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Paper No. 74
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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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LUYE PHARMA GROUP LTD., LUYE PHARMA(USA) LTD., SHANDONG LUYE PHARMACEUTICAL CO., LTD., and NANJING LUYE PHARMACEUTICAL CO., LTD.,
Petitioner,

v.

ALKERMES PHARMA IRELAND LTD. and ALKERMES CONTROLLED THERAPEUTICS, INC.,
Patent Owner.

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Case IPR2016-01096
Patent 6,667,061 B2

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Before LORA M. GREEN, ROBERT A. POLLOCK, and JACQUELINE T. HARLOW, *Administrative Patent Judge*.

GREEN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
Determining That Claims 1–13 and 17–23 Have Not Been Shown to Be Unpatentable
*35 U.S.C. § 318(a) and 37 C.F.R. § 42.73*

# I. INTRODUCTION

Luye Pharma Group Ltd., Luye Pharma (USA) Ltd., Shandong Luye Pharmaceutical Co., Ltd., and Nanjing Luye Pharmaceutical Co., Ltd. (collectively "Petitioner") filed a Petition requesting an *inter partes* review of claims 1–13 and 17–23 of U.S. Patent No. 6,667,061 B2 (Ex. 1001, "the '061 patent"). Paper 5 ("Pet."). Alkermes Pharma Ireland Limited and Alkermes Controlled Therapeutics, Inc. (collectively, "Patent Owner") filed a Preliminary Response to the Petition. Paper 11 ("Prelim. Resp."). We determined that the information presented in the Petition and the Preliminary Response demonstrated that there was a reasonable likelihood that Petitioner would prevail in challenging claims 1–13 and 17–23 as unpatentable under 35 U.S.C. § 103(a). Pursuant to 35 U.S.C. § 314, we instituted trial on November 30, 2016, as to those claims of the '061 patent. Paper 13 ("Institution Decision" or "Dec. Inst.").

Patent Owner filed a Response (Paper 33, "PO Resp."), to which Petitioner filed a Reply (Paper 40). Patent Owner filed Observations on the Cross-Examination of Patrick DeLuca (Paper 50), to which Petitioner filed a Response (Paper 59). Patent Owner was authorized to file a paper identifying what it considered to be new and improper arguments in Petitioner's Reply (Paper 44), to which Petitioner was allowed a response (Paper 46). Patent Owner filed a Motion to Exclude (Paper 51), to which Petitioner filed an Opposition (Paper 57), and Patent Owner filed a Reply (Paper 62). Petitioner also filed a Motion to Exclude (Paper 47), to which Patent Owner filed an Opposition (Paper 56), and Petitioner filed a Reply (Paper 61). With authorization from the Board, Petitioner filed a second Motion to Exclude (Paper 70), to which Patent Owner filed an Opposition

(Paper 71), and Petitioner filed a Reply (Paper 72). Oral hearing was held on August 28, 2017, and a transcript of that hearing has been entered into the record. Paper 73 ("Tr.").

We have jurisdiction under 35 U.S.C. § 6. Petitioner bears the burden of proving unpatentability of the challenged claims, and the burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, Petitioner must establish facts supporting its challenge by a preponderance of the evidence. *See* 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

Based on the record before us, we conclude that Petitioner has failed to demonstrate by a preponderance of the evidence that claims 1–13 and 17–23 of the '061 patent are unpatentable. Moreover, we *dismiss* Patent Owner's Motion to Exclude as improper. We also deny Petitioner's Motions to Exclude in part, and dismiss in part.

### *A. Related Proceedings*

Petitioner filed a second request for *inter partes* review seeking cancellation of claims 1–13 and 17–23 of the '061 patent on other grounds. Pet. 1; Prelim. Resp. 1 n.1. That petition for *inter partes* review, IPR2016-01095, was *denied*. IPR2016-01095, Paper 13.

### *B. The '061 Patent*

The '061 patent issued on December 23, 2003, with J. Michael Ramstack, M. Gary I. Riley, Stephen E. Zale, Joyce M. Hotz, and Olufunmi L. Johnson as the listed co-inventors. Ex. 1001. According to the '061 patent, it is drawn "to injectable suspensions having improved injectability." *Id.* at 1:13–14.

The ’061 patent discloses:

> Injectable suspensions are heterogeneous systems that typically consist of a solid phase dispersed in a liquid phase, the liquid phase being aqueous or nonaqueous. To be effective and pharmaceutically acceptable, injectable suspensions should preferably be: sterile; stable; resuspendable; syringeable; injectable; isotonic; and nonirritating. The foregoing characteristics result in manufacturing, storage, and usage requirements that make injectable suspensions one of the most difficult dosage forms to develop.

*Id.* at 1:17–25.

The ’061 patent teaches that viscosity enhancers are added to injection vehicles to prevent settling of particles, but notes that viscosity is kept low to facilitate mixing and make the suspension easier to inject. *Id.* at 2:25–30. According to the ’061 patent, it was “unexpectedly discovered that injectability is improved, and in vivo injectability failures significantly and unexpectedly reduced, by increasing the viscosity of the fluid phase of an injectable suspension.” *Id.* at 4:57–60. The ’061 patent teaches that “is in contrast to conventional teachings that an increase in the viscosity hinders injectability and syringeability.” *Id.* at 4:60–62. The ’061 patent specifically teaches that carboxymethyl cellulose (“CMC”) is a viscosity enhancing agent. *Id.* at 12:14–20.

The ’061 patent specifically teaches the following injection vehicles: Vehicle A: 0.9% saline and 0.1% Tween 20; Vehicle B: 1.5% CMC, 30% sorbitol, and 0.2% Tween 20; and Vehicle C: 3% CMC, 0.1% Tween 20, and 0.9% saline. *Id.* at 9:38–46. According to the ’061 patent, Vehicle A had a viscosity of 1.0 cp, Vehicle B had a viscosity of 24 cp, and Vehicle C had a viscosity of 56 cp. *Id.* at 10:Table 4.

### *C. Illustrative Claim*

Petitioner challenges claims 1–13 and 17–23 of the '061 patent.

Claim 1, the only independent claim of the '061 patent, is representative:

> 1. A composition suitable for injection through a needle into a host, comprising:
>
> microparticles comprising a polymeric binder; and
>
> an injection vehicle, wherein said microparticles are suspended in said injection vehicle at a concentration of greater than about 30 mg/ml to form a suspension, *wherein a fluid phase of said suspension has a viscosity greater than about 20 cp and less than about 600 cp at 20º C.*, wherein the viscosity of said fluid phase of said suspension provides injectability of the composition through a needle ranging in diameter from 18–22 gauge.

Ex. 1001, 18:6–17 (emphasis added).

### *D. Instituted Challenges*

We instituted trial on the following grounds (Pet. 33):

| **References** | **Basis** | **Claims Challenged** |
|---|---|---|
| Johnson[1] and Kino[2] | § 103 | 1–13, 22, and 23 |
| Gustafsson,[3] Ramstack,[4] and the Handbook[5] | § 103 | 1–3, 6–9, 12, 13, and 17–23 |

[1] Johnson et al., U.S. Patent No. 5,654,010, issued August 5, 1997 (Ex. 1009) ("Johnson").

[2] Kino et al., U.S. Patent No. 5,656,299, issued August 12, 1997 (Ex. 1010) ("Kino").

[3] Gustafsson et al., WO 97/14408, published April 24, 1997 (Ex. 1011) ("Gustafsson").

[4] Ramstack et al., WO 95/13799, published May 26, 1995 (Ex. 1005) ("Ramstack").

