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Paper 12
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PROLLENIUM US INC.,

Petitioner,

v.

ALLERGAN INDUSTRIE, SAS,

Patent Owner.

IPR2020-00084
Patent 9,089,519 B2

Before JOHN G. NEW, SHERIDAN K. SNEDDEN, and ROBERT A. POLLOCK, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

DECISION
Instituting *Inter Partes* Review
35 U.S.C. § 314(a)

I. INTRODUCTION

Petitioner Prollenium US Inc. filed a Petition (Paper 1, "Petition") requesting *inter partes* review of claims 1–8 of US Patent 9,089,519 B2 (Ex. 1001, "the '519 patent"). Patent Owner Allergan Industrie SAS (the "Patent Owner") timely filed a Preliminary Response. Paper 11 ("Prelim. Resp.").

Under 35 U.S.C. § 314, the Board "may not authorize an *inter partes* review to be instituted unless … the information presented in the petition … and any response … shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least one of the claims challenged in the petition." Upon consideration of the Petition and the Preliminary Response we determine that the evidence presented demonstrates a reasonable likelihood that Petitioner would prevail, on Petitioner's Grounds 4 and 5, in establishing the unpatentability of at least one claim of the '519 patent. We determine that Petitioner has not demonstrated a reasonable likelihood it would prevail as to Grounds 1–3. Although the panel finds that Petitioner is not likely to prevail on some Grounds, the Board here institutes on all grounds in the petition. *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").

II. BACKGROUND

A. Related Matters

The parties identify the following consolidated civil action:

> *Allergan USA, Inc. and Allergan Industrie SAS v. Prollenium US Inc. and Prollenium Medical Technologies Inc.*, Civil Action No. 19-126-CFC (D. Del. filed Jan. 22, 2019).)

Paper 4, 1–2.

Petitioner has filed Petitions for *inter partes* review of related U.S. patents as follows: US Patent No. 8,450,475 B2 (the "'475 patent") in IPR2019-01505; US Patent No. 9,238,013 (the "'013 patent") in IPR2019-01508; US Patent No. 8,822,676 B2 (the "'676 patent") in IPR2019-01617; and US Patent No. 9,358,322 B2 (the "'322 patent") in IPR2019-01509. Pet. 68–69.

B. The Asserted Grounds of Unpatentability

Petitioner contends that claims 1–8 of the '519 patent are unpatentable based on the following grounds:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–4	102(a)(1)	PMA P050047/S005[1]
1–4	102(a)(1)	Weinkle[2]
1–4	102(a)(1)	U.S. 2010/0028438 A1[3]
1–8	103	Lebreton[4], Sadozai[5],

[1] Summary Review Memo Template, P050047/S005, Juvederm Ultra Xc And Juvederm Ultra Plus XC (January 6, 2010") ("P050047/S005") (Ex. 1060).

[2] S.H. Weinkle et al., *A Multi-Center, Double-Blind, Randomized Controlled Study of the Safety and Effectiveness of Juvederm® Injectable Gel with and without Lidocaine*, 8 J. COSMETIC DERMATOL. 205–10 (2009) ("Weinkle") (Ex. 1070).

[3] Lebreton (U.S. 2010/0028438 A1, February 4, 2010) (the "'438 application) (Ex. 1072).

[4] Lebreton (US 2006/0194758 A1, August 31, 2006) ("Lebreton") (Ex. 1029).

[5] Sadozai et al. (US 2005/0136122 Al, June 23, 2005) ("Sadozai") (Ex. 1030).

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
1–8	103	P050047[6], Kinney[7]

Petitioner also relies upon the Declaration of its declarant, Dr. Dale P. DeVore (the "DeVore Declaration") (Ex. 1002).

C. The '519 Patent

The '519 patent is generally directed to cohesive soft tissue fillers, for example, dermal and subdermal fillers, based on hyaluronic acids ("HA") and pharmaceutically acceptable salts thereof. Ex. 1001 Abstr. More specifically, the '519 patent teaches soft tissue filler compositions generally comprising: a hyaluronic acid component crosslinked with a crosslinking agent selected from the group consisting of 1,4-butanediol diglycidyl ether (BDDE), 1,4-bis(2,3-epoxypropoxy) butane, 1,4-bisglycidyloxybutane, 1,2-bis(2,3-epoxypropoxy) ethylene and 1-(2,3-epoxypropyl)-2,3-epoxycyclohexane, and 1,4-butanediol diglycidyl ether; and at least one anesthetic agent, generally lidocaine, combined with the crosslinked HA component. Ex. 1001 col. 2, ll. 54–62.

D. Illustrative Claim

Claim 1 is illustrative and recites:

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[6] Inamed Corporation, *Summary Of Safety And Effectiveness Data: JUVEDERM™: Premarket Approval Application (PMA) Number P050047* (June 2, 2006) ("P050047") (Ex. 1074).

[7] B.M. Kinney, *Injecting Puragen Plus into the Nasolabial Folds: Preliminary Observations of FDA Trial*, 26(6) AESTHETIC SURG. J. 741–48 (2006) ("Kinney") (Ex. 1012).

> 1. A first sterile dermal filler composition comprising hyaluronic acid crosslinked with 1,4-butanediol diglycidyl ether (BDDE), and about 0.3% lidocaine by weight, wherein the first composition fills in facial lines and depressions substantially the same as a second sterile dermal filler comprising hyaluronic acid crosslinked with BDDE wherein the second composition does not include lidocaine but otherwise has the same composition as the first composition.

Ex. 1001 col. 19, ll. 16–23.

Independent claims 3 and 5 are similar, but recite, respectively, that the first sterile dermal filler composition "restores fat loss-related tissue volume loss substantially the same," or "is substantially as stable during storage under ambient conditions for at least 3 months," as the second dermal filler. *Id.* at col. 20, ll. 2–3, 12–13.

E. Prosecution History of the '519 Patent

In August and September 2008, Allergan filed a trio of provisional applications (US Appl. Ser. No. 61/085,956, August 04, 2008 (the "'956 application"); US Appl. Ser. No. 61/087,934, August 11, 2008 (the "'934 application"); and US Appl. Ser. No. 61/096,278, September 11, 2008 (the "'278 application") to which the '519 patent claims the priority benefit. Pet. 11.

The parent application of the '519 patent, US Appl. Ser. No. 14/242,747 (the "'747 application") was filed on April 1, 2014, as a continuation of US Appl. Ser. No. 13/419,079 ("the '079 application"), which is, in turn, a continuation of US Appl. Ser. No. 12/393,884 (the "'884 application"). Pet. 13. The Examiner issued a first action Notice of Allowance on October 10, 2014, citing arguments and evidence relied upon by the Patent Owner in the examination of the '884 application. *Id.* (citing Ex. 1049 6–7). Specifically, the then-applicant argued, citing a declaration submitted by the inventor, that a person of ordinary

skill in the art would not have expected a lidocaine-containing HA composition could be sterilized by autoclave. *Id.* (citing Ex. 1023 25–28). Specifically, the then-applicant argued that "it was a surprising and unexpected discovery … that certain [HA] gels … when mixed with lidocaine, could be made to be heat stable and thus useful as dermal fillers." *Id.* at 13–14 (quoting Ex. 1023 23). At the time of this response, some pending claims were directed to BDDE-crosslinked HA, and other claims were directed to HA crosslinked with any crosslinker. *Id.* at 54 (citing Ex. 1023, 18–20 (claims 51–67)).

The Patent Owner also argued that a skilled artisan would have expected that autoclave sterilization would unacceptably reduce the composition's viscosity, thereby making it unsuitable for use as a filler. Pet. 14 (citing Ex. 1023 25). The Examiner accepted these arguments in the '884 application and they were expressly cited again by the Examiner in the reasons for allowance of the '519 patent. *Id.* (citing Ex. 1049 7).

The '519 patent issued on July 28, 2015 (Ex. 1001).

III. ANALYSIS

A. Claim Construction

In an *inter partes* review for a petition filed on or after November 13, 2018, the "[claims] of a patent … shall be construed using the same claim construction standard that would be used to construe the [claims] in a civil action under 35 U.S.C. § 282(b), including construing the [claims] in accordance with the ordinary and customary meaning of such claims as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *See* 37 C.F.R. § 42.100(b) (2019); *see also Phillips v. AWH Corp.*, 415 F.3d 1303, 1312–14 (Fed. Cir. 2005) (*en banc*). Only those terms that are in controversy need be construed,

and only to the extent necessary to resolve the controversy. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Matal*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) (citing *Vivid Techs., Inc. v. America Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

In a related district court litigation, *Allergan USA, Inc. v. Medicis Aesthetics, Inc.*, Case No. SACV 13-1436 AG (JPRx) (C.D. Calif.), 2014 WL 5488895 (C.D. Calif. Aug. 12, 2014),[8] the district court judge entered a claim construction order following a *Markman* hearing. Ex. 1027. Petitioner proposes constructions for certain claim terms, *viz.*, "sterile," "stable," and "freely released *in vivo*" that are consistent with those of the district court. Pet. 15–18. The Patent Owner does not concede that Petitioner's proposed constructions are the correct interpretation of these claims under the *Phillips* standard, but does not expressly contest any of Petitioner's proposed constructions. Prelim. Resp. 18–19.

We find that resolving the parties' dispute regarding whether we should institute *inter partes* review does not require any express claim construction at this stage of the proceedings.

B. A Person of Ordinary Skill in the Art

Petitioner proposes that a person of ordinary skill, at and before the priority date of the patent, would have been: (1) a scientist involved in the development of dermal fillers; (2) would have an advanced degree, such as an M.S., M.D., or Ph.D.; and (3) possessed several years of experience developing dermal fillers for cosmetic use, including HA-based dermal fillers. Pet. 14. Petitioner contends that

[8] This case relates to the '795 patent, which issued from the '884 application, of which the application that issued as the '519 patent is a continuation. *See* Pet. 19; Ex. 1027.

such a skilled artisan 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. *Id.* (citing Ex. 1002 ¶¶ 69–72).

Petitioner also states that a person of ordinary skill in the art would also have been aware of the process by which FDA reviews dermal filler products, and how FDA communicates the results of such reviews to the public. Pet. 14. Specifically, Petitioner posits that a skilled artisan would have known that once the FDA approved a dermal filler, the Agency would have posted information about that filler on its webpage. *Id.* (citing Ex. 1002 ¶¶ 73–75; Ex. 1032 227).

