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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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.

Case IPR2016-01096
Patent 6,667,061 B2

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

GREEN, *Administrative Patent Judge*.

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

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.").

Institution of an *inter partes* review is authorized by statute when "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 1 of the claims challenged in the petition." 35 U.S.C. § 314; *see* 37 C.F.R. §§ 42.4, 42.108. Upon considering the Petition and the Preliminary Response, we determine that Petitioner has demonstrated a reasonable likelihood that it would prevail in showing the unpatentability of claims 1–13 and 17–23. Accordingly, we institute an *inter partes* review of those claims.

A. Related Proceedings

Petitioner states that it has 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, is being decided concurrently with the instant proceeding.

B. The '061 Patent (Ex. 1001)

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 1:12–14.

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 "microparticles" and "microspheres" refer to "particles that contain an active agent or other substance dispersed or dissolved within a polymer that serves as a matrix or binder of the particle," wherein the "polymer is preferably biodegradable and biocompatible." *Id.* at 5:14–19.

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. The '061 patent specifically teaches that CMC is a viscosity enhancing agent. *Id.* at 12:14–20.

C. Challenged Claims

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 20° 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, 18:6–16 (emphasis added).

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–13 and 17–23 of the '061 patent on the following grounds (Pet. 4):

References	Basis	Claims Challenged
Johnson[1] and Kino[2]	§ 103	1–13 and 17–23
Gustafsson,[3] Ramstack,[4] and the Handbook[5]	§ 103	1–13 and 17–23

Petitioner relies also on the Declaration of Patrick Deluca, Ph.D. (Ex. 1002).

II. ANALYSIS

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.

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

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 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).

Petitioner offers explicit constructions of several claim terms (Pet. 19–22), as does Patent Owner (Prelim. Resp. 9–12). On the present record, we determine that none of the claim terms require explicit construction for purposes of this Decision. *See, e.g.*, *Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) ("[C]laim terms need only be construed 'to the extent necessary to resolve the controversy.'") (quoting *Vivid Techs, Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

B. Obviousness over Johnson and Kino

Petitioner asserts that claims 1–13 and 17–23 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 contends that Petitioner has not established a reasonable likelihood that claims 1–13 and 17–23 is rendered obvious by the combination of references relied upon by Petitioner. Prelim. Resp. 14–32.

i. 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. Johnson teaches that "[a] preferred size range for microparticles is from about 1 to about 180 microns in diameter." *Id.* at 4:60–62.

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.

ii. 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. In addition, according to Kino, the sustained release injection may be made more stable by adding a filler such as sorbitol or mannitol, drying to form a solid preparation, which is then used by adding a dispersion medium, such as water, before injection. *Id.* at 4:52–60.

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.

iii. Analysis

a. Claims 1–3, 6–9, 12, and 13

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.

Patent Owner responds that neither Johnson nor Kino teaches the required viscosity limitation. Prelim. Resp. 14. Moreover, Patent Owner

asserts that Petitioner is relying on Johnson's disclosure of the injection vehicle, and the claimed suspension is formed after the microparticles are suspended in the injection vehicle. *Id.* at 15. Patent Owner contends, therefore, that Petitioner has not explained how the ordinary artisan "would have determined the viscosity of the fluid phase of the suspension[ ] of Johnson . . . from disclosures related to the compositions of their injection vehicles prior to formation of a suspension or to show that the viscosity of the injection vehicle[ ] of Johnson . . . would be the same as that of the fluid phase of their suspensions." *Id.* at 15–16. Specifically, Patent Owner asserts that Petitioner has failed to account for how the microspheres may affect the viscosity of the injection vehicle. *Id.* at 16. In addition, Patent Owner argues that the challenged claim require measuring the viscosity at 20°C, and Johnson does not specify the temperature at which the viscosity should be measured. *Id.* at 16–17.

In addition, Patent Owner quotes *Continental Can Co. U.S.A. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991) for the proposition that in order to establish inherency, "the missing characteristic must be ***necessarily present***, or inherent, in the single anticipating reference." Prelim. Resp. 17. Patent Owner contends that Petitioner has "failed to establish that [the ordinary artisan] would have inevitably measured the viscosity of the Johnson . . . formulations at 20ºC or that viscosity of the formulations would be between 20 cp and 600 cp." *Id.* at 18.