[5] HANDBOOK OF PHARMACEUTICAL EXCIPIENTS, 78–81, 135–138, 294–298, 329–330, 375–378, 420–421, 439–442, 477–482 (Ainley Wade and Paul J

Petitioner relies on the Declaration of Patrick P. Deluca, Ph.D. (Ex. 1002), as well as his Supplemental Declaration (Ex. 1024).

Patent Owner relies on the Declarations of Cory J. Berkland, Ph.D., (Ex. 2014), Robson F. Storey, Ph.D. (Ex. 2054), and Stevin Gehrke, Ph.D. (Ex. 2059).

## II. ANALYSIS

Petitioner bears the burden of proving unpatentability of the challenged claims, and that burden of persuasion never shifts to Patent Owner. *Dynamic Drinkware*, 800 F.3d at 1378. To prevail, Petitioner must establish the facts supporting its challenge by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). Below, we explain why Petitioner has failed to meet its burden with respect to the challenged claims.

### *A. Claim Construction*

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. *See* 37 C.F.R. § 42.100(b); *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–45 (2016) (upholding the use of the broadest reasonable interpretation standard). Under that standard, we presume that a claim term carries its "ordinary and customary meaning," which "is the meaning that the term would have to a person of ordinary skill in the art in question" at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). *See also Trivascular, Inc. v. Samuels*, 812 F.3d 1056, 1062 (Fed. Cir. 2016) ("Under a broadest reasonable interpretation, words of the claim must be given their

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Weller, ed., Am. Pharm. Ass'n & Pharm. Press 2nd ed. 1994) (Ex. 1008) ("the Handbook").

plain meaning, unless such meaning is inconsistent with the specification and prosecution history."). Any special definition for a claim term must be set forth in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

In the Institution Decision, we determined that none of the terms in the challenged claims require express construction at that time. Dec. Inst. 6 (citing *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) (noting that only claim terms which are in controversy need to be construed, and then only to the extent necessary to resolve the controversy)); *see also Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co. Ltd.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017). Petitioner offers explicit constructions of several claim terms (Pet. 19–22), as did Patent Owner in its Preliminary Response (Prelim. Resp. 9–12). In its full Response, Patent Owner states that there is no need to expressly construe any of the claim terms. PO Resp. 13–14. On the present record, we agree with Patent Owner and determine that none of the claim terms require explicit construction for purposes of this Decision.

*B. Level of Ordinary Skill in the Art*

Petitioner contends that at the time of invention, the ordinary artisan would have had "at least a bachelor's degree and/or a number of years of industry training or experience in one or more the following fields: pharmaceutical formulation, chemistry, pharmaceutical science, polymer chemistry, pharmaceutics, pharmaceutical technology, pharmacokinetics, and/or pharmacology." Pet. 19 (citing Ex. 1002 ¶¶ 8–13).

Patent Owner responds that the ordinary artisan "would have a bachelor's degree in one of the following fields: pharmaceutical formulation,

chemistry, polymer science, or a related field, and one or two years of industry training or experience in those field(s)." PO Resp. 8 (citing Ex. 2014 ¶ 21; Ex. 2054 ¶ 27).

We conclude that, for practical purposes, there is little difference between Petitioner's and Patent Owner's definitions of the ordinary artisan. Thus, our analysis would be the same under either Petitioner's or Patent Owner's definition. In addition, the level of ordinary skill in the art in this case is reflected by the prior art of record. *See Okajima v. Bourdeau,* 261 F.3d 1350, 1355 (Fed. Cir. 2001).

### *C. Obviousness over Johnson and Kino*

Petitioner contends that claims 1–13, 22, and 23 are rendered obvious by the combination of Johnson and Kino. Pet. 23–38. Petitioner presents a claim chart demonstrating where the limitations of the challenged claims may be found in the relied upon references. *Id.* at 32–38. Patent Owner disagrees with Petitioner's contentions, asserting that the Petition fails to demonstrate the obviousness of the challenged claims by a preponderance of the evidence. PO Resp. 14–34.

#### *i. Overview of the Prior Art Relied Upon*

We find the following as to the teachings of the relevant prior art.

##### *a. Overview of Johnson (Ex. 1009)*

Johnson "relates to a composition, and methods of forming and using said composition, for the sustained release of biologically active, stabilized human growth hormone (hGH)." Ex. 1009, 1:42–45. The method of forming the composition includes the steps of "dissolving a biocompatible polymer in a polymer solvent to form a polymer solution, dispersing particles of biologically active, stabilized hGH in the polymer solution, and

then solidifying the polymer to form a polymeric matrix containing a dispersion of said hGH particles." *Id.* at 1:52–57.

Example 7 of Johnson evaluated "the pharmacokinetic profiles of different hGH sustained release formulations as compared to more traditional methods of administering hGH." *Id.* at 12:19–24. Monkeys were administered a dose of 160 mg of hGH sustained release microspheres in 1.2 ml of injection vehicle using a 20 gauge needle. *Id.* at 12:37–42. Johnson teaches that the "injection vehicle was an aqueous vehicle containing 3% w/v Carboxymethyl Cellulose (sodium salt), 1% v/v Tween 20 (Polysorbate 20) and 0.9% sodium chloride." *Id.* at 12:42–45.

*b. Overview of Kino (Ex. 1010)*

Kino teaches:

> With the aim of improvement in compliance at the time of maintenance therapy with hydrophobic antipsychotic drugs, the present inventors have conducted intensive studies on the development of a sustained release pharmaceutical preparation in which a drug itself is used as an active ingredient without modification. As the result, it was found that a drug can be released at an almost constant rate extending over 1 week or more by including a hydrophobic antipsychotic drug in the form of microcrystals having an average particle size of 10 μm or less, desirably 5 μm or less, into a base comprising a biodegradable high molecular weight polymer having in vivo histocompatibility to make a sustained release microsphere preparation and administrating it by subcutaneous or intramuscular injection.

Ex. 1010, 1:66–2:12.

Kino teaches that the microspheres may be made into a sustained release injection by preparing an aqueous suspension along with a dispersing agent, such as polysorbate 80 or CMC, a preservative, and an isotonic agent, such as sodium chloride or sorbitol. *Id.* at 4:38–44. Kino teaches also that

when used as a suspension for injection, the particle size of the microparticles "may be a range which can satisfy their dispersibility and needle-passing property, for example, in the range of from about 0.5 to about 400 μm, more preferably from about 0.5 to about 200 μm, most preferably from about 15 to 50 μm as an average particle size." *Id.* at 4:32–37.

*ii. Analysis*

A claim is unpatentable under 35 U.S.C. § 103(a) if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness, i.e., secondary considerations. *Id.* (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966)).

In addition, the Court of Appeals for the Federal Circuit has acknowledged that "inherency may supply a missing limitation in an obviousness analysis." *PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1194–95 (Fed. Cir. 2014). The Federal Circuit has cautioned, however, that the use of inherency in an obviousness analysis must be carefully circumscribed. *Id.* at 1195. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference.'" *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (quoting *Continental Can Co. v. Monsanto Co.*,

948 F.2d 1264, 1268 (Fed. Cir. 1991)). Inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981). For example, where the practice of a prior art example sometimes, but not always, yields the claimed product, anticipation is not established. *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047–48 (Fed. Cir. 1995).