The Patent Owner points to the Board's related findings in a prior *inter partes* proceeding, IPR2017-01906, which involved the '795 patent. Prelim. Resp. 20. In that proceeding, the Board adopted a definition of the level of skill of a person of ordinary skill in the art consistent with Petitioner's characterizations (1)–(3), *supra*. *Id.* The Patent Owner rejects Petitioner's additional qualifications respecting "products for which approvals were being publicly sought" and awareness "of the process by which FDA reviews dermal filler products and how FDA communicates the results of such review to the public." *Id.* The Patent Owner notes that Petitioner fails to offer any reason why the Board's previous definition of a person of ordinary skill in the art is incorrect, or any reason why the Board should accept Petitioner's new definition. *Id.*

We do not find the Patent Owner's argument persuasive. The Patent Owner specifically objects to the additional qualification proposed by the Petitioner as being characteristic of a person of ordinary skill in the art, *viz.*:

> A POSITA 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. In particular, the POSITA would have known that once FDA had approved a dermal filler, the FDA would have hosted information about that filler on its webpage.

See Pet. 14. We find that whether a person of ordinary skill in the art, as defined by the petitioner in the prior proceedings would have also had this specific knowledge, as part of the performance of her qualifications and duties, is a finding of fact. Petitioner has presented testimony, *via* the DeVore Declaration, that:

> The POSITA would be aware of both currently marketed dermal fillers, as well as those being publicly tested by medical device companies. The POSITA would have been aware of the process by which FDA reviews applications for new dermal filler products, as well as how the results of those reviews are communicated to the public.

Ex. 1002 ¶ 70.

The Patent Owner presents no evidence or testimony to rebut Dr. DeVore's opinion, and we consequently agree with the Petitioner's definition of a person of ordinary skill in the art would have the additional knowledge and abilities testified to by Dr. DeVore. We find this to be particularly so because the qualifications recited as defining a person of ordinary skill in the art typically define the broad contours of an artisan's education and capabilities and do not speak to every particular aspect of their knowledge and duties. Given that, we adopt for our present purposes that a person of ordinary skill in this particular art would be "aware of the process by which FDA reviews dermal filler products, and how FDA communicates the results of such reviews to the public." Pet. 14. The Patent Owner may adduce evidence at trial to rebut this definition.

C. Grounds 1, 2, and 3: Anticipation of Claims 1–4 by PMA P050047/S005, Weinkle, or the '438 application, respectively

1. Priority claims of the '519 patent

For the cited prior art references to anticipate claims 1–4 of the '519 patent, the '519 patent must not be able to claim the priority benefit of the '956, '934, or

’278 applications (the “priority applications”), thereby rendering the cited references eligible as prior art. Petitioner argues that the effective filing date of claims 1–4 is the actual filing date of the application that issued as the’519 patent, April 1, 2014, rather than the claimed priority date, because the parent applications do not provide sufficient support for the claims as filed. Pet. 18–19.

a. Alleged lack of literal support for claims 1–4

Petitioner first argues that effective filing date of claims 1–4 of the ’519 patent is April 1, 2014 filing date of the ’747 application, the application that issued as the ’519 patent, rather than the earlier priority date(s) claimed by the Patent Owner, because the parent applications do not provide literal support for the claims as filed. Pet. 20. Petitioner points out that independent claims 1 and 3 are directed to sterile dermal fillers comprising BDDE-crosslinked HA and 0.3% lidocaine, and notes that there are no other structural limitations. *Id.* To the contrary, Petitioner contends, each claim is directed to a functional result—the filler’s cosmetic performance. *Id.* Petitioner asserts that claim 1 recites a filler with lidocaine that “fills in facial lines and depressions substantially the same” as an otherwise same filler that does not contain lidocaine. *Id.* Similarly, argues Petitioner, claim 3 recites a filler with lidocaine that “restores fat loss-related tissue volume loss substantially the same” as an otherwise same filler that does not contain lidocaine. *Id.*

According to Petitioner, no disclosure in the priority documents suggests that the disclosed fillers have the claimed functional characteristics. Pet. 21 (citing Ex. 1002 ¶ 146). Petitioner asserts that the there are no comparative tests in the ’956, ’934, or ’278 applications from which equivalent performance could be deduced or inferred, and that no example shows that the claimed fillers fill in facial

lines and depression, or restore fat loss-related tissue volume loss at all, much less that they do so substantially the same relative to a comparative filler that does not contain lidocaine. *Id.* (citing Ex. 1002 ¶¶ 146–147).

Petitioner contends that, although filling facial lines and depressions or restoring fat loss-related tissue volume loss may be intended objectives of the claimed dermal fillers, as they are with all dermal fillers, compositions having those characteristics are not demonstrated or described anywhere in the priority documents, much less in enough detail to identify how the "fill[ing]" or "restor[ing]" is performed in either lidocaine or non-lidocaine fillers. Pet. 21 (citing, e.g., Ex. 1082 col. 1, ll. 30–34; also citing *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1349–50 (Fed. Cir. 2010) (*en banc*)). Petitioner contends that the disclosure is silent as to how any composition—whether prior art or supposedly inventive filler—performs at filling or whether and how the disclosed embodiments perform "substantially the same" at filling facial lines or restoring tissue volume loss. *Id.* Therefore, argues Petitioner, there is nothing in the specification of the claimed priority documents that would clearly allow a person of ordinary skill in the art to recognize fillers having the claimed performance. *Id.* (citing Ex. 1002 ¶¶ 144–147, 152).

The Patent Owner responds that each of the '956, '934, and '278 applications discuss the ability of these compositions to retain their viscosity so that they can function to fill in facial lines and restore fat loss-related tissue volume. Prelim. Resp. 23. By way of example, the Patent Owner notes that these priority applications state: "Soft tissue fillers have been developed to help fill in facial lines and depressions, and for restoring volume of tissues due to fat loss." *Id.* (quoting Ex. 1013 11; Ex. 1028 4; Ex. 1044 16). The Patent Owner further argues that these priority applications further describe problems that soft tissue

fillers exhibited in performing these functions, disclosing that: "The development of HA-based fillers which exhibit ideal in vivo properties as well as ideal surgical usability has proven difficult." *Id.* (quoting Ex. 1013 12; Ex. 1028 5; Ex. 1044 17). Furthermore, argues the Patent Owner, in the case of HA-injectable compositions, the priority applications attribute these problems to lidocaine-induced degradation, disclosing that: "HA-based injectable compositions which incorporate lidocaine during the manufacturing process are prone to partial or almost complete degradation prior to injection, particularly during high temperature sterilization steps and/or when placed in storage for any significant length of time." *Id.* at 23–24 (quoting Ex. 1013 12; Ex. 1028 5; Ex. 1044 17). The Patent Owner contends that the '956, '934, and '278 applications subsequently characterize the invention as solving the degradation problem, leading to improved stability and comparable performance to HA-based compositions lacking lidocaine. *Id.* at 24 (citing Ex. 1013 13–14; Ex. 1028 6–7; Ex. 1044 18).

The Patent Owner contends that support for claims 1–4 can also be found in the '956, '934, and '278 applications *via* their disclosures with respect to the stability experiments involving the claimed compositions. Prelim. Resp. 25. The Patent Owner responds that, because the claimed compositions are stable, they are able to perform the filling features recited in claims 1–4. *Id.* The Patent Owner points to the tables provided in the priority applications summarizing the "stability testing results on the composition manufactured in accordance with the invention." *Id.* (quoting Ex. 1013 25; Ex. 1028 18; Ex. 1044 29). According to the Patent Owner, the data in the Table show that the extrusion force of the compositions containing lidocaine remained constant over a period of 3–9 months, and thus maintain their integrity to function as claimed over a period of 3–9 months. *Id.*

The Patent Owner argues further that the '956, '934, and '278 applications also include figures and discussion that demonstrate changes in viscosity between the autoclaved samples with and without lidocaine. Prelim. Resp. 25. The Patent Owner points to these figures as demonstrating that the viscosity at 0.1 Hz of BDDE-crosslinked cohesive Samples 4, 5, and 6, which embody the invention, did not decrease to any appreciable extent (not greater than about 30%) when lidocaine was added and the combination was autoclaved. *Id.* (citing Ex. 1013 40–44; Ex. 1028 39–43; Ex. 1044 43–45).

Summarizing, the Patent Owner contends that the '956, '934, and '278 applications convey to a person of skill in the art that, because the lidocaine-containing samples embodying the claimed invention retain their viscosity and extrusion force, and consequently solve the lidocaine degradation problem, they are able to perform the filling functions as well as identical compositions lacking lidocaine. Prelim. Resp. 26.

We agree with the Patent Owner. The priority applications, as exemplified by the '956 application, expressly state that: "Soft tissue fillers have been developed to help fill in facial lines and depressions, and for restoring volume of tissues due to fat loss, thereby temporarily restoring a smoother, more youthful appearance." Ex. 1013 11. The '956 applications continues:

> The search for fillers that do not provoke allergic reactions has brought about the development of hyaluronic acid (HA)-based products. In December 2003, the first HA-based filler was approved by the FDA. This was soon followed by other HA-based fillers.
>
> Hyaluronic acid, also known as hyaluronan, is a naturally occurring, water soluble polysaccharide, specifically a glycosaminoglycan, which is a major component of the extracellular matrix and is widely distributed in animal tissues. Hyaluronic acid has excellent biocompatibility and does not cause allergic reaction when implanted

> into a patient. In addition, hyaluronic acid has the ability to bind to large amounts of water, making it an excellent volumizer of soft tissues.
> ….
> Crosslinked HA is formed by reacting uncrosslinked HA with a crosslinking agent under suitable reaction conditions. Methods of preparing HA based soft tissue fillers including both crosslinked and uncrosslinked HA are well known.

Id. at 11–12.