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." (emphasis added). We acknowledge that Johnson does not specifically teach that viscosity limitation. As noted by Petitioner, however,

Johnson teaches an injection vehicle comprising 3% w/v CMC, 1 % polysorbate 20, and 0.9% sodium chloride. Pet. 24; Ex. 1009, 12:42–45. The '061 patent teaches Vehicle C, which comprises 3% CMC, 0.1% Tween 20 (i.e., polysorbate 20), and 0.9% saline, has a density of 56 cp. Ex. 1001, 9:45; 10:Table 4. 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.* at 12:14–20.

Petitioner further relies on the Declaration of Dr. Tracy (Ex. 1018), submitted during prosecution, to demonstrate that the viscosity of the injection vehicle of Johnson would have a viscosity greater than about 20 cp. Pet. 25. The Tracy Declaration looked at test Example 2 of Kino. 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.

Thus, Dr. Tracy based his estimate of the viscosity of the injection vehicle of Kino solely on the amount of CMC in the injection vehicle. The Tracy Declaration, therefore, is further evidence that the injection vehicle of Johnson would have a viscosity at 20ºC close to that of Vehicle C of the '061 patent, as each has 3.0% CMC.

Patent Owner's argument premised on *Continental Can* does not convince us otherwise. Inherency does not require intent or recognition that a prior art process achieve a result which is claimed. "Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art." *MEHL/Biophile Intern. Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999). Thus, "[m]ere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991). Thus, the fact that the ordinary artisan may not have recognized that the injection vehicle of Johnson may have a viscosity greater than about 20 cp at 20ºC does not affect the inherency analysis.

Patent Owner's argument that Petitioner does not take into account how the microspheres may affect the viscosity of the injection vehicle is also not convincing at this stage of the proceeding. Claim 1 specifies that the "*fluid phase* of said suspension has a viscosity greater than about 20 cp and less than about 600 cp at 20º C." (emphasis added). The fluid phase of the suspension would be the injection vehicle. That is supported by the Specification of the '061 patent, as, for example, Table 4 provides the

viscosity of Vehicles A, B, and C, and not the viscosity of suspension after the microparticles were added. Ex. 1001, 10:Table 4; *see also id.* at 10:12–13 (noting that "[d]ensities were measured for Vehicles A, B, and C"). In that regard, as we noted above, the Declaration of Dr. Tracy only took into account the amount of CMC in stating that the fluid phase of Test Example 2 of Kino would have a viscosity less than 7 cp at 20ºC. Ex. 1018 ¶ 5.

As to Petitioner's use of the Declaration of Dr. Tracy, Patent Owner argues also that the Declaration does not support Petitioner's contention that the ordinary artisan would have understood that the injection vehicle of Johnson meets the claimed viscosity limitation. Prelim. Resp. 19–20. According to Patent Owner, that Declaration was directed to the formulation of Kino, and "Dr. Tracy did not state that [the ordinary artisan] could always determine viscosity based solely on the concentration of CMC in an injection vehicle or fluid phase of a suspension, without accounting for additional components, such as polysorbate 80, sodium chloride or microspheres of various active ingredients." *Id.* at 20. In addition, Patent Owner argues that the Tracy Declaration is not a patent or printed publication under 35 U.S.C. § 311(b), as it was filed during prosecution more than two years after the earliest filing date of the challenged patent. *Id.* at 20.

Patent Owner argues further that Dr. Tracy is not an ordinary artisan, but exceeds the knowledge of the ordinary artisan, and thus his Declaration does not reflect what would have been known by the ordinary artisan. *Id.* at 20–21. Thus, Patent Owner asserts, Petitioner offers "no independent evidence that [the ordinary artisan] would have understood the formulations in Johnson . . . to ***necessarily*** meet the claimed viscosity limitation present in

each challenged claim of the '061 patent." *Id.* at 21. Patent owner argues that although Petitioner relies on its declarant, Dr. DeLuca, Dr. DeLuca relies only on the Tracy Declaration for support. *Id.* (citing Ex. 1002 ¶¶ 60, 61). According to Patent Owner, that reliance is in error, because, as argued above, the Tracy Declaration is not prior art, and nor is it a patent or printed publication, and thus Dr. DeLuca's testimony is unsupported. *Id.*