Petitioner relies on Johnson for teaching "microspheres suspended in an aqueous injection vehicle." Pet. 24 (citing Ex. 1009, 10:64–66; Ex. 1002 ¶¶ 54, 59). Petitioner contends that "Johnson teaches a solution of 3% w/v carboxymethyl cellulose (low viscosity), polysorbate 20, and sodium chloride used as the injection vehicle; the same components as used in Vehicle C of the '061 Patent." *Id.* (citing Ex. 1009, 12:39–42; Ex. 1002 ¶¶ 55, 59). Petitioner asserts further that Johnson teaches that a concentration of microparticles of 133 mg/ml, which, Petitioner argues, is greater than the concentration of a minimum of 30 mg/ml required by the challenged claims. *Id.* at 24–25 (citing Ex. 1009, 12:39–42; Ex. 1002 ¶¶ 54, 59). In addition, Petitioner notes that the "formulation is suitable for injection into a patient via a 20 gauge needle, which is within the claimed range of 18–22 gauge." *Id.* at 25 (citing Ex. 1009, 12:39-42; Ex. 1002 ¶¶ 54, 59).

Petitioner acknowledges that "Johnson is silent as to the viscosity of the . . . formulation." *Id.* Petitioner contends, however, that the ordinary artisan would understand that CMC is a viscosity enhancing agent, and that it "would be considered the viscosity-controlling component of an injection vehicle." *Id.* (citing Ex. 1008, 78; Ex. 1002 ¶ 61).

Petitioner notes further that during prosecution, the applicants relied on the Declaration of Dr. Mark A. Tracy (Ex. 1018), in which Dr. Tracy "offered the conclusion that Kino taught a viscosity less than 7 cp based solely on the amount of CMC present in the Kino examples." Pet. 25. Thus, Petitioner asserts, the ordinary artisan "would appreciate that the injection vehicle disclosed in Johnson would have substantially the same viscosity of the preferred embodiment of the '061 Patent and as a result fall within the scope of claim 1." *Id.* (citing Ex. 1002 ¶¶ 60, 61).

According to Petitioner:

> Based on the Patent Owner's admission during prosecution of the '061 Patent, the Tracy Declaration, and what would be known to [the ordinary artisan], [the ordinary artisan] would reasonably expect the injection vehicle of Johnson — having 3% CMC — to have a viscosity greater than 27cp at 20°C and certainly within the claimed range of 20-600cp at 20°C. Johnson therefore teaches every limitation of claims 1-3. (Ex. 1002 ¶ 60, 61).

*Id.* at 25–26; *see also id.* at 33 (claim chart) (citing Ex. 1002 ¶¶ 27, 54, 59, 61).

Petitioner is, therefore, relying on the doctrine of inherency in contending that the injection vehicle of Johnson inherently has the viscosity required by the challenged claims. *See* Tr. 11[6] (Petitioner's counsel noting that they are relying inherency to meet the viscosity limitation); *see also* PO

[6] Petitioner also argued during the oral hearing that it would have been obvious to one of ordinary skill in the art to optimize viscosity. Tr. 16–17. Petitioner pointed to pages 7–9 of its Petition to support that assertion. Tr. 23. Those pages, however, as noted during the argument (Tr. 23–24), were in the Background section of the Petition discussing improving injectability, and did not explain how the combination of Johnson and Kino rendered the claimed viscosity obvious.

Resp. 2 ("Petitioners argue that the injection vehicle formulations disclosed in the primary references of both grounds, Johnson and Gustafsson, would ***inherently*** have viscosities between 20 cp and 600 cp at 20ºC as claimed in the '061 patent.").

Patent Owner responds that Petitioner has not met the high burden of establishing inherency, and, in particular, has "failed to establish that the type or grade of CMC used in the Johnson or Gustafsson vehicles would ***necessarily*** have achieved the claims viscosity." PO Resp. 2; *id.* at 14 ("Johnson does not expressly or inherently meet the viscosity limitations of the claims.").

Patent Owner argues that, as acknowledged by both the Petition (Pet. 25) and the Decision on Institution (Dec. Inst. 9–10), Johnson does not specify the viscosity of its injection vehicle. PO Resp. 16. Moreover, Patent Owner asserts, Johnson "provides insufficient information to ascertain the viscosity of its injection vehicle or to conclude that it is ***necessarily*** the same as that of a preferred embodiment of the '061 patent." *Id.* (citing Ex. 2014 ¶¶ 81, 87.)

In particular, Patent Owner notes that "Petitioners rely on Johnson's disclosure of an injection vehicle comprised of 3% CMC, 1% polysorbate 20, and 0.9% sodium chloride." *Id.* at 18 (citing Pet. 24). Patent Owner states that it "asked Dr. Stevin Gehrke to make the Johnson vehicle using commercially available CMCs." *Id.* (citing Ex. 2059 ¶¶ 5-12; Ex. 2014 ¶¶ 47-50). According to Patent Owner, "Dr. Gehrke recorded the viscosity at 20ºC as 6.03 cp when the vehicle was made with Ashland 7ULC CMC and 9.41 cp when the vehicle was made with Ashland 7ELC1 CMC,

which both fall below the claimed range." *Id*. (citing Ex. 2059 ¶¶ 7, 12; Ex. 2014 ¶¶ 47-50).

Patent Owner asserts that Petitioner did not offer any testing data of its own, but rather, asserts based on the Tracy Declaration that CMC is the viscosity controlling component, and, thus, the ordinary artisan could predict the viscosity based only on the amount of CMC in the formulation. *Id.* at 18–19 (citing Pet. 25; Ex. 2016, 252:18–253:7; Ex. 2014 ¶¶ 76–86).

Patent Owner argues further that Petitioner has not demonstrated that "Johnson disclosed a specific type and grade of CMC that would ***necessarily*** cause the viscosity of its vehicle to fall within the claimed range at 20ºC," or that "all available grades and types of CMC would ***necessarily*** cause Johnson's vehicle to fall within the claimed viscosity range." PO Resp. 20–21. Patent Owner notes in particular that Johnson does not specify the type or grade of CMC that it used. *Id.* at 21 (citing Ex. 2014 ¶¶ 51–56; Ex. 2016, 227:9–11, 230:14–231:21). The claimed injection vehicle, Patent Owner asserts, requires a particular viscosity, that is, a viscosity greater than about 20 cp and less than about 600 cp at 20º C. *Id*. Petitioner has not shown, Patent Owner asserts, "that the Johnson vehicle is inevitably such a vehicle." *Id.* at 22 (citing Ex. 2014 ¶¶ 81, 87).

Patent Owner argues additionally that even if the CMC of Johnson is considered to be the viscosity controlling component, the absence of any disclosure in Johnson as to the grade and type of CMC used in its injection vehicle "makes it impossible to establish that the viscosity is ***necessarily*** in the claimed range." *Id.* (citing Ex. 2014 ¶¶ 51–61; Ex. 2016, 147:10–16, 176:2–24). There were a wide variety of grades and types of CMC that were available at the time of invention, which, Patent Owner argues, "could yield

a wide-range of possible viscosities for CMC solutions, even at a fixed concentration." *Id.* (citing Ex. 1008, 79; Ex. 2034, 15; Ex. 2014 ¶¶ 37–41, 51–61; Ex. 2016, 183:1–6).

According to Patent Owner, Petitioner's own reference, the Handbook, supports that many viscosities are possible, as its states that "aqueous 1% w/v solutions [of CMC] with ***viscosities of 5-4000 mPas (5-4000 cP)*** may be obtained." PO Resp. 22 (quoting Ex. 1008, 79). Patent Owner also cites the 1999 Aqualon brochure (Ex. 2034) as well as Dow Chemical (Ex. 2036) as demonstrating that a range of viscosities for solutions containing the products are possible. *Id.* at 23 (citing Ex. 2034, 6, 15; Ex. 2036; Ex. 2014 ¶¶ 41, 53–55). In addition, Patent Owner argues, as supported by the 1999 Aqualon brochure, if medium or high grade CMC were used in the injection vehicle of Johnson, viscosities higher than those claimed could result. *Id.* at 23–24 (citing Ex. 1008, 79, Table 1; Ex. 2014 ¶¶ 60–61; Ex. 2034, 15; Ex. 2014 ¶¶ 60–61; Ex. 2016, 230:14–231:21).