> The '956 application further discloses that:
>
> The next step in the manufacturing process comprises the step of crosslinking the hydrated, alkaline NaHA gel with a suitable crosslinking agent. The crosslinking agent may be any agent known to be suitable for crosslinking polysaccharides and their derivatives via their hydroxyl groups. Suitable crosslinking agents include but are not limited to, for example, 1,4-butanediol diglycidyl ether (or 1,4-bis(2,3-epoxypropoxy)butane or 1,4-bisglycidyloxybutane=BDDE), 1,2-bis(2,3-epoxypropoxy)ethylene and 1-(2,3-epoxypropyl)-2,3-epoxycyclohexane.

Id. at 18. The priority applications thus disclose that HA dermal fillers crosslinked with BDDE, as claimed in the '519 patent, were well-known in the art at the time of filing. Indeed, Petitioner's declarant, Dr. DeVore, testifies that it was known in the art, as of August 2008, that:

> Facial dermal fillers are a class of implantable medical devices that are used to fill wrinkles or add volume to portions of the face where facial tissue has been lost. Dermal fillers are viscous liquid compositions which are injected using a syringe into a patient's face in order to restore lost volume and remove facial wrinkle lines and folds.

Ex. 1002 ¶ 78. Dr. DeVore further attests that:

> Although many different compounds can be used to crosslink HA, as of August 2008 the vast majority of dermal fillers were prepared from a small number of crosslinker compounds: 1,4-butanediol diglycidyl ether ("BDDE"), divinylsulfone ("DVS"), p-phenylene-bis(ethylcarbodiimide) ("BDCI"), and diepoxyoctane ("DEO")….

Ex. 1002 ¶ 85. It is therefore evident to us that, as of the time of filing of the priority applications, it was well known in the art, as attested to by Dr. DeVore, that dermal fillers were used for "fill[ing] wrinkles or add[ing] volume to portions of the face where facial tissue has been lost," and that, among such dermal fillers, HA crosslinked with BDDE was not only a commonly used and well understood formulation, but was known by the trade name of Juvéderm Ultra Plus. *See id.* ¶ 192.

Furthermore, the Examples in the priority applications demonstrate that adding lidocaine to BDDE-crosslinked HA-based dermal fillers results in compositions that demonstrate essentially similar thermal stability and viscosity properties possessed by BDDE-crosslinked HA based dermal fillers[9] without lidocaine, i.e., both compositions behave in the same way as dermal fillers "fill[ing] wrinkles or add[ing] volume to portions of the face where facial tissue has been lost." Figure 6 of the '956 application is reproduced below:

[9] In viewing these data, we have concerns about the lack of repetitive sampling and concurrent statistical analysis in the Examples of the priority applications as well as in the Specification of the '519 patent. Nevertheless, the data presented support a *prima facie* argument that the thermal stability properties of the samples are similar, the which point is not disputed by the parties at this time.

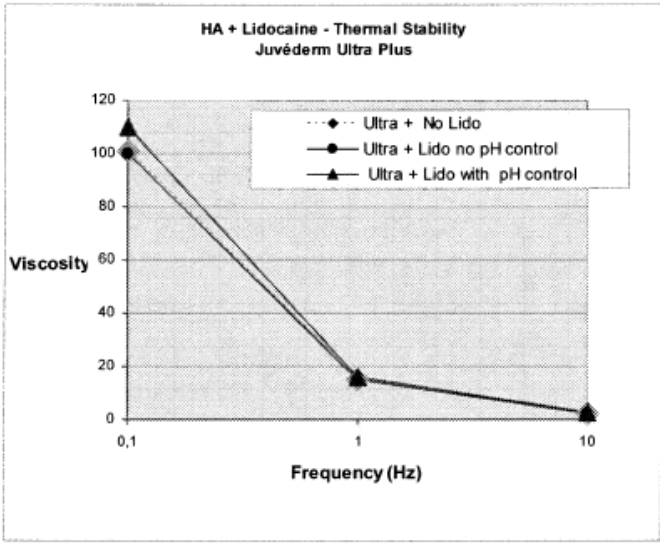

Figure 6 of the '956 application demonstrates the post-sterilization thermal stability of a commercially available BDDE-crosslinked HA dermal filler (Juvéderm Ultra Plus): (1) without lidocaine; (2) with 0.3% lidocaine; and (3) with 0.3% lidocaine and with pH adjusted to 7.2

Figure 6 of the '965 application (and the other priority applications) thus demonstrates that a BDDE-crosslinked HA-based dermal filler exhibits similar viscosities post-autoclaving whether paired with 0.3% lidocaine or sterile water (control). We agree that a person of ordinary skill in the art would have comprehended, from these disclosures of the priority documents, that a BDDE-crosslinked HA-based dermal filler containing 0.3% lidocaine would act in the same manner as the commercially-available, BDDE-crosslinked HA dermal filler (Juvéderm Ultra Plus) in its intended purpose of "fill[ing] wrinkles or add[ing] volume to portions of the face where facial tissue has been lost." Or, as Petitoner's declarant declarant opines:

> Because the POSITA would expect the lidocaine to be voided from the gel quickly after implantation, the POSITA would have expected the lidocaine-containing gel *to have substantially the same clinical performance, including the claimed filling in facial lines and wrinkles (claim 1) and restoring fat loss related tissue volume loss*, as an otherwise same gel that did not contain lidocaine.

Ex. 1002 ¶ 196 (emphasis added). We therefore do not find convincing Petitioner's argument that claims 1–4 of the '519 patent lack literal support in the disclosures of the '956, '934, and '278 applications.

b. Whether the disclosed species support claims 1–4

Petitioner next argues that the species disclosed in the '956, '934, and '278 applications do not describe the full scope of the fillers recited in the claims. Pet. 22 (citing Ex. 1002 ¶ 152). Petitioner notes that, in an unpredictable art, the disclosure of many species will not describe a genus if the genus is much broader than the species. *Id.* (citing *Abbvie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301 (Fed. Cir. 2014)). According to Petitioner, the Patent Owner has repeatedly argued that the claims were patentable because it was not expected that lidocaine could be combined with hyaluronic acid and that it was an unexpected discovery that cohesive gels could be successfully combined with lidocaine. *Id.* at 23 (citing Ex. 104 ¶¶ 5–10; Ex. 1023, 23–25).

Petitioner asserts that the claims of the '519 patent are broad, requiring only the presence of BDDE-crosslinked HA and 0.3% lidocaine. Pet. 23. The claims cover fillers with essentially any degree of crosslinking, any particle size, any amount of free HA and almost any ratio of high and low molecular weight HA. *Id.* (Ex. 1002 ¶¶ 149–150). However, Petitioner argues the '956, '934, and '278 applications disclose only three species, each of which is a cohesive gel having 6% crosslinking or less. *Id.* (citing Ex. 1001 col. 15, ll. 38–52).

Petitioner contends that, in view of the breadth of the claims, the Patent Owner's repeated assertions that the art was unpredictable compels a finding that the claims are not entitled to the claimed priority date, even if one or more of the species disclosed therein might have the claimed performance. Pet. 24. Petitioner

argues that the '519 patent and the priority documents all contend that it was unpredictable whether lidocaine could be added to a dermal filler. *Id.* (citing Ex. 1001 col. 2, ll. 26–31). Petitioner also observes that the '956 application (which is incorporated by reference into each of the priority applications) explicitly states that it was "recognized" by the "conventional knowledge in the art" that adding lidocaine to HA compositions resulted in degradation. *Id.* (citing Ex. 1013 col. 4, ll. 14–20) (emphasis added).

Petitioner also points to the Declaration of inventor Dr. Pierre Lebreton (the "Lebreton Declaration" (Ex. 1024)), submitted during examination, which states that "shortly prior to August 4, 2008," "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." Pet. 25 (quoting Ex. 1024 ¶¶ 4–5). Petitioner asserts that the Lebreton Declaration states that it was discovered that a subset of dermal fillers, e.g., cohesive gels, could be successfully combined with lidocaine: "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." *Id.* (quoting Ex. 1024 ¶ 15).

Summarizing, Petitioner contends that the alleged breadth of the claims, the alleged lack of a sufficient number of examples, and the Patent Owner's asserted unpredictability of the art compel a finding that the claims are not described by any of the claimed priority documents. Pet. 26.

The Patent Owner responds that claims 1–4 are drawn to sterile dermal filler compositions containing BDDE-crosslinked HA and 0.3% lidocaine that perform the claimed filler functions that are substantially the same as identical dermal fillers lacking lidocaine. Prelim. Resp. 27–28 (citing Ex. 1001 col. 19, ll. 16–20).

According to the Patent Owner, the claims therefore require a specific polymer (crosslinked HA), a specific crosslinker (BDDE), a specific anesthetic (lidocaine), and a specific amount of the anesthetic (0.3%). *Id.* at 28.

The Patent Owner notes that Petitioner acknowledges that the priority applications describe three species embodying the claimed invention. Prelim. Resp. 28 (citing Pet. 23). The Patent Owner asserts that the '956, '934, and '278 applications each describe Samples 4–6, which correspond to Juvéderm Refine, Juvéderm Ultra Plus, and Juvéderm Voluma. *Id.* (citing Ex. 1013 26; Ex. 1028 19; Ex. 1044 30). The Patent Owner argues that these samples all contain BDDE-crosslinked HA and (in Test 2) 0.3% lidocaine as recited in claims 1–4. *Id.* The Patent Owner contends that the text of the priority applications shows that when Samples 4–6 are mixed with lidocaine, the resulting compositions are stable with autoclaving. *Id.* Furthermore, argues the Patent Owner, the priority applications demonstrate the free release of lidocaine from the Juvéderm Ultra Plus gel (Sample 5). *Id.* (citing Ex. 1013 29; Ex. 1028 22; Ex. 1044 34). The Patent Owner therefore argues that the three species disclosed in the priority applications adequately support claims 1–4.

We do not find Petitioner's arguments persuasive. We agree with Petitioner that the Examples of the '956, '934, and '278 applications disclose three species, each of which is a cohesive gel having 6% crosslinking or less (i.e., Samples 4–6). *See* Pet. 23. However, the priority applications also disclose that "[c]rosslinked HA is formed by reacting uncrosslinked HA with a crosslinking agent under suitable reaction conditions. Methods of preparing HA based soft tissue fillers including both crosslinked and uncrosslinked HA are well known." *See, e.g.*, Ex. 1013 2. The priority applications further disclose that:

> The next step in the manufacturing process comprises the step of crosslinking the hydrated, alkaline NaHA gel with a suitable

> crosslinking agent. The crosslinking agent may be any agent known to be suitable for crosslinking polysaccharides and their derivatives via their hydroxyl groups.… The use of more than one crosslinking agent or a different crosslinking agent is not excluded from the scope of the present invention. In is [sic] particularly preferred embodiment, the crosslinking agent comprises or consists of 1,4-butanediol diglycidyl ether (BDDE).