Patent Owner asserts further:

> Petitioners use impermissible hindsight to selectively rely on the Tracy declaration. Dr. Tracy clearly states that, assuming measurement at 20ºC and consistent with the art at the time of the invention, the viscosities of the injection vehicles in Kino are significantly less than 20 cp. (Exh. 1018 at ¶¶ 4-5.) Nevertheless, Petitioners ignore this teaching and ask the Board to focus only on Dr. Tracy's statements elsewhere in his declaration. Petitioners, however, cannot pick and choose one portion of his declaration to support a viscosity disclosure while blatantly ignoring another portion, relied upon by the Examiner, that proves Kino is not invalidating prior art with respect to the invention. *See, e.g.*, *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1348 (Fed. Cir. 2010) (warning against relying on hindsight to pick and choose among isolated elements from the prior art).

Id. at 22.

We do not find Patent Owner's arguments in this regard convincing at this stage of the proceeding. It is irrelevant that Dr. Tracy may not be one of ordinary skill in the art. Dr. Tracy is testifying as to the inherent property of an injection vehicle, and inherency need not be coterminous with the knowledge of those of ordinary skill in the art. *MEHL/Biophile Intern. Corp.*, 192 F.3d at 1365. Thus, the challenge is based on Johnson and Kino, and the Declaration of Dr. Tracy, as discussed above, is evidence that the injection vehicle of Johnson would inherently meet the viscosity limitation of challenged claim 1.

As to claims 6–9, 12 and 13, Petitioner notes that claim 6 adds a tonicity agent, and claim 7 specifies that the tonicity agent is sodium chloride. Pet. 27. Claims 8 and 12 depend from claims 2 and 6, respectively, and add a wetting agent, and claims 9 and 13 "specify that the wetting agent is 'selected from the group consisting of polysorbate 20, polysorbate, 40, and polysorbate 80.'" *Id.* at 27–28. According to Petitioner, "Johnson teaches carboxymethyl cellulose (sodium), a viscosity enhancing agent, sodium chloride, a tonicity agent, and polysorbate 20, a wetting agent, alone or in combination, and therefore teaches every element of claims 6-9 and 12-13." *Id.* at 28 (citing Ex. 1009, 12:42–45; Ex. 1002 ¶ 63).

After considering the Petition and Preliminary Response, we determine that Petitioner has demonstrated a reasonable likelihood that claims 1–3, 6–9, 12, and 13 are obvious over the cited prior art.

b. Claims 4, 5, 10, and 11

Petitioner notes that claim 4 adds the limitation of a density enhancing agent, and claim 5 specifies that the density enhancing agent is sorbitol. Pet. 26. As to claim 10, Petitioner notes that that it depends from claim 4, and adds a wetting agent, and claim 11 specifies "that the wetting agent is 'selected from the group consisting of polysorbate 20, polysorbate, 40, and polysorbate 80.'" *Id.*

Petitioner relies on Kino for teaching the addition of fillers, such as sorbitol, and wetting agents, such as polysorbate 80, to microparticle suspensions, and that sorbitol is known to enhance the stability of such suspensions. *Id.* at 27 (citing Ex. 1010, 4:38–40, 4:52–56; Ex. 1002 ¶¶ 56, 62).

Patent Owner responds that Petitioner has not established why the ordinary artisan would have combined Johnson and Kino, with a reasonable expectation of success of arriving at the claimed invention. Prelim. Resp. 24–25. At best, Patent Owner asserts, Petitioner relies on impermissible hindsight. *Id.* at 25.

Specifically, as to claims 4, 5, 10, and 11, Patent Owner asserts that the reason provided by Petitioner is to increase the density to stabilize the formulation; however, Patent Owner argues, neither Johnson nor Kino suggest that the formulation need to be stabilized, or that increasing the density would be desirable. *Id.* at 26.

We agree with Patent Owner that the Petition does not point to any teaching in Johnson or Kino that establishes that increasing the density would be desirable. As noted by Petitioner (Pet. 27), however, Kino teaches that adding a filler such as mannitol or sorbitol to microspheres before freezing allows for more stable sustained release injections. Ex. 1010, 4:52–60. Thus, Petitioner has sufficiently demonstrated on this record that the ordinary artisan would have had a reason to use a filler such as mannitol or sorbitol in the final sustained release compositions of Johnson.

