Braun Melsungen AG, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (informative) ("the *Becton Dickinson* factors").

1. Becton Dickinson Factors (a) through (d)

With respect to factors (a) through (d), Patent Owner argues that "the same art and arguments the Petition advances were considered, and ultimately rejected, throughout the extensive prosecution history of the '795 Patent." Prelim. Resp. 26.

With respect to the primary reference of Ground 2, Patent Owner argues that the Examiner's rejection in view of Lebreton was successfully overcome during the prosecution of the '795 patent. *Id.* at 27–28. With regard to the secondary reference Sadozai, Patent Owner contends this reference "is cumulative of art considered and distinguished during prosecution of the '795 patent." *Id.* at 29.

Petitioner, however, argues that "Allergan's argument that Lebreton was 'distinguished' in prosecution is inaccurate; Allergan never overcame the *prima facie* cases made by the Examiner. Instead, every patent was allowed based on Allergan's proffered unexpected results, primarily the unsubstantiated inventor declaration." Reply, 1–2. Petitioner's assertion is supported by the relevant prosecution history, as further discussed below. *See e.g.,* section I(C)(3), above.

Petitioner also argues that the asserted grounds combine Lebreton with "substantially different secondary references (Sadozai, etc.) than used by the Examiner and provide arguments and evidence (including the unrebutted DeVore testimony) not considered by the Examiner." Reply 2–6. We find particularly persuasive for the purpose of our § 325(d) analysis, Petitioner's contention that, whereas Calais and Wang, cited by the

Examiner, "merely *suggest* lidocaine . . . *could* be added to a crosslinked HA gel . . . [,] Sadozai directly refutes the inventor's declaration that lidocaine would degrade a HA gel during high temperature sterilization." Reply 2–3 (citations omitted). *Oticon Medical AB v. Cochlear Limited*, IPR2019-00975 (PTAB Oct. 16, 2019) (Paper 15) (precedential as to sections II.B and II.C).

On balance, factors (a) through (d) do not weigh in favor of exercising our discretion to deny institution under §325(d).

2. Becton Dickinson Factor (e)

As to factor (e), Patent Owner asserts that "Petitioner fails to meets its burden to demonstrate how the Examiner allegedly erred in his review of the prior art during prosecution." Prelim. Resp. 31. According to Petitioner, the Examiner's error in allowing these claims "was induced by the declaration." Reply 6. Although Petitioner's analysis is not contrary to the present record, whether the Examiner "erred" by relying on the Lebreton Declaration is subsumed into our analysis of factor (f), below.

3. Becton Dickinson Factor (f)

Even if we were to accept at face value Patent Owner's arguments regarding factors (a) through (d), they would be outweighed by our analysis of factor (f): "the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the asserted prior art or arguments," which in this case, relates to Petitioner's arguments and evidence regarding the Lebreton Declaration. *See generally*, Pet. 47–51; Reply 6–7.

a) Paragraphs 4–10 of the Lebreton Declaration

The Lebreton Declaration presents two general arguments. First, that one of ordinary skill in the art would have known that the addition of lidocaine to crosslinked HA dermal filler compositions was incompatible

with high temperature sterilization. *See* Ex. 1024 ¶¶ 4–10.[14] Petitioner, in arguments supported by the testimony of its expert Dr. DeVore, however, directs us to substantial evidence to the contrary. In particular, Petitioner identifies evidence that one of ordinary skill in the art would have understood that lidocaine-containing crosslinked HA dermal fillers could be sterilized with high temperatures and that such products were approved by the FDA for commercial sale. *See e.g.*, Pet. 45–46 (citing Ex. 1002 ¶¶ 209–210).

Patent Owner appears to take the position that the Lebreton Declaration would have provided the Examiner with a complete picture of the prior art because he "was aware of the very references and teachings Petitioner alleges were absent" in the Declaration. Prelim. Resp. 32 (arguing that the Examiner specifically considered Lebreton and Sadozai, which Patent Owner contends are cumulative to references considered during prosecution of the '795 patent). The current record, however, further includes the presently unrebutted testimony of Dr. DeVore, and the question of whether the secondary references before the Examiner were truly cumulative is a matter of factual dispute that can be addressed at trial. *See* Reply 2–5. Moreover, the record indicates that the Examiner overlooked the relevance of the working examples disclosed in Kinney and Reinmuller during examination. These factors weigh against exercising our discretion under § 325(d), as do the parties' arguments with respect to Cui, discussed above.