Id. at 18. The priority applications additionally disclose that:

> The step of crosslinking may be carried out using means known to those of skill in the art. Those skilled in the art appreciate how to optimize the conditions of crosslinking according to the nature of the HA, and how to carry out the crosslinking to an optimized degree. The degree of crosslinking is preferably sufficient for the final hydrogel composition obtained from the present methods to remain implanted at the injection site without excessive diffusion away from this injection site. In some embodiments of the present invention, the degree of crosslinking is at least about 2% to about 20%, and more preferably is about 4% to about 12%, wherein the degree of crosslinking is defined as the percent weight ratio of the crosslinking agent to HA-monomeric units in the composition.

Id. at 18. The priority applications thus disclose that: (1) optimizing the crosslinking of HA with BDDE was well known within the art of dermal fillers; (2) for the purposes of the claimed invention, the degree of crosslinking is at least about 2% to about 20%, and more preferably is about 4% to about 12%, and that (3) as explained *supra*, the Examples demonstrate that a commercially-available dermal filler, in which the HA was 6% crosslinked with BDDE (i.e., Juvéderm Ultra Plus) exhibited thermal stability when combined with 0.3% lidocaine that was comparable to that demonstrated by the same dermal filler without lidocaine.

Petitioner argues that claims 1–4 of the ’519 patent are not sufficiently supported by the disclosures of the ’956, ’934, and ’278 applications because (as the Patent Owner argued during examination) the art of dermal fillers is so

unpredictable that a person of ordinary skill would not have received sufficient guidance from the priority applications to practice the claimed invention. Petitioner points to the statements of the Lebreton Declaration in support of this contention.

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

Ex. 1024 ¶¶ 5–10. We find that the Lebreton Declaration asserts, at most, that it would have been uncertain to a person of ordinary skill in the art that combining lidocaine with a BDDE-crosslinked HA-based dermal filler would have the same thermal stability properties as the same BDDE-crosslinked HA-based dermal filler without lidocaine – a supposition contradicted by Trials 1–3 disclosed by the

priority Declarations. Furthermore, and as we explain *infra*, the statements of the Lebreton Declaration are unsupported by any factual evidence of record.

Petitioner, however, argues that the art is not uncertain, and that the lack of degradation caused by the addition of 0.3% lidocaine would have been entirely expected by a person of ordinary skill in the art. The DeVore Declaration, upon which Petitioner expressly relies, attests that:

> Moreover, in my opinion a POSITA, at least "shortly prior to" August 4, 2008, would have believed that lidocaine *could* be added to a HA gel. As explained throughout much of this declaration, the prior art explicitly taught that lidocaine *had* been successfully combined with several other crosslinked-HA dermal fillers, leading to (at least) the products Prevelle Silk, Elevess, and Puragen Plus. The POSITA would have been aware of these products and would have also been aware of the references cited in "Grounds" of the Petition and this declaration, as well as other publications such as Toth and Hanke. Each of these references except for Hanke explicitly describe a crosslinked-HA dermal filler combined with lidocaine, and the POSITA would have understood Hanke's HA composition was crosslinked as well. Further a POSITA would have understood that each of the commercial products, as described in the various references cited, would have been sterilized and "sufficiently stable" (to use Lebreton's words from his declaration) in order to obtain FDA approval and be competitive in the marketplace. Thus, the prior art and documents cited here contradict Lebreton's opinions in his declaration about the knowledge of the POSITA.

Ex. 1002 ¶ 208 (internal reference omitted). Petitioner cannot credibly argue simultaneously that the art was so uncertain that a person of ordinary skill would not have understood that the addition of 0.3% lidocaine would not degrade a crosslinked HA-based dermal filler and also argue that the art was certain enough that a skilled artisan would have understood "that lidocaine had been successfully combined with several other crosslinked-HA dermal fillers." *Id.* Furthermore, the statement of the DeVore Declaration is supported by evidence of record (*See* Ex.

1021 (Toth[10] and Hanke[11], quoted *supra*)), whereas the assertions of the Lebreton are not. We therefore determine that the opinions expressed in this passage of the DeVore Declaration are, at least with respect to the degree of certainty in the art, more credible than those of the DeVore Declaration.

Finally, even were we, *arguendo*, to agree that the '956, '934, and '278 applications did not provide sufficient support for claims 1–4, the '519 patent also claims the priority benefit of the '884 application (*see* II E, *supra*). The Specification of US 8,357,795 B2 (the "'795 patent," which issued from the '884 application) discloses the same stability tests as the priority applications. *See* Ex. 1082 cols. 15–17, ll. 21–2). Furthermore, the Specification of the '795 patent discloses:

> The step of crosslinking may be carried out using any means known to those of ordinary skill in the art. Those skilled in the art appreciate how to optimize conditions of crosslinking according to the nature of the HA, and how to carry out crosslinking to an optimized degree.
>
> Degree of crosslinking for purposes of the present disclosure is defined as the percent weight ratio of the crosslinking agent to HA-monomeric units within the crosslinked portion of the HA based composition. It is measured by the weight ratio of HA monomers to crosslinker (HA monomers:crosslinker).
>
> The degree of crosslinking in the HA component of the present compositions is at least about 2% and is up to about 20%.

[10] C.A. Toth et al., *Preclinical Evaluation of a Novel Hyaluronic Acid 28 mg/mI, Lidocaine 0.3% Stable Combination Product*, 56(2) J. AMER. ACAD. DERMATOL. SUPPL. AB94 (2007) ("Toth").

[11] C.W. Hanke et al., *Effectiveness and Durability of a Hyaluronic Acid 28 mg/ml, Lidocaine 0.3% Stable Combination Product as Demonstrated in a Multicenter, Randomized Trial*, 56(2) J. AMER. ACAD. DERMATOL. SUPPL. AB94 (2007) ("Hanke").

> In other embodiments, the degree of crosslinking is greater than 5%, for example, is about 6% to about 8%.
>
> In some embodiments, the HA component is capable of absorbing at least about one time its weight in water. When neutralized and swollen, the crosslinked HA component and water absorbed by the crosslinked HA component is in a weight ratio of about 1:1. The resulting hydrated HA-based gels have a characteristic of being highly cohesive.
>
> The HA-based gels in accordance with some embodiments of the invention may have sufficient cohesivity such that the gels will not undergo substantial phase separation after centrifugation of the gel at 2000 rd/min for 5 minutes. In another embodiment, the gels have the characteristic of being capable of absorbing at least one time their weight of water and have sufficient cohesivity such that when swollen with water at a gel/water weight ratio of about 1:1, the gels maintain their integrity, for example, when subjected to centrifugation.

Id. at col. 10, ll. 11–45. The Specification of the ’795 patent provides even more specific disclosures concerning claims 1–4 of the ’519 patent. The ’884 application was filed on February 26, 2009, which antedates the allegedly anticipatory references relied upon by the Examiner: (1) P050047/S005 (dated January 6, 2010) (Ex. 1060); (2) Weinkle (published September 2009) (Ex. 1070); and (3) the ’438 application (filed February 4, 2010) (Ex. 1072). We conclude that these additional disclosures of the ’884 application provide further, and sufficient, support for claims 1–4 of the ’519 patent. Because the filing date of the ’884 application antedates the dates of the art references cited by Petitioner, we determine that P050047/S005, Weinkle, and the ’438 application do not qualify as prior art to the ’519 patent, we find that the evidence presented does not demonstrate a reasonable likelihood that Petitioner would prevail on Grounds 1–3.

D. Ground 4: Obviousness of Claims 1–8 over Lebreton and Sadozai

1. Overview of Lebreton

Lebreton teaches dermal filler compositions, including BDDE-crosslinked HA dermal filler obtained by crosslinking a mixture of low and high molecular weight HA starting materials. Ex. 1029 ¶¶ 43–45. Lebreton teaches that such fillers have improved properties relative to fillers using only high or only low molecular weight HA. *Id.* at ¶¶ 21–24. Lebreton teaches that the fillers can be formulated at pH between 6.5 and 7.5, preferably between 7 and 7.4, and even more preferably between 7.1 and 7.3, and that the pH can be controlled using the appropriate buffer solution. *Id.* at ¶ 48. The '519 patent cites Lebreton in explaining how selection of various HA components in dermal fillers was known to affect characteristics such as extrusion force, elastic modulus, and viscous modulus, among others. Ex. 1001 col. 9, ll. 30–40.

Lebreton teaches two examples in which a mixture of high molecular weight and low molecular weight HA is crosslinked with BDDE in the presence of sodium hydroxide. Ex. 1029 ¶¶ 80–92. The resulting mixture is neutralized to pH 7.2 using a phosphate buffer and dialyzed, then mechanically homogenized, loaded into a syringe, and sterilized in an autoclave. *Id.*

2. Overview of Sadozai

Sadozai teaches p-phenylene-bis(ethylcarbodiimide) ("BDCI")–crosslinked HA dermal fillers that include lidocaine. Ex. 1030 ¶¶ 7, 85. Sadozai teaches that its dermal fillers may include an anesthetic that can increase the stability of the dermal filler relative to the same filler without the anesthetic. *Id.* at ¶ 68.

Sadozai teaches examples of nine crosslinked HA gels prepared by crosslinking HA with BDCI. Ex. 1030 ¶ 85. Sadozai further teaches several

examples in which one of the crosslinked HA samples (Example 5) is reconstituted in a phosphate buffer containing 0.3% lidocaine hydrochloride (Buffer 4). *Id.* at ¶¶ 90, 100, 102. The resulting gel is loaded into a syringe and autoclaved, after which the storage modulus (which is related to viscosity) of the lidocaine-containing crosslinked HA is higher than an otherwise identical crosslinked HA without lidocaine. *Id.* at ¶¶ 90, 107 (relating storage modulus to viscosity).