Patent Owner argues that Johnson and Kino are directed to "vastly different subject matter," as Johnson is drawn to compositions for sustained release of hGH, which is soluble in a water-based system, whereas Kino relates to microspheres containing risperidone, which lacks affinity for water. Prelim. Resp. 28. Moreover, Patent Owner asserts, Kino is drawn to low viscosity compositions, which comprise 0.5% CMC, whereas the compositions of Johnson contain 3% CMC. *Id.* at 28–30. Thus, given the conventional wisdom that low viscosity compositions were better for

injectable compositions, Patent Owner asserts that the ordinary artisan would not have combined Johnson and Kino as suggested by Petitioner. *Id.* at 29–30. Patent Owner contends, therefore, that Petitioner has not established a reasonable expectation of success of combining Johnson with Kino to arrive at the claimed invention. *Id.* at 31. Specifically, Patent Owner contends that the prior art "establishes that increased viscosity hinders injectability." *Id.*

We do not find Patent Owner's arguments convincing at this stage of the proceeding. Both Johnson and Kino are drawn to the use of sustained release microsphere compositions. In addition, Johnson teaches an injection vehicle containing 3% CMC, and, thus, provides a reasonable expectation of success of achieving an injection vehicle containing 3% CMC, as well as a filler, such as sorbitol or mannitol. Note that all that is required is a reasonable expectation of success, not absolute predictability of success. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

After considering the Petition and Preliminary Response, we determine that Petitioner has demonstrated a reasonable likelihood that claims 4, 5, 10, and 11 are obvious over the cited prior art.

c. Claims 17–21

Petitioner notes that claim 17 depends from claim 1, and "requires that the microparticles 'further comprise an active agent encapsulated within said polymeric binder.'" Pet. 28. Claim 18 specifies that the polymeric binder is selected from a Markush group that includes a copolymer of poly(glycolic acid) and poly-d,l-lactic acid, and claim 19, also dependent from claim 17, specifies that the "polymeric binder is poly(d,l-lactide-co-glycolide) having

a molar ratio of lactide to glycolide in the range of from about 85:15 to about 50:50." *Id*. at 28–29.

As to claims 20 and 21, Petitioner notes that they depend from claims 17 and 19, and "specify that the 'active agent is selected from the group consisting of risperidone, 9-hydroxyrisperidone, and pharmaceutically acceptable salts thereof.'" *Id.* at 29.

Petitioner relies on Johnson for teaching entrapping active substances in microparticles for sustained release, as well as teaches the use of poly(lactide-co-glycolide) as a polymeric binder. *Id*. (citing Ex. 1009, 1:45–49, 3:55–60; Ex. 1002 ¶ 64).

Petitioner relies on Kino for teaching "that daily dose maintenance therapy to treat mental disease is undesirable due to patient compliance and that improvements in sustained release antipsychotics are necessary." *Id.* (citing Ex.1010, 1:12-2:13; Ex. 1002 ¶ 65). Petitioner also relies on Kino as teaching that "improvements to compliance of maintenance therapy with antipsychotic drugs can be obtained with injections of sustained release preparations," wherein the antipsychotic drug may be risperidone. *Id.* at 29–30 (Ex. 1010, 1:65–2:3, 2:41; Ex. 1002 ¶ 65).

Petitioner asserts that the ordinary artisan would have improved the injectibility of a suspension of risperidone microparticles to increase patient compliance, and, thus, would have looked "to combine sustained release microparticles . . . to improve the injectability of the suspension." *Id.* (citing Ex. 1002 ¶ 66).

Patent Owner responds that "nothing in Johnson or Kino indicates that selectively combining their teachings would lead to improved suspension injectability or that improved injectability would impact patient

compliance." Prelim. Resp. 27. Patent Owner argues further that "nothing in Johnson or Kino suggests the higher viscosity injection vehicle of Johnson would be appropriate for the Kino compositions comprising risperidone as an active ingredient." *Id.* at 30.