As to the Tracy Declaration, Patent Owner notes that it was originally submitted with Application No. 09/577,875 ("the '875 Application"), "Dr. Tracy explained that 'CMC is the viscosity-controlling component ***of the injection vehicle of Test Example 2***'" of Kino, as it used a 0.5% CMC solution isotonized with mannitol. PO Resp. 11 (citing Ex. 1018 ¶ 5). Table 1 of the Tracy Declaration, which Patent Owner states "summarizes the information Dr. Tracy relied upon in reaching his conclusions regarding Kino test Example 2," is reproduced below:

**Table 1: Vehicles of the '875 Application and Kino Test Example 2**

| '875 Application (Formula 1) | '875 Application (Formula 2) | Kino Test Example 2 |
|---|---|---|
| 1.5% by volume CMC, 30% by volume sorbitol, 0.2% by volume Tween 20 | 0.75% by volume CMC, 15% by volume sorbitol, 0.2% by volume Tween 20 | 0.5% CMC isotonized with mannitol |
| Viscosity: 27 cp at 20°C | Viscosity: 7 cp at 20°C | No viscosity disclosed. |
| (Exh. 2053 at 12:10-14.) | (Exh. 2053 at 12:14-17.) | (Exh. 1010 at 6:29-31.) |

*Id.* at 11–12.

According to Patent Owner, "[b]ecause Kino did not disclose the viscosity of its Test Example 2, in order to make a comparison between Kino Test Example 2 and the '875 application, Dr. Tracy had to assume that the Kino CMC was the same as that used in the '875 application." *Id.* at 12 (citing Ex. 2014 ¶¶ 83-85; Ex. 2016, 176:2-24). Patent Owner asserts "[t]hat assumption and conclusion were also consistent with Kino's use of physiological saline alone in three of the four exemplified vehicles, all of which had a viscosity of 1 cp—far below the claimed viscosity range." *Id.* at 12–13 (citing Ex. 1010, 6:19, 6:43–44, 7:8–9; Ex. 2014 ¶¶ 78–85).

Patent Owner contends that the Tracy Declaration does not support that CMC is the viscosity controlling components of Johnson's injection vehicle, as the declaration does not relate to Johnson. *Id.* at 20 (citing Ex. 2014 ¶¶ 77–81). Patent argues further that "the grade and type of CMC in Johnson's vehicle and how the vehicle is prepared are . . . highly relevant to the viscosity of the injection vehicle." *Id.* That is, Patent Owner argues, although "the grade and type of CMC and preparation of the vehicles ***may*** be the same in Johnson as in the '875 application, Johnson provides no such

information and Petitioners do not and cannot establish that this is ***necessarily*** the case." *Id*.

Challenged independent claim 1 requires that the "fluid phase of said suspension has a viscosity greater than about 20 cp and less than about 600 cp at 20º C." As noted in the Decision on Institution and discussed above, Johnson does not specifically teach that viscosity limitation. Dec. Inst. 10. Petitioner relies on Johnson's teaching an injection vehicle comprising 3% w/v CMC, 1 % polysorbate 20, and 0.9% sodium chloride. Pet. 24. As we noted further in the Decision on Institution, the '061 patent teaches Vehicle C, which comprises 3% CMC, 0.1% Tween 20 (i.e., polysorbate 20), and 0.9% saline, and has a viscosity of 56 cp. Dec. Inst. 11 (citing Ex. 1001, 9:45; 10:Table 4). In the Decision on Institution, we determined that the evidence of record at that time sufficiently established a reasonable likelihood that as the injection vehicle of Johnson and Vehicle C are substantially the same, except for the concentration of polysorbate 20, the injection vehicles would be expected to have similar, if not the same viscosities, especially as the '061 patent teaches that CMC is a viscosity enhancing agent. *Id*. Based on the argument and evidence developed during trial, however, we determine that Petitioner has not demonstrated by a preponderance of the evidence that the Johnson vehicle inherently has the viscosity required by the challenged claims.

In that regard, we note that Petitioner must "meet a high standard in order to rely on inherency to establish the existence of a claim limitation in the prior art in an obviousness analysis—the limitation at issue necessarily must be present, or the natural result of the combination of elements

explicitly disclosed by the prior art." *PAR Pharm., Inc.*, 773 F.3d at 1195–96.

As noted by Dr. Berkland, Dr. Gehrke[7] made the vehicle of Johnson using "two different types of low viscosity CMC: 7ULC and 7ELCI from Ashland." Ex. 2014 ¶ 48; Ex. 2059 ¶¶ 6–7. According to Dr. Berkland:

> each of these Ashland CMCs yielded a Johnson vehicle with a viscosity below 20 cp when measured at 20ºC and thus fall outside the range claimed in the '061 patent. ([Ex. 2059] ¶ 12.)

**TABLE A – JOHNSON VEHICLES (EXH. 2059, GEHRKE DECL.)**

| Formulation | Viscosity (cp) at 20°C | RPM |
|---|---|---|
| 3% Ashland 7ULC CMC, 0.9% NaCl, 1% polysorbate 20 | 6.03 cp | 200 |
| 3% Ashland 7ELC1 CMC, 0.9% NaCl,1% polysorbate 20 | 9.41 cp | 200 |

Ex. 2014 ¶ 50.

The testing performed by Dr. Gehrke is the only data provided during the proceeding of testing of the vehicle of Johnson, and demonstrates that viscosities lower than those required by the claim were obtained. The data provided by Dr. Gehrke, therefore, is evidence that the injection vehicle of Johnson would not necessarily have the viscosity required by the challenged claims.

Moreover, the Handbook (Ex. 1008), supports the finding that a solution having the same percentage of CMC may not necessarily all have the same viscosity. Specifically, the Handbook teaches:

> *Viscosity:* various grades of carboxymethylcellulose sodium are commercially available which have differing aqueous

[7] We note that Petitioner elected not to take the deposition of Dr. Gehrke. Tr. 63.

> viscosities; aqueous 1% w/v solutions with viscosities of 5-4000 mPa s (5-4000 cP) may be obtained. An increase in concentration results in an increase in aqueous solution viscosity. Viscosities of various grades of carboxymethylcellulose sodium are shown in Table I. . . .
>
> **Table I: Viscosity of aqueous carboxymethylcellulose sodium solutions at 25°C.**
>
| Grade | Concentration (% w/v) | Viscosity (mPa s) |
|---|---|---|
| Low viscosity | 4 | 50-200 |
| Medium viscosity | 2 | 400-800 |
| High viscosity | 1 | 1500-3000 |

Ex. 1008, 79 (footnote omitted). Thus, the Handbook is further evidence that the percentage of CMC used is not determinative of the viscosity of the solution, but that a solution with various viscosities may be obtained. Petitioner has not presented any evidence demonstrating that even if these difference in viscosities were taken into account, the solution of Johnson would *necessarily* have the viscosity required by the challenged claims. *See* Tr. 14 (Petitioner's counsel acknowledging that it has not performed any testing).

That finding is also supported by the testimony of Petitioner's expert, Dr. DeLuca. Dr. DeLuca testifies:

> Q. Okay. Is it because the CMC that comes from two different suppliers can have different characteristics?
>
> A. They could, yes.
>
> Q. They could have different viscosity ranges?
>
> A. They could vary in viscosity range, yeah.
>
> Q. So it was important to you to consider different suppliers of CMC in coming up with your opinion today because the characteristics of the CMC can vary from supplier to supplier, right?
>
> A. Yes.