3. Obviousness over Lebreton and Sadozai

Petitioner argues that Lebreton teaches two examples in which a mixture of high molecular weight and low molecular weight HA is crosslinked with BDDE in the presence of sodium hydroxide. Pet. 35. According to Petitioner, the resulting mixture is adjusted to a physiological pH, mechanically homogenized, loaded into a syringe, and sterilized with an autoclave. *Id.* (citing Ex. 1029 ¶¶ 80–92). Petitioner acknowledges that Lebreton's compositions do not contain lidocaine.

Petitioner argues that Sadozai discloses BDCI-crosslinked HA dermal fillers that include lidocaine. Pet. 35 (citing Ex. 1030 ¶¶ 7, 85; Ex. 1002 ¶ 128). Petitioner contends that Sadozai teaches that the dermal fillers may include an anesthetic that can increase the stability of the dermal filler relative to an equivalent filler without the anesthetic. *Id.* (citing Ex. 1030 ¶ 68). Petitioner asserts that Sadozai discloses nine crosslinked HA gels prepared by crosslinking HA with another known crosslinker, p-phenylene-bis(ethylcarbodiimide) ("BDCI"), and further discloses at least one crosslinked HA sample which is reconstituted in a phosphate buffer containing 0.3% lidocaine hydrochloride (Buffer 4), and is then loaded into a syringe and autoclaved (Example 5). *Id.* at 35–36 (citing Ex. 1030 ¶¶ 90, 100, 102). Petitioner argues that Sadozai teaches that the storage modulus (which is related to viscosity) of the lidocaine-containing

crosslinked HA was higher than an otherwise same crosslinked HA without lidocaine. *Id.* at 36 (citing Ex. 1030 ¶ 107); Ex. 1002 ¶ 129 (relating storage modulus to viscosity)).

Petitioner argues that, at the time of filing of the '519 patent, lidocaine had been successfully incorporated into compositions containing HA crosslinked with the three other conventional crosslinking agents: (1) 1,4-divinylsulfone ("DVS"); (2) diepoxyoctane ("DEO"); and (3) BDCI. Pet. 9–10, 16 (citing Ex. 1059 col. 7, ll. 1–17; Ex. 1002 ¶¶ 121–123; Ex. 1012 742; Ex. 1002 ¶¶ 117, 130–131; Ex. 1050 1; Ex. 1002 ¶¶ 114–116). Petitioner asserts that two products had, at the time of filing, already received FDA approval by the earliest filing date of challenged patent, and that the third (Puragen Plus) was approved in Europe and undergoing clinical trials in the U.S. *Id.* at 36 (citing Ex. 1020 8; Ex. 1012 742; Ex. 1002 ¶¶ 117, 130–131; Ex. 1052 (Prevelle Silk); Ex. 1019 4 (Anika's Elevess, (an implementation of Sadozai); Ex. 1002 ¶ 115). Petitioner contends that a composition containing BDDE-crosslinked HA and lidocaine was a derivative and predictable next step in view of the success of the other three clinically-used crosslinkers. *Id.* Petitioner asserts that, at minimum, adding lidocaine to Lebreton would have been obvious to try. *Id.*

Petitioner argues further that the prior art would have suggested, to a skilled artisan, a reasonable expectation of success in adding lidocaine to the BDDE-crosslinked HA of Lebreton to produce a lidocaine-containing dermal filler. Pet. 37. Petitioner contends that the repeated successful use of lidocaine across the remaining spectrum of crosslinked HA dermal fillers would have prompted a person of ordinary skill in the art to, at minimum, attempt the combination. *Id.* Petitioner points to its declarant, Dr. DeVore's opinion that HA gels crosslinked with DVS, BDCI, or DEO share many more similarities with BDDE-crosslinked

gel than there are differences. *Id.* (citing Ex. 1002 ¶¶ 187, 199–200). Once crosslinked, Dr. DeVore opines, all four crosslinkers are devoid of reactive or unstable functional groups which a skilled artisan might suspect would unfavorably react in the presence of lidocaine. *Id.* (*see* Ex. 1002 ¶¶ 199–200).

Furthermore, argues Petitioner, lidocaine had been successfully incorporated into dermal fillers containing more significant chemical differences than the various crosslinked HA compositions. Pet. 37. Petitioner notes that, in the cosmetic field alone, lidocaine had been successfully incorporated into fillers based on synthetic polymers, bovine collagen, and human collagen. *Id.* (citing Ex. 1002 ¶ 113). Petitioner asserts that there is therefore no credible reason why the POSITA would have not expected that lidocaine could be successfully incorporated into a BDDE-crosslinked HA gel as well. *Id.*

The Patent Owner does not expressly contest Petitioner's arguments with respect to the obviousness of the claims, but argues, rather, that the Board should exercise its discretion to deny institution on Ground 4, and on Ground 5, under 35 U.S.C. § 325(d). Prelim. Resp. 33–50. We address these arguments *infra*. However, based upon Petitioner's arguments, we find that, with respect to Ground 4, the prior art cited by Petitioner teaches the limitations of claims 1–8, and that a person of ordinary skill in the art would have been motivated to combine the references with a reasonable expectation of success. We therefore conclude that there is a reasonable likelihood that the Petitioner will prevail at trial upon this ground.

E. Ground 5: Obviousness of Claims 1–8 over P050047and Kinney

1. Overview of P050047

P050047 is a printed publication with a publication date of no later than June

30, 2006. Ex. 1074. The Juvéderm family of dermal fillers received premarket approval ("PMA") from the FDA on June 2, 2006, based on P050047, filed by Inamed Corporation[12] ("Inamed"). *Id.* According to the Food & Drug Administration (FDA) Notice in the Federal Register, the "Safety and Effectiveness Data" for Juvéderm was available on FDA's website by June 30, 2006. Ex. 1075 56,158 (listing the Juvéderm gel implants among the "List of Safety and Effectiveness Summaries for Approved PMAs Made Available" in the second quarter of 2006).

2. Overview of Kinney

Kinney teaches a clinical study comparing two dermal fillers: (1) Restylane, which had been on the market for several years, and (2) Puragen Plus, which was undergoing FDA clinical trials. Ex. 1012 741–742. Kinney teaches that Restylane is an injectable dermal filler containing 20 mg/mL of BDDE-crosslinked HA particles with a high concentration of "minimally modified HA molecules." *Id.* Kinney further teaches that a "major disadvantage" of existing HA based fillers was the pain that accompanied injection. *Id.* at 741. Kinney also teaches Puragen Plus, a dermal filler containing 20 mg/mL of DEO-double crosslinked HA particles and lidocaine hydrochloride (0.3%), which was then undergoing clinical trials. *Id.* at 742. Kinney teaches that injection with Puragen Plus caused minimal or no pain for patients, especially when compared to Restylane. *Id.* at 746.

3. Obviousness over P050047 and Kinney

Petitioner argues that P050047 discloses sterile BDDE-crosslinked HA gels formulated at a concentration of 22-26 mg/mL suspended in a physiological buffer.

[12] The Patent Owner subsequently acquired Inamed. *See* Pet. 4.

Pet. 46 (citing Ex. 1074 1). Petitioner notes that these gels are given the trade name Juvéderm and are indicated for the correction of moderate to severe facial wrinkles and folds. *Id.* According to Petitioner, P050047 discloses Juvéderm 30HV, which is intended for use in certain types of wrinkles. *Id.* (citing Ex. 1074, 2).

Petitioner argues that Kinney teaches results of a clinical trial of "Puragen Plus," a DEO-crosslinked HA dermal filler that includes 0.3 wt% lidocaine, and which provides a "relatively pain-free injection." Pet. 46 (citing Ex. 1012 742). Petitioner contends that Kinney teaches that injection of the lidocaine-containing filler resulted in less pain than injection with a filler that did not contain lidocaine, such as known products Restylane and Puragen (the predecessor of Puragen Plus), and that all patients preferred the lidocaine-containing filler. *Id.* (citing Ex. 1012 746).

It is Petitioner's position that a person of ordinary skill in the art would have been motivated to add lidocaine to the Juvéderm 30HV product described by P050047, because Kinney teaches patients preferred Puragen Plus over Restylane (a BDDE-crosslinked HA filler), due to it containing lidocaine for pain reduction. Pet. 46 (citing Ex. 1012 746; Ex. 1002 ¶ 189). Petitioner contends that a skilled artisan would have been motivated to add lidocaine to Juvéderm, with the expectation that it would reduce pain and increase patient demand in the marketplace. *Id.* at 46–47 (citing Ex. 1002 ¶ 189). Furthermore, Petitioner argues, because BDDE and DEO are each bis-epoxide crosslinkers resulting in the same type of crosslink bonds, a person of ordinary skill would have reasonably expected that lidocaine would function analogously in both of the crosslinked gels. *Id.* at 47 (citing Ex. 1002 ¶ 195).

The Patent Owner responds that the Board should decline to initiate *inter partes* review on Ground 5 because Petitioner fails to prove that P050047 qualifies as a printed publication under pre-AIA 35 U.S.C. § 102(b). Prelim. Resp. 29. The Patent Owner argues that P050047 is an FDA Premarket Approval ("PMA") document entitled "Summary of Safety and Effectiveness Data," and summarizes the features of Juvéderm 30, Juvéderm 24 HV, and Juvéderm 30HV, which are HA-BDDE crosslinked fillers that lack lidocaine. *Id.* at 30 (citing 1074 1–2). The Patent Owner notes that Petitioner points Exhibit 1075, arguing that P050047 was included in a listing of approved PMAs published on the FDA's website no later than June 30, 2006. *Id.* (citing Pet. 4).

The issue, according to the Patent Owner, is not whether P050047 was listed on the FDA's website by June 30, 2006, more than one year before the filing date of the '519 patent (i.e., more than one year before August 4, 2008). Prelim. Resp. 30. Rather, the Patent Owner argues, the issue is whether P050047 was available to a person of ordinary skill in the art exercising reasonable diligence before the critical date. *Id.* (citing, e.g., *SRI Int'l, Inc. v. Internet Sec. Sys., Inc.*, 511 F.3d 1186, 1194 (Fed. Cir. 2008)).