We agree with Patent Owner that Petitioner has not demonstrated a reasonable likelihood that claims 17–21 are rendered obvious by the combination of Johnson and Kino. Petitioner offers only the conclusory statement that the ordinary artisan "would look to combine sustained release microparticles . . . to improve the injectability of the suspension." Pet. 30. Such a conclusory statement, without more, is not sufficient to support the obviousness analysis. In *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 415 (2007), although the Supreme Court emphasized "an expansive and flexible approach" to the obviousness question, it also reaffirmed that "[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, *there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *Id.* at 418 (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added).

After considering the Petition and Preliminary Response, we determine that Petitioner has not demonstrated a reasonable likelihood that claims 17–21 are obvious over the cited prior art.

d. Claims 22 and 23

Petitioner notes that claim 22 depends from claim 1, and "specifies that the 'mass median diameter of said microparticles is less than about 250 μm.'" Pet. 30. Claim 23 "specifies that the 'mass median diameter of said microparticles is in the range of from about 20 μm to about 150 μm.'" *Id.*

Petitioner contends:

> Johnson teaches sustained release microparticles that include a polymer, such as poly(lactide-co-glycolide). (Exs.1009, at 1:45-49, 3:55-60; 1002 ¶ 67.) Johnson teaches that such microparticles have a diameter between 1 to about 180 microns. (Exs.1009, at 4:60-62; 1002 ¶ 67.) Johnson does not describe how the microparticles are measured, but [the ordinary artisan] would reasonably expect that the mass median diameter of the Johnson microparticles would fall within the range recited by claims 22 and 23. Kino teaches microparticles having a diameter of 0.5 to about 400 μm, or preferably 0.5-200 μm and most preferably 15-50 μm. (Exs.1010, at 4:34-37; 1002 ¶68.) Kino explains that their microspheres are screened to remove any oversized particles. (Exs.1010, at 4:29-30; 1002 ¶68.) [The ordinary artisan] would reasonably expect that the mass median diameter of the Kino microparticles would fall within the range recited by claims 22 and 23.

Id. at 31.

After considering Petitioner's challenge and evidence, we determine that Petitioner has demonstrated a reasonable likelihood that claims 22 and 23 are obvious over the cited prior art.

e. Conclusion

Petitioner has demonstrated a reasonable likelihood that claims 1–13, 22, and 23 are rendered obvious by the combination of Johnson and Kino. Petitioner, however, has failed to demonstrate a reasonable likelihood that claims 17–21 are rendered obvious by that combination.

C. Obviousness over Gustafsson, Ramstack, and the Handbook

Petitioner asserts that claims 1–13 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 contends that Petitioner has not established a reasonable

likelihood that the challenged clams are rendered obvious by the combination of Gustafsson, Ramstack, and the Handbook. Prelim. Resp. 14–24, 32–40.

i. 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.

ii. Overview of Ramstack (Ex. 1005)

Ramstack is drawn to the preparation of micrparticles 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 micropaticles 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.

iii. 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.

The Handbook teaches further that polysorbates, such as polysorbate 80, may be used as a wetting agent in the formulation of parenteral suspensions. *Id.* at 376.

iv. Analysis

a. Claims 1–3, 6, 7, 17–19

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, 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.* at 25 (citing Ex. 1008 at 78, Ex. 1002 ¶ 61).

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.

Patent Owner responds that none of Gustafsson, Ramstack, or the Handbook teaches the claimed viscosity limitation. Prelim. Resp. 14. Moreover, Patent Owner asserts that Petitioner is relying on Gustafsson's

disclosure of the injection vehicle, and the suspension is formed after the microparticles are suspended in the injection vehicle. *Id.* at 15. Patent Owner contends that Petitioner has not explained how the ordinary artisan "would have determined the viscosity of the fluid phase of the suspension[ ] of . . . Gustafsson from disclosures related to the compositions of their injection vehicles prior to formation of a suspension or to show that the viscosity of the injection vehicle[ ] of . . . Gustafsson would be the same as that of the fluid phase of their suspensions." *Id.* at 15–16.

Specifically, Patent Owner asserts that Petitioner has failed to account for how the microspheres may affect the viscosity of the injection vehicle. *Id.* at 16. In addition, Patent Owner argues that the challenged claim require measuring the viscosity at 20°C, and Johnson does not specify the temperature at which the viscosity should be measured. *Id.* at 16–17.