Ex. 2081, 102:22–103:13; *see also* Paper 50, 5 (pointing out Dr. DeLuca's testimony in this regard). Again, as the viscosity can change depending not just on its grade, but also on the supplier, the preponderance of the evidence does not support Petitioner's contention that the injection vehicle of Johnson would necessarily have the claimed viscosity.

We have considered Petitioner's arguments and evidence made in its Reply, but the Reply does not persuade us otherwise.

Petitioner, in its Reply, responds that injection vehicles having a viscosity over 20 cp were known. Reply 3–4 (citing Ex. 1024 ¶¶ 11–12; Ex. 1028, 6:37–7:3). Petitioner, however, did not rely on that assertion that the viscosities required by the claims were known in challenging the claims of the '061 patent. Petitioner relied on Johnson's teaching of "a solution of 3% w/v carboxymethyl cellulose (low viscosity), polysorbate 20, and sodium chloride used as the injection vehicle; the same components as used in Vehicle C of the '061 Patent." Pet. 24. Thus, the Petition relied on inherency, arguing that the ordinary artisan would appreciate that the injection vehicle disclosed in Johnson would have substantially the same viscosity of the preferred embodiment of the '061 Patent and as a result fall within the scope of claim 1 (*id.* at 25), rather than contending that it would have been obvious based on the teachings of Johnson and Kino to provide an injection vehicle having the viscosity required by the challenged claims.

Petitioner argues further that "Johnson specifically identifies 'low viscosity' CMC in the examples, and [an ordinary artisan] would appreciate that this implies the same CMC was used by Johnson throughout." Reply 11–12 (footnote omitted). Patent Owner, through its expert Dr. Gehrke, Petitioner asserts, did not test low viscosity CMC, but tested extra-low and

ultra-low CMCs that were not pharmaceutical grade. *Id.* at 13 (citing Ex. 1024 ¶¶ 57–58). Petitioner contends that the CMCs tested were specifically chosen by Patent Owner "to ensure the desired results." *Id.* In particular, Petitioner contends that the ordinary artisan at the time of invention would have chosen "commercially-available pharmaceutical-grade CMC -- not a special-order non-pharmaceutical-grade CMC -- in preparing an injection vehicle," and, thus, Dr. Gehrke's testing is not relevant to the issues in this proceeding. *Id.* at 10–11 (citing Ex. 1024 ¶ 44).

Petitioner responds further that Patent Owner does not demonstrate that the CMCs used by Dr. Gehrke that yield viscosities outside of the range required by the challenged claims were available at the time of invention. Reply 8, 10. Petitioner asserts that Patent Owner's expert did not choose the CMCs, and Patent Owner's expert, Dr. Berkland, testified that he did not know if they were available at the time of invention. *Id.* at 10 (citing Ex. 1024 ¶ 43; Ex. 1031, 217:18–218:10; Ex. 2059 ¶ 6).

Specifically, as to the Aqualon Brochure (Ex. 2034), Petitioner notes that it has a revision date of April 2002, and that the revision supersedes all previous editions. *Id.* at 8. Thus, Petitioner asserts, it is unclear if any of Aqualon's CMCs were available at the time of invention. *Id.* (citing Ex. 2034, 29; Ex. 1024 ¶ 32). Similarly, Petitioner contends, the Dow brochure has a copyright date of 2017, the Ashland catalog's is 2016, and the Spectrum CA193 Safety Data Sheet has a revision date of January 22, 2015. *Id.* at 8–9 (citing Ex. 2036; Ex. 2038; Ex. 2040; Ex. 1024 ¶ 32). Thus, Petitioner argues that Patent Owner "has simply done nothing to refute Petitioners arguments regarding the inherency of the viscosity limitation of the Patent claims." *Id.* at 9.

The Petition relies on Johnson for teaching a solution of 3% w/v carboxymethyl cellulose (low viscosity), polysorbate 20, and sodium chloride used as the injection vehicle. Pet. 24 (citing Ex. 1009, 12:39–42; Ex. 1002 ¶¶ 55, 59). Johnson, although teaching an injection vehicle "containing 3% w/v Carboxymethyl Cellulose (sodium salt), 1% v/v Tween 20 (Polysorbate 20) and 0.9% sodium chloride" (Ex. 1009, 12:42–45), does not specify in the example using that vehicle, Example 7, that the CMC used was low viscosity. Petitioner is relying on Johnson's teaching of the use of a low viscosity CMC in other examples, such as Example 5 and 6 (Ex. 1009, 10:18, 11:1), to infer that Johnson must have used low viscosity CMC in Example 7. *See* Reply 11–12. That is, however, an inference, and as Johnson did not specify the type and grade of CMC it used in Example 7, as discussed above, Petitioner has not established that the injection vehicle of Johnson would necessarily have the viscosity required by the challenged claims. And even if we were to accept Petitioner's inference and assume Example 7 of Johnson used low viscosity CMC, Petitioner has not established that the viscosity would necessarily be within the claimed range.

We recognize that Dr. DeLuca, in his Declaration, testifies that "[i]nstead of using pharmaceutical grade CMC, which is what an experienced formulator would use in preparing a pharmaceutical injectable suspension, Dr. Gehrke's tests used ultra-low viscosity CMC and extra-low viscosity CMC." Ex. 1024 ¶ 43. According to Dr. DeLuca, "[u]ltra-low and extra-low viscosity grades of CMC were not intended to be used for suspending particles in an injection vehicle for pharmaceutical applications." *Id.* ¶ 57. Dr. DeLuca testifies further:

> I understand that Dr. Berkland testified that ultra-low viscosity and extra-low viscosity CMC belong in the low viscosity category. (Ex.1031, 216:13-218:1) I disagree. Dr. Berkland bases his determination on the 2016 Ashland brochure, which as I mentioned above, does not show that these components were available at the time of the invention. And, according to the Handbook, which lists pharmaceutically acceptable excipients, they were not. (Ex.1008, 79.) An[d] even if they were available, which Patent Owners have not shown, the Handbook describes low viscosity CMC at a 4% concentration as having a viscosity of 50-200cp. In contrast, according to Patent Owners' Exhibits 2062 and 2063, a 6% concentration of ultra-low viscosity CMC has a viscosity of only 10-25cp and a 6% concentration of extra-low viscosity CMC has a viscosity of 35-60cp. Accordingly, ultra-low and extra-low CMC do not fall within the "low" viscosity range of a pharmaceutically acceptable CMC, which is the only type [an ordinary artisan] would use in an injectable suspension.

*Id.* ¶ 58.

Dr. DeLuca, however, does not cite to any evidence to support his assertion that low viscosity pharmaceutically acceptable CMC is the only type of CMC that the ordinary artisan would use in an injectable suspension. In fact, in contradiction to his statement that the ordinary artisan would use "pharmaceutical" grade CMS, Dr. DeLuca testified in deposition that he has used food grade CMC in studying vehicles for drug delivery. Ex. 2081, 134:7–135:3; *see* Paper 50, 1. Thus, we determine that Dr. DeLuca's statement that the ordinary artisan would only use low viscosity pharmaceutical grade CMC in an injectable suspension is entitled to little weight. *See* 37 C.F.R. § 42.65(a) ("Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.").