The Patent Owner notes that Petitioner's declarant, Dr. DeVore, testifies as to what a person of ordinary skill in the art would have been aware of, and would have done, with respect to P050047. Prelim. Resp. 30–31 (citing Ex. 1002 ¶¶ 70–75, 155–159). However, the Patent Owner observes, Dr. DeVore's curriculum vitae indicates that he is not a person of ordinary skill in the art, as determined in the prior, related IPR2017-01906, and which the Patent Owner urges to adopt in these proceedings. *Id.* at 31.

According to the Patent Owner, Petitioner offers no evidence that, under the Board's previous definition, a skilled artisan would have routinely reviewed PMA

approvals and would have located P050047 before the critical date by exercising reasonable diligence. Prelim. Resp. 31–32. The Patent Owner notes that Petitioner contends that a person of ordinary skill would have known how to search the FDA's online database to locate PMA notices and would have "recognized Inamed's Juvéderm gel implant product as a relevant dermal filler because Inamed was a known developer of HA-based dermal fillers." *Id.* at 32 (citing Pet. 5). However, argues the Patent Owner, the real question is whether a skilled artisan would have routinely searched that database and, seeing notice of Inamed's PMA, would have searched for P050047. *Id.*

The Patent Owner contends that the evidence cited by Petitioner fails to support its position. Prelim. Resp. 32. By way of example, the Patent Owner points to Petitioner's Exhibit 1039, a January 2008 publication, which cites P050047, as well as PMA documents for "two other products." *Id.* (citing Pet. 5).

The Patent Owner notes that Petitioner also relies on various issues of the "Skin Therapy Letter" journal (Ex. 1076). *Id.* The Patent Owner contends that Petitioner argues that these issues include a recurring section titled "Update on Drugs" that gives notice of FDA approvals, and asserts that this simple listing would have prompted a POSITA to seek out FDA PMAs. *Id.* (citing Pet. 5–6).

However, the Patent Owner contends that Petitioner's statements about these references are no more than unsupported speculation. Prelim. Resp. 32. According to the Patent Owner, references to P050047 and awareness of FDA approvals by reviewing updates in "Skin Therapy Letter" do not prove that a person of ordinary skill in the art would have routinely searched the FDA's database for PMA approvals and would have located P050047 before the critical date. *Id.* at 32–33. The Patent Owner observes that all of the references that Petitioner cites are directed at M.D.s, and that Dr. DeVore does not hold that

degree and does not provide evidence that a skilled artisan possessing an M.D. would search FDA databases for PMA approvals. *Id.* at 33. Similarly, argues the Patent Owner, knowledge of Inamed's activity in the area of dermal fillers does not prove that a person of ordinary skill would have located P050047 before the critical date. *Id.* Consequently, the Patent Owner argues, Petitioner fails to show that P050047 qualifies as a printed publication and qualified prior art to the '519 patent. *Id.*

We do not find the Patent Owner's argument persuasive. As we have explained in III.B *supra*, Dr. DeVore has testified that:

> The POSITA would be aware of both currently marketed dermal fillers, as well as those being publicly tested by medical device companies. The POSITA would have been aware of the process by which FDA reviews applications for new dermal filler products, as well as how the results of those reviews are communicated to the public.

Ex. 1002 ¶ 72. Although the Patent Owner attacks Dr. DeVore's testimony as "unsupported speculation," the Patent Owner presents no evidence or testimony of record to rebut Dr. DeVore's opinion. *Id.* at 32; *see In re De Blauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984) (holding that arguments and conclusions unsupported by factual evidence carry no evidentiary weight). We consequently agree with the Petitioner's definition of a person of ordinary skill in the art would have the additional knowledge and abilities testified to by Dr. DeVore, and would therefore have been aware of the P050047 reference, for the reasons attested by Dr. DeVore. We find this to be particularly so because the qualifications recited as defining a person of ordinary skill in the art typically define the broad contours of an artisan's education and capabilities and do not speak to every particular aspect of their knowledge and duties.

The Patent Owner additionally attacks Dr. DeVore's testimony, based upon his experience, as not being reflective of that of a person of ordinary skill in the art. The Patent Owner also criticizes Dr. DeVore's testimony, because Dr. DeVore does not hold an M.D. degree. The Patent Owner observes that all of the references that Petitioner cites are directed at M.D.s, and that Dr. DeVore does not hold that degree and does not provide evidence that a skilled artisan possessing an M.D. would search FDA databases for PMA approvals. *See* Prelim. Resp. 30–31, 33. We fail to see the relevance of these arguments. If, as the Patent Owner seems to argue, Dr. DeVore's qualifications exceed those of a person of ordinary skill in the art, whether by dint of his academic qualifications and work history, or his personal knowledge and experience, we fail to see how this precludes Dr. DeVore from opining as to what would be the knowledge of a person of ordinary skill in the art. *See*, *e.g.*, Ex. 1002 ¶¶ 69–72. Such testimony is capable of being challenged by the Patent Owner at trial, and evaluated by the Board in light of both parties' arguments.

Furthermore, although Dr. DeVore does not hold an M.D. degree, he does, indisputably, hold a Ph.D. in the related area, and has extensive experience in the field of dermal fillers. *See* Ex. 1002 4–9. The definition of a person of ordinary skill in the art, as agreed to by both parties in the related district court proceedings, would be: (1) a scientist involved in the development of dermal fillers; (2) would have an advanced degree, such as an M.S., M.D., or Ph.D.; and (3) possessed several years of experience developing dermal fillers for cosmetic use, including HA-based dermal fillers. *See, e.g.*, Pet. 14; Prelim. Resp. 20. By these criteria, Dr. DeVore is at least a person of ordinary skill in the art and can testify to the understanding and ability of an ordinarily skilled artisan at the time of filing. We consequently agree with Petitioner that the P050047 reference, for the purpose of

this Decision to Institute qualifies, as a printed publication under pre-AIA 35 U.S.C. § 102(b), and as prior art for Ground 5.

As with respect to Ground 4, the Patent Owner does not expressly contest Petitioner's arguments with respect to the obviousness of the claims, but argues, rather, that the Board should exercise its discretion to deny institution on Ground 4, and on Ground 5, under 35 U.S.C. § 325(d). Prelim. Resp. 33–50. We address these arguments *infra*. However, based upon Petitioner's arguments, we find that, with respect to Ground 5, the prior art cited by Petitioner teaches the limitations of claims 1–8, and that a person of ordinary skill in the art would have been motivated to combine the references with a reasonable expectation of success. We therefore conclude that there is a reasonable likelihood that the Petitioner will prevail at trial upon this ground.

F. Exercise of Discretion on Grounds 4 and 5 under 35 U.S.C. § 325(d)

The Patent Owner urges us to exercise our discretion under 35 U.S.C. § 325(d) and deny institution of Grounds 4 and 5. Prelim. Resp. 33. The Patent Owner argues that the factors set forth in our decision in *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, No. IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) (precedential as to § III.C.5, first paragraph) militate in favor of denying institution of *inter partes* review. *Id.* at 33–34. The Patent Owner contends that the same, or cumulative, art and arguments advanced by Petitioner were considered and, ultimately, rejected throughout the extensive prosecution history of the '519 patent. *Id.* at 34.

Specifically, the Patent Owner asserts that Petitioner's declarant, Dr. DeVore, disagrees with the inventor and the Examiner with respect to the unexpected results evidence that formed the basis for allowing the '519 patent

claims. Prelim. Resp. 34. However, argues the Patent Owner, a mere difference of opinion is not sufficient to warrant institution based on references and arguments the Examiner already considered. *Id.* (citing *Apple Inc. v. Qualcomm Inc.*, IPR2018-01453, Paper 7 at 10–15 (PTAB Feb. 27, 2019) (denying institution under § 325(d) where Petitioner relied on the same art that the Examiner considered, and the challenge was merely Petitioner's declarant disagreeing with the Examiner's interpretation of the art)); *Apotex, Inc. v. Celgene Corp.*, No. IPR2018-00685, Paper 8 at 25–26 PTAB Sept. 27, 2018) (denying institution where "[e]ssentially, Petitioner and [Petitioner's declarant] disagree with the Examiner's conclusion that, on balance, the subject matter of the claims would not have been obvious….").

The factors set forth in *Becton, Dickinson* are:

(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 distinguishes 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 prior art or arguments.

Becton, Dickinson, IPR2017-01586, Paper 8 at 17–18.

More recently, the Board explained a two-part framework that the Board uses under § 325(d):

> (1) whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office; and
>
> (2) if either condition of first part of the framework is satisfied, whether the petitioner has demonstrated that the Office erred in a manner material to the patentability of challenged claims.

Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH, IPR2019-01469, Paper 6 at 8 (PTAB Feb. 13, 2020) (precedential). The Board explained that the *Becton, Dickinson* factors "provide useful insight into how to apply the framework under 35 U.S.C. § 325(d)." *Id.* at 9. We consider these factors in turn.

1. *Becton, Dickinson* factors (a)–(d)

i. Lebreton

With respect to Lebreton, the Patent Owner argues that the reference not only appears on the face of the '519 patent, but is expressly cited and incorporated by reference in the specification of the '519 patent. Prelim. Resp. 35 (citing Ex. 1001 col. 9, ll. 36–40).

The Patent Owner points out that Lebreton was also the primary reference relied upon by the Examiner during prosecution of the '795 and '676 patents, of which the '519 patent is a continuation. Prelim. Resp. 35. The Patent Owner contends that Petitioner advances the same obviousness arguments, based upon Lebreton that were presented and successfully overcome during prosecution. *Id.* at 35–36. The Patent Owner notes that Petitioner argues that Lebreton discloses BDDE-crosslinked HA dermal fillers without lidocaine and that a skilled artisan could have successfully incorporated lidocaine into Lebreton's BDDE-crosslinked gels. *Id.* at 36 (citing Pet. 35–38). The Patent Owner contends that this is the same

argument based on the same primary reference that the Examiner raised in rejections dated May 31, 2011 and December 27, 2011 during prosecution of the '795 patent and on August 30, 2013 during prosecution of the '676 patent (parent applications to the '519 patent), that Allergan successfully overcame. *Id.* (citing Ex. 1023 45–46, 79–80; Ex. 2005 70).

ii. Sadozai

The Patent Owner argues that Sadozai appears on the face of the '519 patent and was considered by the Examiner during prosecution. Prelim. Resp. 36 (citing Ex. 1001, 2). The Patent Owner argues further that Sadozai, is either the same as, or cumulative of, the prior art that was considered, and distinguished, during prosecution of the '519 patent. Prelim. Resp. 36 (citing Pet. 35–36). The Patent Owner contends that Sadozai (Ex. 1030) is cumulative of Wang[13] (Ex. 1047), Calias[14] (Ex. 1048), and Marko[15] (Ex. 2004), and was considered by the Examiner during prosecution. *Id.* (citing Ex. 1001 2).