Patent Owner quotes *Continental Can Co. U.S.A. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991) for the proposition that in order to establish inherency, "the missing characteristic must be ***necessarily present***, or inherent, in the single anticipating reference." Prelim. Resp. 17. Patent Owner contends that Petitioner has failed to establish that the ordinary artisan "would have inevitably measured the viscosity of the Johnson or Gustafsson formulations at 20ºC or that viscosity of the formulations would be between 20 cp and 600 cp." *Id.* at 18. Patent Owner argues also, as it did as to the challenge over Johnson, that the Tracy Declaration does not support Petitioner's contention that the ordinary artisan would have understood that the injection vehicle of Gustafsson meets the claimed viscosity limitation. *Id.* at 19–22.

We have considered Patent Owner's arguments, but do not find them persuasive at this stage of the proceeding. As noted above with the challenge based on Johnson and Kino, Gustafsson teaches an injection vehicle containing 3% CMC, and the evidence currently of record supports Petitioner that such an injection vehicle would inherently meet the viscosity limitation of independent challenged claim 1.

Patent Owner contends also that Gustafsson does not teach a microparticle as required by the challenged claims. Prelim. Resp. 22. Patent Owner asserts that "[t]he '061 patent defines 'microparticles' to mean 'particles that contain an active agent or other substance dispersed or dissolved within a polymer that serves as a matrix or binder of the particle.'" *Id.* (citing Ex. 1001, 5:15–18). In the microparticles of Gustafsson, however, Patent Owner asserts, the active agent "is entrapped in the core microparticle, and this core microparticle is then dried and subsequently coated with polymer so as to avoid any 'substantial or detrimental exposure of the active substance to organic solvent.'" *Id.* at 22–23. Patent Owner contends that Petitioner has not addressed how the microparticles of Gustafsson meet the limitation of "microparticles" as set forth in the '061 patent. *Id.* at 23.

We do not find Patent Owner's arguments persuasive at this stage of the proceeding. As Patent Owner notes, the '061 patent defines microparticles as "particles that contain an active agent or other substance dispersed or dissolved within a polymer that serves as a matrix or binder of the particle." Ex. 1001, 5:15–18. Thus, the definition of microparticle set forth by the '061 patent does not exclude a coating, such as that used by Gustafsson. The microparticles of Gustafsson meet that limitation, as the

active is entrapped, that is, dispersed or dissolved in the polymer of the microparticle, before the microparticle is coated. Ex. 1011, 7:3–10.

After considering the Petition and Preliminary Response, we determine that Petitioner has demonstrated a reasonable likelihood that claims 1–3, 6, 7, 17–19 are obvious over the cited prior art.

b. Claims 4, 5, 10, and 11

Petitioner notes that claim 4 adds the limitation of a density enhancing agent, and claim 5 specifies that the density enhancing agent is sorbitol. Pet. 41. As to claim 10, Petitioner notes that that it depends from claim 4, and adds a wetting agent, and claim 11 specifies "that the wetting agent is 'selected from the group consisting of polysorbate 20, polysorbate, 40, and polysorbate 80.'" *Id.*

Petitioner relies on Ramstack for teaching an aqueous vehicle containing CMC, mannitol, and Tween 80. *Id.* (citing Ex. 1005, 37:6; Ex. 1002 ¶¶ 58, 72). Petitioner asserts that the ordinary artisan would understand that that ingredients such as mannitol or sorbitol would increase the density of the injectable suspension. *Id.* (citing Ex. 1002 ¶¶ 72–74).

Petitioner then relies on the Handbook for teaching that wetting agents, such as Tween 80, mannitol, and sorbitol are commonly used in intramuscular injections. *Id.* at 42 (citing Ex. 1009, 294, 375, 477; Ex. 1002 ¶¶ 32, 72–74.

Patent Owner responds that Petitioner has not provided a reason to combine Gustafsson, Ramstack, and the Handbook, but only offers "conclusory and vague statements." Prelim. Resp. 33. Specifically, Patent Owner argues that Petitioner states that one would have combined Gustafsson and Ramstack to enhance the density of the aqueous solution, but

neither Gustafsson nor Ramstack teaches or suggests that the density of the solution needs to be enhanced. *Id.* at 34.