[14] As noted in the Petition, these "statements were *not* limited to BDDE-crosslinked HA [as presently claimed and] Allergan and the inventor cited no prior art references to support the inventor's opinions." Pet. 45 (citing Ex. 1024 ¶¶ 4–8 and Ex. 1023, 24–28).

b) Paragraphs 11–15 of the Lebreton Declaration

With reference to Example 4 of the incorporated provisional applications, the Lebreton Declaration further asserts that "other HA gels" mixed with lidocaine (represented by samples 4 and 5) "surprisingly and unexpectedly" maintained their viscosity and elasticity after high temperature sterilization as compared to gel samples 1, 2, and 3. Ex. 1024 ¶¶ 11–15. There appears to be no dispute at this juncture that the lidocaine-gel compositions of samples 4 and 5 comprise BDDE-crosslinked soft tissue filler compositions within the scope of the challenged claims. Petitioner, nonetheless, contends this portion of the Lebreton Declaration does not provide support for unexpected results because, first, samples 1–3 do not represent the closest prior art and, second, even though samples 1 and 2 show less drop in viscosity after sterilization as compared to samples 4–6, this difference is merely a matter of degree rather than kind. Pet. 48–50 (citations omitted).

We find particularly interesting Dr. DeVore's presently uncontested testimony that:

> Allergan's experiment and its interpretation of the results fundamentally misunderstands the point of stability testing. The consideration whether a crosslinked HA composition would be suitable as a dermal filler depends on its *final* viscosity, not how much the viscosity drops during sterilization. It is irrelevant if the viscosity drops by 5%, 50%, or even 90%, so long as the sterilized final product has the desired viscosity and is shelf stable.

Ex. 1002 ¶ 218. This testimony was not available to the Examiner during patent prosecution. Nor was Dr. DeVore's testimony that Sample 1 is irrelevant as a mixture of uncrosslinked HA and a polymer other than HA, whereas "[t]he final viscosity of samples 2 and 3 in each test (~75–375

PA*s) is substantially the same as the final viscosities of Samples 4–6 (~50–09 PA*s), all of which are within the range of marketed dermal fillers (50–1,200 PA*s)." *Id.* at ¶ 219. In support of that contention, Dr. DeVore points to the priority documents as identifying samples 2 and 3 as corresponding to FDA-approved dermal fillers Hylaform and Restylane, respectively. *See id.* at ¶¶ 221–222 (citing Ex. 1013, 26:7; Ex. 1028, 19:7).

Dr. DeVore further testifies that:

> During the prosecution of '795 patent, Allergan stated that Sample 3, when combined with lidocaine without pH adjustment, exhibited a 35% reduction in viscosity, while Sample 4 exhibited a 30% reduction in viscosity in the same test. EX1023, 26–27. During the prosecution of this application, Allergan argued that the claimed compositions exhibited a "much lower" reduction in viscosity.

Id. at ¶ 223.

> In my opinion, even if viscosity reduction by itself was a meaningful measure of suitability (it is not), there is no meaningful difference between a 30% and 35% reduction in viscosity. . . . Determining whether 30% is significantly different from 35% would require statistical analysis, such as required in FDA submissions. Such analysis is not present in the challenged patents. Thus, it is impossible to tell if the difference between Sample 3 and Sample 4, when pH is not controlled, is real or not.

Id. at ¶ 224.

We do not, on the present record, find Dr. DeVore's testimony "conclusory" and without a "well-reasoned rationale or objective support" as Patent Owner contends. Prelim. Resp. 36. To the contrary, Dr. DeVore's testimony weighs against exercising our discretion under § 325(d). We, nonetheless, look forward to Patent Owner's testing of Dr. DeVore's opinions at trial.

4. Conclusion

In sum, upon weighing the relevant Becton Dickinson factors, we determine that, although the grounds may rely on the same or substantially the same art or arguments previously presented to the Office, Petitioner has demonstrated sufficiently how the Office erred in a manner material to the patentability of the challenged claims in reliance on the Lebreton Declaration to overcome the prior art. Thus, we decline to exercise our discretion under 35 U.S.C. § 325(d) to deny institution of the Petition.

IV. CONCLUSION

On the present record, we find Petitioner shows sufficiently that the cited references would have taught or suggested each element of claims 26–39, and set forth a sufficient rationale for why a person of ordinary skill would have been motivated to combine these teachings and suggestions to arrive at the invention recited in those claims. Petitioner has established a reasonable likelihood of prevailing in demonstrating that claims 26–39 would have been obvious over the combinations of prior art set forth in the asserted grounds.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), that an *inter partes* review of claims 26–39 of the '795 patent is instituted with respect to all grounds set forth in the Petition; and

FURTHER ORDERED, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4(b), that the *inter partes* review of the '795 patent shall commence on the entry date of this Order, and notice is hereby given of the institution of a trial.

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