In addition, the Ashland Reference Guide provides the following table characterizing Bondwell, Blanose, and Aqualon CMCs:

**Physical Properties**

| CMC Category | | DS Type | | | Viscosity limits, mPa•s @ 25 °C | |
|---|---|---|---|---|---|---|
| Grade | Type | 7 | 9 | 12 | Range | Concentration |
| L | Ultra Low | 7UL | | 12UL | 10 - 25 | 6% |
| | Extra Low | 7EL | 9EL | | 20 - 60 | 6% |
| | Low-Low | 7L1 | | | 90 - 130 | 6% |
| | Low-Medium | 7L2 | | | 150 - 250 | 6% |
| | | 7L3 | | | 400 - 750 | 6% |
| | Low-High | 7L | | | 25 - 50 | 2% |
| M | Medium-Low | 7M1 | | | 50 - 100 | 2% |
| | | 7M2 | 9M2 | | 100 - 200 | 2% |
| | Medium | 7 M | | | 300 - 600 | 2% |
| | | 7M8 | 9M8 | 12M8 | 200 - 800 | 2% |
| | Medium-High | 7M31 | 9M31 | 12M31 | 1500 - 3100 | 2% |
| | | 7M65 | 9M65 | | 3000 - 6500 | 2% |
| H | High-Low | 7H | | | 1500 - 2500 | 1% |
| | High | 7H4 | 9H4 | | 2500 - 4500 | 1% |
| | | 7H5S | | | 3500 - 5500 | 1% |
| | High-High | 7H9 | | | 4000 - 9000 | 1% |

Ex. 2038, 40. Thus, the Ashland Reference Guide characterizes ultra-low and extra-low CMC's as grade L (low viscosity). *See* Ex. 2081, 208:11–14 (Dr. DeLuca acknowledging that Ashland classified its 7UL and 7EL CMCs as low viscosity grade).

Moreover, Dr. DeLuca, states in his Reply Declaration the above table reproduced from the Ashland Reference Guide is not consistent with the Handbook, as the Handbook describes low viscosity CMC at a 4% concentration as having a viscosity of 50-200cp, whereas the Ashland Reference Guide shows that ultra-low and extra-low CMCs have a viscosity

around 10–60 cP at a 6% concentration. Ex. 1024 ¶ 58. Table I of the Handbook (reproduced above), however, only refers to three grades of CMC: low viscosity, medium viscosity, and high viscosity, and is, thus, consistent with the above reproduced chart from the Ashland Reference Guide. That is, the Ashland Reference Guide also only lists three grades of CMC: low viscosity, medium viscosity, and high viscosity. In addition, the Handbook refers to "Typical Properties" of CMC, and also states that 1% solutions of 5–4000 cp may be obtained, and the ordinary artisan would not read that as encompassing all available CMCs. Ex. 1008, 79. Although the Ashland Reference Guide may not have been publicly available at the time of invention, we find it be relevant as to the various grades of CMCs, and, for the reasons noted above, determine that it is consistent with the chart provided in the Handbook, which both parties appear to agree is prior art to the invention.

As to the exact viscosities of the different grades, however, we find neither the chart in the Ashland Reference Guide nor the chart in the Handbook to be on point as neither chart discusses the viscosity at a 3% solution of the CMC, which is the percentage used by Johnson, wherein the viscosity was measured at 20ºC, which is the temperature at which the viscosity should be measured as specified by the challenged claims. As noted above, Petitioner has not provided any evidence that even if we were to accept its contention that Johnson must have used a low viscosity CMC as defined by the Handbook, all of those CMCs would necessarily have provided an injection vehicle wherein the claimed viscosity of about 20cp and less than about 600 cp at 20ºC when the CMC was present at 3% w/v.

Moreover, as to the commercial availability of the CMCs used by Dr. Gehrke in his Declaration, Dr. DeLuca acknowledged that as shown in US Patent No. 6,231,657 (the ’657 patent”, Ex. 2076) and US Patent No. 6,475,632 (“the ’632 Patent”, Ex. 2074), Blanose 7UL and 7EL were commercially available during the relevant time frame. Specifically, Dr. Deluca testified:

> Q. So these two patents confirm that Blanose 7ULC® and Blanose 7ELC® were commercially available as of the time of the invention, correct?
>
> MR. VAN BUSKIRK: Objection as to form. Which two patents?
>
> MR. WONG: '657 and '632.
>
> MR. VAN BUSKIRK: Thank you.
>
> Q. It's the two U.S. patents.
>
> A. Yeah, the Blanose patents were available. Whether they were Aqualon, I'm not sure.
>
> Q. But you would agree, at least, that Blanose 7UL® and 7EL® were commercially available as of the time of the invention, right?
>
> A. Yes.

Ex. 2081, 167:9–25. Dr. DeLuca’s testimony, therefore, is evidence that extra-low and ultra-low CMCs were available at the time of invention.

To the extent Petitioner argues that Patent Owner “has simply done nothing to refute Petitioners arguments regarding the inherency of the viscosity limitation of the Patent claims” (Reply 9), we note that the burden of persuasion always remains with Petitioner, and never switches to Patent Owner. And for the reasons discussed above, Petitioner has not established by a preponderance of evidence of record that the injection vehicle of Johnson inherently has the viscosity required by the challenged claims. That

is, the preponderance of the evidence of record does not support a finding that the injection vehicle of Johnson necessarily has a viscosity greater than about 20 cp and less than about 600 cp at 20ºC as required by independent claim 1.

Petitioner responds that Patent Owner, during prosecution, did not test the formulation of Kino, or perform testing comparing its formulation to that of Kino, but relied on the Tracy Declaration to compare their injection vehicle with that of Kino. Reply 9 (citing Ex. 1010; Ex. 1018; Ex. 1002 ¶ 44; Ex. 1024 ¶¶ 46–52). Petitioner asserts that "[w]hat is sauce for the goose is sauce for the gander" as Petitioner is relying on "the very logic that allowed [Patent Owner] to obtain the challenged claims in the first place." *Id*. at 10. Petitioner notes that neither the '061 patent or Kino describes the type and grade of CMC used, contending "[i]f the CMC mattered, then [Patent Owner] should not have been able to rely upon Tracy to overcome Kino." Reply 13 (citing Ex. 1024 ¶¶ 51, 59).

We have considered Petitioner's position as to the Tracy declaration, but Petitioner does not convince us that the declaration supports a finding that the vehicle of Johnson necessarily has the claimed viscosity. In particular, Dr. Tracy declared:

> Test Example 2 of the Kino patent uses a 0.5% sodium carboxymethyl cellulose (CMC) solution isotonized with mannitol as the injection vehicle. Based upon my knowledge and experience, the CMC is the viscosity-controlling component of the injection vehicle of Test Example 2 of the Kino patent. That CMC is the viscosity-controlling component.is exemplified by the two injection vehicles disclosed on page 10, lines 10-17 of the '875 application as originally filed. The Formula 1 injection vehicle described on page 10 of the '875 application contains 1.5% CMC, and has a

> viscosity of approximately 27 cp at 20°C. The Formula 2·injection vehicle described on page 10 of the '875 application contains 0.75% CMC, and has a viscosity of approximately 7 cp at 20°C. By reducing the CMC from 1.5% to 0.75%, the viscosity dropped from 27 cp to 7 cp. Based upon my knowledge and experience, and the disclosure on page 10, lines 10-17 of the '875 application, the viscosity of the CMC injection vehicle as the fluid phase of a suspension containing the microspheres of Test Example 2 of the Kino patent is less than 7 cp at 20°C.

Ex. 1018 ¶ 5.

As can be seen in the above paragraph, Dr. Tracy states how he came to the conclusion that the viscosity of Test Example 2 of Kino is less than 7 cp. Dr. Tracy does not state that he relied on test data, or state that all suspensions having a CMC concentration of 0.5% would have a viscosity of less than 7 cp. In addition, Petitioner has not pointed to any evidence demonstrating that the Examiner misunderstood the declaration. And, importantly, the declaration does not demonstrate that the injection vehicle of Johnson necessarily would have the claimed viscosity.