The Patent Owner notes that Petitioner argues that because Sadozai teaches a lidocaine-containing HA composition that was sterilized and FDA-approved, a person of ordinary skill in the art would have expected that adding lidocaine to Lebreton's BDDE-crosslinked HA fillers would have created stable fillers. Prelim. Resp. 37 (citing Pet. 54–56). However, the Patent Owner argues, Sadozai does not describe sterile lidocaine-containing BDDE-crosslinked HA. *Id.* The Patent Owner asserts that Wang, Calias, and Marko likewise described HA crosslinked

[13] Wang (US 2005/0271729 A1, December 8, 2005) ("Wang").

[14] Calias et al. (US 6,521,223 B1, February 18, 2003) ("Calias").

[15] Marko et al. (US 2004/0101959 A1, May 27, 2004) ("Marko").

with agents other than BDDE. *Id.* Therefore, the Patent Owner argues, Sadozai, adds nothing to Wang, Calias, and Marko, nor does it describe the free release of lidocaine *in vivo*, as required by claims 2, 4, and 8. *Id.* Rather, the Patent Owner asserts that Sadozai states that "[t]he crosslinked HA can function as a vehicle which provides the controlled or sustained release of the bioactive agent." *Id.* (quoting Ex. 1030 ¶ 59). The Patent Owner contends that "[c]ontrolled or sustained release" is the opposite of free release. *Id.*

iii. P050047

The Patent Owner repeats the argument presented *supra*, that P050047 is not a printed publication. Prelim. Resp. 37–38. However, the Patent Owner argues, even if, *arguendo*, the P050047 is a printed publication, it is merely cumulative of Lebreton (Ex. 1029). *Id.* at 38. The Patent Owner contends that P050047, like Lebreton, discloses BDDE-crosslinked HA gels that lack lidocaine. *Id.* (citing Ex. 1074 1–2). The Patent Owner again argues that this issue was raised by the Examiner during prosecution of the '519 patent, which was ultimately allowed. *Id.*

iv. Kinney

Turning to the Kinney reference, the Patent Owner argues that Kinney was considered by the Examiner during prosecution of the '519 patent. Prelim. Resp. 38. The Patent Owner asserts that Kinney is cumulative of Lebreton (Ex. 1029), Wang (Ex. 1047), Calias (Ex. 1048), and Marko (Ex. 2004), all of which were cited by the Examiner during prosecution of the '795 patent. *Id.*

According to the Patent Owner, Petitioner relies on Kinney (Ex. 1012) for its disclosure that (1) "injection with the lidocaine-containing filler [Puragen Plus] resulted in less pain than injection with a filler that did not contain lidocaine, such

as known products Restylane and Puragen (the predecessor of Puragen Plus) and that all patients preferred the lidocaine-containing filler" and (2) a person of ordinary skill in the art would have been motivated to include lidocaine in an HA filler and would have expected BDDE and DEO crosslinking agents to behave similarly. Prelim. Resp. 38–39 (citing Pet. 46–47).

The Patent Owner contends that Petitioner merely repeats the same arguments set forth by the Examiner with respect to the references that the Patent Owner overcame during prosecution of the '519 patent family. Prelim Resp. 39. Specifically, the Patent Owner argues, these are similar to the arguments that the Examiner advanced during prosecution of the '519 patent family in the context of Wang, Calias, and Marko. *Id.* The Patent Owner argues that, like Kinney, Wang and Calias both describe the inclusion of an anesthetic (e.g., lidocaine) into crosslinked HA compositions, and Marko discloses crosslinked hydrogels compositions containing 0.3% by weight lidocaine. *Id.* (citing Ex. 1023 47).

Summarizing, the Patent Owner argues that Petitioner relies upon the same or cumulative art used by the Examiner during prosecution, and makes the same arguments that were successfully overcome and that, consequently, factors *Becton-Dickinson* factors (a)–(d) support denial of *inter partes* review institution. Prelim. Resp. 39.

2. *Becton, Dickinson* factor (e)

The Patent Owner argues that Petitioner has failed to meet the burden of demonstrating how the Examiner allegedly erred in his review of the prior art during prosecution. Prelim. Resp. 41. The Patent Owner contends that Petitioner argues that the Examiner erred in his analysis because he "had an incomplete picture of the prior art." *Id.* (quoting Pet. 66). The Patent Owner repeats that the

Examiner either considered the references (i.e., Lebreton, Kinney, and Sadozai) or that P050047 is cumulative of Lebreton. *Id.* at 41–42.

The Patent Owner argues further that Petitioner's argument that inventor Lebreton's declaration was "unsubstantiated and erroneous" is unsupported by evidence, and that Dr. DeVore's criticism of the data is misplaced. Prelim. Resp. 42 (quoting Pet. 65). The Patent Owner contends that Petitioner's arguments, based on the DeVore Declaration, do not rebut the experiments cited in the Specification and in the Lebreton Declaration, or the Examiner's conclusion of unexpected results. *Id.*

With respect to the Cui reference[16] (Ex. 1025), the Patent Owner observes that Petitioner and Dr. DeVore criticize Cui, because Cui did not compare BDDE-crosslinked HA gels with FDA-approved crosslinking agents, and because Cui was not prior art. Prelim. Resp. 43 (citing Pet. 60–61). The Patent Owner argues, to the contrary, that Cui teaches such crosslinking agents. *Id.* (citing Ex. 1025 1506). The Patent Owner notes that Petitioner, and Petitioner's declarant, Dr. DeVore, fail to point to any evidence refuting Cui's disclosures that BDDE-crosslinked hyaluronic acid gels were known to be sensitive to heat sterilization relative to other crosslinked HA gels. *Id.* The Patent Owner argues further that whether Cui qualifies as prior art is irrelevant. *Id.* at 44. The Patent Owner asserts that post-filing information and data can be used to demonstrate unexpected results. *Id.* (citing *Knoll Pharm. Co. v. Teva Pharm. USA, Inc.*, 367 F.3d 1381, 1385 (Fed. Cir. 2004)).

[16] Y-j Cui et al., *The Comparison of Physicochemical Properties of Four Cross-linked Sodium Hyaluronate Gels with Different Cross-linking Agents*, 369–98 ADV. MATERIALS RES. 1506–512 (2012).

With respect to Petitioner's argument that Sadozai and Kinney both disclose lidocaine-containing crosslinked HA fillers that had viscosities similar to crosslinked HA fillers without lidocaine, the Patent Owner contends that this argument fails to address unexpected results in the context of the limitations set forth in the claims, e.g., the requirement of claims 2, 4, and 8 that lidocaine be freely released *in vivo*, and the storage stability recited in claims 6 and 7. *Id*. at 44.

3. *Becton, Dickinson* factor (f)

Finally, the Patent Owner contends that Petitioner fails to present any new evidence weighing in favor of institution. Prelim. Resp. 46. The Patent Owner repeats that the references relied upon by the Examiner were of record and/or cumulative of references relied upon by the Examiner, and that the DeVore Declaration is conclusory and fails to provide a well-reasoned rationale or objective support for the proposed grounds. *Id.* (citing Ex. 1002 ¶¶ 19, 140, 180).

Furthermore, the Patent Owner argues that Dr. DeVore's opinion that the claimed invention is obvious represents an over-simplified view of the invention, aided by the benefit of hindsight. Prelim. Resp. 47. According to the Patent Owner, Dr. DeVore discusses how it would have been obvious to modify individual features of the invention claimed in the '519 patent—for example, choice of crosslinker, HA concentration, gel hardness, particle size and distribution, free HA, pH, sterility, and viscosity. *Id.* at 47–48 (citing Ex. 1002 ¶¶ 82–100). Dr. DeVore states these "different factors […] could be routinely modified in order to obtain a crosslinked-HA filler having a desired spectrum of clinical characteristics." *Id.* at 48 (quoting Ex. 1002 ¶ 102). The Patent Owner contends that Dr. DeVore analyzes these factors in isolation, failing to address the interplay between these factors, and that persons of ordinary skill in the

contemporaneous art would have recognized that modifying one variable affects the impact of other aspects of the composition. *Id.* (citing Ex. 1014 1091–1092; Ex. 1022 78; Ex. 1005 124). The Patent Owner contends that Dr. DeVore offers no new evidence to rebut the Examiner's conclusion that the claimed inventions exhibited unexpected results. *Id.* at 49.

G. The Board's Decision with respect to the Patent Owner's argument with respect to 35 U.S.C. § 325(d)

We decline to accept the Patent Owner's invitation to exercise our discretion under Section 325(d) and not institute *inter partes* review.

1. *Becton, Dickinson* factors (c)

Despite the Patent Owner's assertions to the contrary, we find that the Patent Owner (the then-Applicant) did not overcome the combined teachings of Lebreton, Sadozai, P050047, and Kinney during prosecution. To the contrary, the then-Applicant persuaded the Examiner that, despite the Examiner's *prima facie* conclusion that the claims were obvious over the prior art, secondary considerations, *viz*., the allegedly unexpected results disclosed in the Lebreton Declaration, sufficed to persuade the Examiner that the proposed claims were patentable. *See* Ex. 1023 8.