We agree with Patent Owner that Petitioner has not demonstrated a reasonable likelihood that claims 4, 5, 10, and 11 are obvious over the cited prior art. As the Supreme Court pointed out in *KSR*, "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. Rather, the Court stated:

> [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements *in the way the claimed new invention does* . . . because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Id. at 418-419 (emphasis added); *see also id.* at 418 (requiring a determination of "whether there was an apparent reason to combine the known elements *in the fashion claimed* by the patent at issue") (emphasis added).

Here, Petitioner points to where each of the elements are independently found in the cited prior art. The only reason to combine provided by Petitioner, however, is that the ordinary artisan would understand that ingredients such as mannitol or sorbitol would increase the density of the suspension. What is lacking from Petitioner's analysis is a reason, with rational underpinning, as to why the ordinary artisan would want to increase the density.

After considering the Petition and Preliminary Response, we determine that Petitioner has not demonstrated a reasonable likelihood that claims 4, 5, 10, and 11 are obvious over the cited prior art.

c. Claims 8, 9, 12, and 13

Petitioner notes that claim 8, which is dependent from claim 2, adds a wetting agent, and claim 9 specifies that the wetting agent "is 'selected from the group consisting of polysorbate 20, polysorbate, 40, and polysorbate 80.'" Pet. 43.

Petitioner notes further that claim 12, which is dependent from claim 6, adds a wetting agent, and claim 13 specifies that the wetting agent "is 'selected from the group consisting of polysorbate 20, polysorbate, 40, and polysorbate 80.'" *Id.* at 44.

Petitioner asserts that Gustafsson teaches all of the elements of claim 1 and 6, and Ramstack teaches an injection vehicle that includes 0.1% Tween 80. *Id.* at 44. Petitioner contends that both Gustafsson and Ramstack teach an injection vehicle that includes CMC, that CMC is a known viscosity enhancing agent, and that Tween 80 is a known wetting agent. *Id.* Thus, Petitioner contends, the ordinary artisan would have added a wetting agent, such as Tween 80, "to an injection vehicle to assist in suspendability." *Id.* at 44–45.

As to claims 8, 9, 12, and 13, Patent Owner argues that the only reason provided by Petitioner to combine Gustafsson and Ramstack to add a wetting agent, such as Tween 80, is to aid in suspendability. Prelim. Resp. 34. Patent Owner asserts that Petitioner relies on its Declarant, Dr. DeLuca to support that assertion, but argues that Dr. DeLuca does not provide a

reason as to why the ordinary artisan would have wanted to improve suspendability. *Id.* at 34–35 (citing Ex. 1002 ¶ 74; Ex. 1014, 288)

We do not find Patent Owner's arguments persuasive at this stage of the proceeding. Gustafsson teaches that CMC is added as an aid to suspension (Ex. 1011, 18:21–24), and, thus, provides a reason to adding other agents which may aid with suspendability, such as Tween 80. Ramstack demonstrates that it was known to add Tween 80 to injection vehicles to sustained release formulations comprising microparticles.

After considering the Petition and Preliminary Response, we determine that Petitioner has demonstrated a reasonable likelihood that claims 8, 9, 12, and 13 are obvious over the cited prior art.

d. Claims 20 and 21

As to claims 20 and 21, Petitioner notes that they depend from claims 17 and 19, and "specify that the 'active agent is selected from the group consisting of risperidone, 9-hydroxyrisperidone, and pharmaceutically acceptable salts thereof.'" Pet. 45. Petitioner asserts, however, that "Gustafsson teaches that the active may be any substance desirable for sustained or controlled release as a microparticle." *Id.* at 46 (citing Ex. 1011, 6:33–35; Ex. 1002 ¶ 79).

Petitioner notes that Ramstack teaches the use of polymers, such as 75:25 dl (polylactide-co-glycolide), may be used in a biodegradable polymer that incorporates a biologically active substance such as risperidone. *Id.* at 46 (citing Ex. 1005, Abstract, 5:19–22, 35:1–36:26, Example 2, Example 3; Ex. 1002 ¶ 80. Petitioner asserts, therefore, that the ordinary artisan "would expect to combine the risperidone microspheres of Ramstack and the

injection vehicle of Gustafsson with a reasonable expectation of success." *Id.* at 46–47 (citing Ex.1002 ¶ 80).