Thus, we determine that Petitioner has not established that the injection vehicle of Johnson necessarily has the required viscosity required by the challenged claims. As that is the only basis set forth in the Petition as to why the prior art meets the viscosity limitation, Petitioner has failed to establish that the combination of Johnson and Kino renders claims 1–13, 22, and 23 obvious.

Petitioner argues further that the ordinary artisan "focuses on suspendability and injectability when preparing parenteral suspensions," and, thus, it would have been obvious to the ordinary artisan "to adjust the viscosity to determine what is needed to achieve injectability and

suspendability." Reply 15 (citing Ex. 1002 ¶ 19; Ex. 1024 ¶¶ 19–20, 66–69, 71).

Petitioner's argument in that regard is one of obviousness, rather than inherency. Petitioner does not point, however, where it made that specific obviousness argument in the Petition, and we decline to consider such an argument made for the first time in a Reply. *See Wasica Finance GmbH v. Continental Automotive Systems, Inc.*, 853 F.3d 1272, 1286 (Fed. Cir. 2017) (noting that it is improper for a petitioner to bring new theories on unpatentability in its reply, rather than explaining how the challenge as set forth in the petition is correct).

Patent Owner argues also that objective indicia of non-obviousness, such as unexpected results and commercial success support the patentability of the challenged claims. PO Resp. 59–61. As we conclude that the preponderance of evidence of record does not support Petitioner's obviousness challenge, we need not address Patent Owner's evidence of secondary indicia.

*D. Obviousness Over Gustafsson, Ramstack, and the Handbook*

Petitioner contends that claims 1–3, 6–9, 12, 13, and 17–23 are rendered obvious by the combination of Gustafsson, Ramstack, and the Handbook. Pet. 38–56. Petitioner presents a claim chart demonstrating where the limitations of the challenged claims may be found in the relied upon references. *Id.* at 49–56. Patent Owner disagrees with Petitioner's contentions, asserting that the Petition fails to demonstrate the obviousness

of the challenged claims by a preponderance of the evidence. PO Resp. 34–59.

*i. Overview of the Prior Art Relied Upon*

We find the following as to the teachings of the relevant prior art.

*a. Overview of Gustafsson (Ex. 1011)*

Gustafsson is drawn to sustained release parentally administrable formulations. Ex. 1011, 6:16–19. Gustafsson teaches the use of polymers such as linear polyesters based on lactic acid, glycolic acid, or mixtures thereof, which Gustafsson refers to as "PLGA." *Id.* at 1:27–31. Gustafsson teaches that the microparticles have an average diameter in the range of 10–200 μm, preferably from 20–100 μm. *Id.* at 7:30–33. Although Gustafsson specifically teaches the use of proteins as the active agent, Gustafsson teaches that it is "useful for all active substances which may be utilized in parental administration." *Id.* at 6:23–26, 6:33–35.

According to Gustafsson:

> the invention is based on the idea on entrapping the active ingredient in microparticles without using any organic solvent, working up the microparticles to the dry state and subsequently coating the microparticles with a biodegradable polymer using an air suspension technique to remove, very rapidly, any organic solvent used for the polymer coating to avoid any substantial exposure of the active substance to organic solvent.

*Id.* at 7:3–10.

In Example 6 (*id.* at 17), Gustafsson looked at the release of bovine serum albumin ("BSA") from coated microspheres in female rats. *Id.* at 18:17–19. Gustafsson injected 200 μl of a suspension containing 163 mg/ml of microparticles, in which the vehicle for injection was "physiological sodium chloride solution containing 3% of sodium carboxymethylcellulose

as [a] suspension aid," wherein the suspension was injected using a 21 gauge needle. *Id.* at 18:21–24.

*b. Overview of Ramstack (Ex. 1005)*

Ramstack is drawn to the preparation of microparticles that encapsulate an active agent. Ex. 1005, 1:14–17. Ramstack teaches that a wide variety of active agents may be encapsulated in the microparticles (*id.* at 30:1–32:18), including antibodies and enzymes (*id.* at 32:6–7), and specifically teaches that the active agent may be risperidone (*id.* at 8:21–22). According to Ramstack the "most preferred polymer for use in the practice of this invention is poly(dl-lactide-co-glycolide)," wherein "the molar ratio of lactide to glycolide in such a copolymer be in the range of from about 85:15 to about 50:50." *Id.* at 16:28–31.

Ramstack teaches that the microparticles are stored as a dry material, but are suspended in a suitable pharmaceutical liquid vehicle before administration, such as a 2.5 wt. % solution of CMC. *Id.* at 29:27–31. Ramstack provides an example of an aqueous vehicle comprising 0.75% CMC, 5% mannitol, and 0.1% Tween 80, wherein after the microparticles are suspended in that vehicle, they are quickly frozen, and lyophilized. *Id.* at 37:5–9. For injection into dogs, the "dry microparticles were syringe-loaded and resuspended in the syringe with an injection vehicle comprised of 2.5 wt% carboxymethyl cellulose (CMC)." *Id.* at 38:6–8.

*c. Overview of the Handbook (Ex. 1008)*

The Handbook of Pharmaceutical excipients teaches that CMC has viscosity-increasing properties, noting that viscous aqueous solutions are used to suspend powders intended for parental administration. Ex. 1008, 78.

*ii. Analysis*

Petitioner relies on Gustafsson for teaching a sustained release formulation containing an active agent, wherein the formulation may be used with any active agent. Pet. 39 (citing Ex. 1011, Abstract, 6:33–35; Ex. 1002 ¶¶ 57, 69). Petitioner relies also on the teaching of Gustafsson of an injection vehicle "that includes a sodium chloride solution containing carboxymethyl cellulose and microparticles in a concentration of greater than 30mg/ml, wherein the resulting suspension is suitable for suspension in a solution suitable for injection into a patient via a 21 gauge needle." *Id.* (citing Ex.1011, 18:19–24; Ex. 1002 ¶¶ 57, 69).

Petitioner acknowledges that Gustafsson does not specify the viscosity, but contends that the ordinary artisan would understand that CMC is a viscosity enhancing agent, and that it "would be considered the viscosity-controlling component of an injection vehicle." *Id.* (Ex. 1002 ¶ 70).

Petitioner contends:

> According [to] the Tracy Declaration, a solution that includes 1.5% CMC provides viscosity of 27cps. (Ex.1002 ¶ 70.) Based on the Patent Owner's admission during prosecution of the '061 Patent, the Tracy Declaration, and what would have been understood [by the ordinary artisan, the ordinary artisan] would reasonably expect the injection vehicle of Gustafsson—having 3% CMC—to have a viscosity greater than 27cp at 20°C and certainly within the claimed range of 20-600cp at 20°C. (*Id.*).

*Id.* at 39–40; *see also id.* at 50 (claim chart) (citing Ex. 1002 ¶¶ 28, 57, 70).

For essentially the same reasons set forth as to Johnson, Patent Owner responds that Petitioner has failed to establish that injection vehicle of Gustafsson inherently has a viscosity as required by the challenged claims. PO Resp. 37–38. In response, Petitioner reiterates its arguments as to the

challenge based on Johnson. Reply 18–19, 21–22. Thus, for the reasons set forth above with respect to the obviousness challenge based on Johnson, we determine that Petitioner has not demonstrated that the injection vehicle of Gustafsson necessarily has the viscosity required by the claims.