Petitioner's declarant, Dr. DeVore, attacks the credibility of the Lebreton Declaration as failing, *inter alia*, to provide any evidentiary support for its characterization of what a person of ordinary skill in the art would have believed "shortly prior to August 4, 2008." Ex. 1002 ¶ 208. We find this assertion persuasive. The Lebreton Declaration cites no evidence of record in support of what a person of ordinary skill would have understood to be the state of the art at

the time of invention, other than the unsupported opinion of the inventor of the '884 application, Dr. Lebreton. Dr. DeVore disagrees with Dr. Lebreton, and provides evidentiary support for his contention that lidocaine could be added to a crosslinked HA composition and sterilized without degrading the composition. *See* Ex. 1002 ¶¶ 197–198. Specifically, Dr. DeVore declares that:

> As explained throughout much of this declaration, the prior art explicitly taught that lidocaine *had* been successfully combined with several other crosslinked-HA dermal fillers, leading to (at least) the products Prevelle Silk, Elevess, and Puragen Plus. The POSITA would have been aware of these products and would have also been aware of the references cited in "Grounds" of the Petition and this declaration, as well as other publications such as Toth and Hanke. Each of these references except for Hanke explicitly describe a crosslinked-HA dermal filler combined with lidocaine, and the POSITA would have understood Hanke's HA composition was crosslinked as well. Further a POSITA would have understood that each of the commercial products, as described in the various references cited, would have been sterilized and "sufficiently stable" (to use Lebreton's words from his declaration) in order to obtain FDA approval and be competitive in the marketplace.

Id. at ¶ 208.

Balancing the statements and evidence presented in the two Declarations, we find Dr. DeVore's to be better supported by evidence than the Lebreton Declaration and, consequently, more credible, and not a mere "difference of opinion," as argued by the Patent Owner. *See* Prelim. Resp. 34. We consequently conclude that, had the evidence in the DeVore Declaration been presented to the Examiner during prosecution of the '884 patent, there is a reasonable likelihood that the Examiner would have maintained the rejection of the claims of the '884 application, and that the '519 patent would not have issued.

We find, similarly, with respect to Grounds 4 and 5, that the DeVore Declaration's assessment of the state of the art, and the knowledge of a person of

ordinary skill in that art, are supported by evidence and, consequently, more persuasive than the unsupported opining of the Lebreton Declaration. We find particularly persuasive Dr. DeVore's conclusion that:

> Because BDDE and DEO are each bis-epoxide crosslinkers, the POSITA would have reasonably expected that Zhao process could be adapted to use BDDE instead of DEO. Both crosslinkers rely on the same chemistry—nucleophilic epoxide opening by the N-acetyl glucosamine primary alcohol, followed by nucleophilic epoxide opening by the glucoronic acid carboxylate. In both cases, epoxide opening results in the presence of a secondary alcohol in the crosslinking chain. Given the high degree of similarity between the two crosslinkers, the POSITA would reasonably expect that lidocaine would function analogously in both crosslinked gels.

Ex. 1002 ¶ 176.

For the same reason, we are not persuaded that the results of Example 4 are necessarily probative of unexpected results. "[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991).

Because we conclude that the statements of the DeVore Declaration, supported by evidence, concerning the state of the art at the time of invention, and the knowledge of a person of ordinary skill in the art, are more credible than the unsupported opinions of the Lebreton Declaration, we find that, had that evidence been before the Examiner, there is a reasonable likelihood that the Examiner would have sustained the *prima facie* conclusion of obviousness under Section 103, discounting what was then interpreted as evidence of unexpected results.

Moreover, as the DeVore Declaration points out, Sadozai directly refutes the Lebreton Declaration's averral that lidocaine would degrade a HA gel during high temperature sterilization. *See* Ex. 1002 ¶¶ 31–35, 39, 43, 49, 130–131, 144. We

accordingly determine that, because Sadozai was of record during examination of the '519 patent, the Examiner erred by failing to appreciate the relevance of the teachings of Sadozai during evaluation of the Lebreton Declaration.

We acknowledge that Lebreton, Sadozai, and Kinney were cited in an IDS, and thus, are the same art previously presented to the Office. Because the "same or substantially the same prior art or arguments previously were presented to the Office" in this case, we next turn to the question of whether Petitioner has sufficiently demonstrated that the Office materially erred in evaluating the art or the arguments, as informed by considering *Becton, Dickinson* factors (e) and (f). *See Advanced Bionics*, IPR2019-01469, Paper 6 at 8, 10; *Becton, Dickinson*, Paper 8 at 24 (considering whether the petitioner has pointed out sufficiently how the examiner erred in its evaluation of the asserted prior art).

2. *Becton, Dickinson* factor (e)

Similarly, we find that Petitioner has pointed out sufficiently how the Examiner erred in evaluating the asserted prior art. *See Advanced Bionics*, IPR2019-01469, Paper 6 at 10–11. Again, we emphasize that the Patent Owner did not overcome the Examiner's conclusion that the claims were obvious over the prior art, but relied, rather, on the Lebreton Declaration as establishing that the claimed composition possessed properties that were unexpected or surprising over the closest prior art. These findings were dependent upon the Lebreton Declaration's unsupported statements concerning the state of the art and the level of knowledge of a person of ordinary skill in the art.

Nor, and for the reasons we have explained *supra*, do we find persuasive the Lebreton Declaration's opinion that the properties exhibited by the claimed composition were unexpected in view of the closest prior art. We find persuasive

Petitioner's argument, supported by evidence adduced in the DeVore Declaration, that:

> [A skilled artisan] would have been aware of commercial lidocaine-containing crosslinked HA dermal fillers such as Elevess, Prevelle Silk and Puragen Plus, as well as the disclosure of the prior art documents cited [in the Petition], including Sadozai and Kinney. Each of these products and references explicitly state, or at minimum suggest, that crosslinked HA lidocaine-containing fillers were sterilizable, and were sufficiently stable to be approved by FDA as a dermal filler.

Pet. 54–55 (citing Ex. 1002 ¶¶ 208–209).

3. *Becton, Dickinson* factor (f)

Factor (f) of *Becton, Dickinson* requires us to inquire whether as to the extent to which additional evidence and facts presented in the Petition warrant reconsideration of prior art or arguments. *Becton, Dickinson*, IPR2017-01586, Paper 8 at 18. Once again, we turn to whether the evidence presented in the DeVore Declaration is sufficient to persuasively challenge that presented in the Lebreton Declaration during examination. The Patent Owner argues that the DeVore Declaration is "conclusory" and fails to provide a well-reasoned rationale or objective support for the proposed grounds. Prelim. Resp. 46. We do not agree.

The Lebreton Declaration asserts that:

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

> 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 a 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.

Ex. 1024 ¶¶ 5–10. Each of these statements represents the opinion of Dr. Lebreton, but we note that they are not supported by any evidence of record in the Declaration.

Also before the Examiner at that time was Cui, which the Patent Owner argues demonstrates that HA crosslinked with BDDE was "known to be especially sensitive to heat sterilization relative to HA gels crosslinked with other, i.e. non-BDDE crosslinkers," so that the discovery of the claimed sterile compositions was, allegedly, unexpected and surprising, given the supposedly unstable nature of HA-based gels crosslinked with BDDE even without the addition of lidocaine. *See* Ex. 1023 28.

In his Declaration, Dr. DeVore notes that: "The statements in the declaration were not limited to fillers containing both BDDE-crosslinked HA and free HA. Moreover, I understand that when the declaration was submitted, the pending claims were not limited to BDDE-crosslinked HA." Ex. 1002 ¶ 206 (citing Ex. 1023 18–20, claims 51–67). Petitioner asserts Dr. DeVore attests that:

> [A] skilled artisan would have been aware of commercial, lidocaine-containing, crosslinked HA dermal fillers such as Elevess, Prevelle Silk and Puragen Plus, as well as the teachings of the prior art documents cited in the Petition, including Sadozai and Kinney. *Id.* at 52–53. *Each of these products and references expressly teach, or suggest, that crosslinked HA lidocaine-containing fillers were sterilizable, and were sufficiently stable to be approved by FDA as a dermal filler*.

Pet. 54–55 (citing Ex. 1002 ¶ 208–209). Similarly, the Dr. Lebreton points to the experiments presented in the Specification of the '884 application, stating that:

> The experiments showed that certain HA gels, when mixed with lidocaine, degraded and became substantially less viscous after high temperature sterilization, specifically autoclave sterilization, as would have been expected by one of ordinary skill in the art. [referring to samples 1, 2, 3, Figs. 1–3].
>
> I discovered that other HA gels, when mixed with lidocaine, maintained their viscosity and elasticity, even after such high temperature sterilization [referring to samples 4, 5, 6, Figs. 4, 5, 7].

Ex.1024 ¶¶ 13–14.

> Responding to these statements, Dr. DeVore states:
>
> In 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 HMPC being used as a dermal filler, either in 2008 or now.
>
> Moreover, 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.
> ….
> Allergan argued the viscosity differences, measured at 0.1 Hz, indicated that Samples 1-3 were not stable to autoclave sterilization. EX1023, 26-27. In my opinion, the data does not support that conclusion. The 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). EX1039, 267.

Ex. 1002 ¶¶ 216–218.

In short, Dr. DeVore points to prior art that is evidence of record to rebut the unsupported statements of the Lebreton Declaration concerning the state of the prior art, as well as a skilled artisan's knowledge of that art. Dr. DeVore also provides evidence-based arguments that undermine the probative value of the tests in Example 4 as indicative of unexpected or surprising results.

Contrary to the Patent Owner's arguments, we do not find these statements to be "conclusory" or lacking in objective support. The Patent Owner may attempt to rebut the statements of the DeVore Declaration at trial, but, in our view, the DeVore Declaration adduces evidence of record and presents arguments that presumptively rebut the Lebreton Declaration and, consequently, warrant denial of the Patent Owner's request that we deny institution.

In sum, having weighed the relevant *Becton Dickinson* factors, we find 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. *Advanced Bionics*, IPR2019-01469, Paper 6 at 8–9. Consequently, we decline to exercise our discretion under 35 U.S.C. § 325(d) to deny institution of the Petition.

V. CONCLUSION

For the reasons we have explained, we conclude that Petitioner has made a sufficiently persuasive showing that the cited references would have taught or suggested the elements of claims 1–8, 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 therefore established a reasonable likelihood of prevailing in demonstrating that claims 1–8 would have been obvious over the combinations of prior art set forth in the asserted grounds.

VI. ORDER

In consideration of the foregoing, it is hereby:

ORDERED, pursuant to 35 U.S.C. § 314(a), that an *inter partes* review of claims 1–8 of the '519 patent is INSTITUTED with respect to all Grounds 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 '519 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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