In that regard, we note that Dr. Gehrke made the vehicle of Johnson using "two different types of low viscosity CMC: 7ULC and 7ELCI from Ashland." Ex. 2014 ¶ 122–124; Ex. 2059 ¶¶ 5–12. As Dr. Berkland explains:

> each of these Ashland CMCs yielded a Gustafsson vehicle with a viscosity below 20 cp when measured at 20ºC and thus outside the range claimed in the '061 patent. ([Ex. 2059] ¶ 12.)

**TABLE B – GUSTAFSSON VEHICLES (EXH. 2059, GEHRKE DECL.)**

| Formulation | Viscosity (cp) at 20°C | RPM |
|---|---|---|
| 3% Ashland 7ULC CMC, 0.9% NaCl | 5.62 cp | 200 |
| 3% Ashland 7ELC1 CMC, 0.9% NaCl | 9.17 cp | 200 |

Ex. 2014 ¶ 124.

Again, for the reasons explained above as to Johnson, the data provided by Dr. Gehrke evidences that the formulation of Gustafsson does not necessarily have the viscosity required by the challenged claims. Thus, Petitioner has failed to demonstrate by a preponderance of the evidence that the combination of Gustafsson, Ramstack, and the Handbook renders claims 1–3, 6–9, 12, 13, and 17–23 are obvious.

*E. Patent Owner's Motion to Exclude (Paper 51)*

Patent Owner uses its Motion to Exclude Evidence as a vehicle to respond to arguments made by Petitioner in its Reply. For example, Patent Owner argues that the Reply "far exceeds the proper scope of a reply by

going above and beyond responding to arguments made in the Patent Owners' Response." Paper 51, 1. A motion to exclude evidence is not the proper vehicle, however, to ask for a paper such as a reply to be stricken from the record. We decline to search through the Motion to determine which portions constitute a proper motion to exclude, and which portions do not relate to a proper motion to exclude. Thus, we decline to consider Patent Owner's Motion to Exclude, *dismissing* it as improper. *See* 37 C.F.R. § 42.63(a) (defining evidence as "affidavits, transcripts of depositions, documents, and things," filed in the form of an exhibit)

*F. Petitioner's Motions to Exclude (Papers 47 and 70)*

In its first Motion to Exclude, Petitioner argues that Exhibits 2034, 2036, 2038–2040, and 2052 should be excluded, as well as the declarations that rely upon them. Paper 47, 2. According to Petitioner, Patent Owner relies on those exhibits "for its assertion that CMC products commercially available at the time of the invention would have produced viscosities below the claimed range." *Id.* at 2–3. Petitioner asserts that the Exhibits are "impermissible hearsay," "lack authentication," and are "irrelevant" as none of the exhibits make it more or less probable that the CMC products were available at the time of invention. *Id.* at 3. In particular, as to authentication, Petitioner argues that Patent Owner has not established that they were available at the time of invention. *Id.* at 5–6.

We conclude that the Exhibits are not hearsay, as they are not offered for the truth asserted therein. Rather, as evidenced by Petitioner's addressing the Exhibits together, rather than pointing out how each separate exhibit has been offered for the truth of the statements made within each exhibit, Patent Owner relies upon them to demonstrate that various types and

grades of CMC, having different viscosities, are known to be commercially available. That is, those Exhibits were "offered simply as evidence of what it described, not for proving the truth of the matters addressed in the document." *See, e.g.*, *Joy Techs., Inc. v. Manbeck*, 751 F. Supp. 225, 233 n.2 (D.D.C. 1990), *judgment aff'd*, 959 F.2d 226 (Fed. Cir. 1992); Fed. R. Evid. 801(c) 1997 Adv. Comm. Note ("If the significance of an offered statement lies solely in the fact that it was made, no issue is raised as to the truth of anything asserted, and the statement is not hearsay."). In addition, the fact that Patent Owner has not established that they were available at the time of invention goes to the weight that should be accorded the Exhibits, and not to whether they are inadmissibly irrelevant. We, thus, *deny* Petitioner's Motion as to Exhibits 2034, 2036, 2038–2040, and 2052. In addition, for the same reason we deny the Motion to Exclude as to those Exhibits, we also deny Petitioner's Motion to Exclude as to the paragraphs of Dr. Gehrke's Declaration and Dr. Berkland's Declaration that rely on those exhibits.

Petitioner argues further that we should exclude Exhibit 2049 should be excluded as hearsay. Paper 47, 12. As we did not rely on Exhibit 2049, we *dismiss* Petitioner's Motion as to that Exhibit as moot.

Petitioner also argues in its first Motion that Exhibits 2022–2030, 2035, 2037, 2042, and 2044 should be excluded as irrelevant. Paper 47 13–14. Specifically, Petitioner asserts that Patent Owner has not established that they were available at the time of invention. *Id.* at 14. Again, that goes to the weight that should be accorded the exhibits, and not to whether they are inadmissibly irrelevant. We, thus, *deny* Petitioner's Motion as to Exhibits 2022–2030, 2035, 2037, 2042, and 2044.

Finally, Petitioner argues that Exhibits 2020, 2021, 2047, and 2056–2058 should be excluded as irrelevant as Patent Owner does not rely upon them, nor has it identified how they are relevant to the proceeding. As pointed out by Patent Owner (Paper 56, 14), Petitioner does not point us to where in the record it objected to those exhibits. 37 C.F.R. § 42.64 (A motion to exclude "must identify the objections in the record and must explain the objections."). We, therefore, *deny* the Motion as to those Exhibits.

Thus, as to Petitioner's first Motion to Exclude, we *deny* it in part *dismiss* it as moot in part.

In its second Motion to Exclude, Petitioner seeks to exclude Exhibits 2073, 2075, 2077–2079, as well as portions of Exhibit 2081 as it objected to the exhibits during deposition, and Patent Owner "made no attempt to overcome the objection during deposition." Paper 70, 2. As we did not rely on those Exhibits in this Decision, we *dismiss* Petitioner's second Motion to exclude as to Exhibits 2073, 2075, 2077–2079, and the portions of Exhibit 2081 that rely on them.

Petitioner argues further that we should exclude Exhibits 2075 and 2077 as failing to comply with 37 C.F.R. § 42.63(b). As we did not rely on those Exhibits in this Decision, we also *dismiss* the motion as moot as to those Exhibits.

Petitioner argues also that Exhibits 2074 and 2076 should be excluded as irrelevant, as Patent Owner has not established that they have a priority date before the date of invention. Paper 70, 3. In addition, Petitioner argues that Exhibits 2074–2079 should be excluded as irrelevant as being directed to non-analogous art. *Id.* at 3. Finally, Petitioner asserts that Exhibits 2073,

2078, and 2079 should be excluded as irrelevant, as Patent Owner has not established that the products were commercially available at the time of invention. Those arguments go more to the weight to be accorded the Exhibits, and not whether they should be excluded. Thus, we *deny* the motion as to Exhibits 2073–2079.

Thus, as to Petitioner's second Motion to Exclude, we *deny* it in part *dismiss* it as moot in part.

## D. CONCLUSION

After considering Petitioner's and Patent Owner's positions and evidence, we conclude that Petitioner has not demonstrated by a preponderance of the evidence that claims 1–13 and 17–23 of the '061 patent are unpatentable as obvious.

## E. ORDER

Accordingly, it is hereby:

ORDERED that Petitioner has failed to demonstrate by a preponderance of the evidence that claims 1–13 and 17–23 of the '061 patent are unpatentable under 35 U.S.C. § 103(a);

FURTHER ORDERED that Patent Owner's Motion to Exclude is *dismissed* as improper;

FURTHER ORDERED that Petitioner's first Motion to Exclude is *denied* in part, and *dismissed* as moot in part, as is Petitioner's second Motion to Exclude; and

FURTHER ORDERED that, because this is a final written decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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