As to claims 20 and 21, Patent Owner argues that Petitioner does not offer a reason as to why the ordinary artisan "would replace the microspheres of Gustafsson with the microspheres of Ramstack and use the injection vehicle and concentration of microspheres of Gustafsson." Prelim. Resp. 35.

We do not find Patent Owner's arguments persuasive at this stage of the proceeding. Gustafsson teaches that its active may be any substance desirable for sustained or controlled release as a microparticle, and teaches an injection vehicle that Petitioner has sufficiently demonstrated meets the limitations of independent claim 1. Thus, it would have been obvious to the ordinary artisan that the injection vehicle of Gustafsson could be used for Ramstack's microparticles, as Gustafsson teaches that its injection vehicle aids in suspending the microparticles (Ex. 1011, 18:21–24).

After considering the Petition and Preliminary Response, we determine that Petitioner has demonstrated a reasonable likelihood that claims 20 and 21 are obvious over the cited prior art.

e. Claims 22 and 23

Petitioner notes that claim 22 depends from claim 1, and "specifies that the 'mass median diameter of said microparticles is less than about 250 μm.'" Pet. 47. Claim 23 "specifies that the 'mass median diameter of said microparticles is in the range of from about 20 μm to about 150 μm.'" *Id.*

Petitioner contends:

> Gustafsson teaches that the microparticles should be smaller than 200 μm so they can pass through an injection needle. (Exs.1011, at 1:19-23; 1002 ¶ 81.) Gustafsson states that the

> preferred average diameter for microparticles is 10-200 μm and most preferably, 40-60 μm. (Exs.1011, at 7:30-33; 1002 ¶ 81.). Gustafsson describes a process for preparing microparticles, which includes sieving the microparticles through a 160μm mesh. (Exs.1011, at 15:8-9; 1002 ¶ 81.) Thus Gustafsson teaches microparticles having a mass median diameter at least falling within the scope of claims 22 and 23. (Ex.10002 [sic] ¶ 81.) [The ordinary artisan] would appreciate that the mass median diameter of the Gustafsson microparticles would fall within the range recited by claims 22 and 23. (Ex.1002 ¶81.)

Id.

Similarly, Petitioner asserts that Ramstack teaches microparticles having a diameter of 1 to 5000 microns, preferably 25-180 microns, and teaches a process for preparing risperidone microparticles wherein the particles are sieved through a 25 to 80 micron sieve. *Id.* at 48 (citing Ex. 1005, 35:24–25; 36:24–25; Ex. 1002 ¶82). Thus, Petitioner asserts, the ordinary artisan would understand that the particles of Ramstack fall within the limitations of claims 22 and 23. *Id.* (citing Ex. 1002 ¶ 82).

After considering Petitioner's challenge and evidence, we determine that Petitioner has demonstrated a reasonable likelihood that claims 22 and 23 are obvious over the cited prior art.

f. Conclusion

Petitioner has demonstrated a reasonable likelihood that claims 1–3, 6–9, 12, 13, and 17–23 are rendered obvious by the combination of Gustafsson, Ramstack, and the Handbook. Petitioner, however, has failed to demonstrate a reasonable likelihood that claims 4, 5, 10, and 11 are rendered obvious by that combination.

D. Secondary Considerations

Patent Owner contends that trial should not be instituted as the Petition "presents no evidence regarding the critical 'objective indicia' of

non-obviousness, which are of record in this proceeding, were considered by the Examiner and are detailed throughout the patent specification." Prelim. Resp. 40. In particular, Patent Owner asserts Applicants

> presented compelling objective evidence that it was unexpected that increasing viscosity of a suspension would result in improved injectability and significantly reduce *in vivo* injectability failures. (Exh. 1001 at 4:47-60, Examples 1-4.) Such findings were unexpected because at the time of the invention, "conventional teachings [showed] that an increase in viscosity hinders injectabilty [sic]." (*Id*. at 4:60-62; *see also* Exh. 1014 at 33 ("Increases in the following characteristics tend to reduce syringeability or make material transfer through the needle more difficult: the viscosity of the vehicle . . . Probably the most important of these factors is viscosity."); Exh. 1014 at 287, 299.)

Id. at 41.

Patent Owner's arguments are not persuasive at this stage of the proceeding. In that regard, we note that the evidence of record currently supports sufficiently Petitioner's position that both Johnson and Gustafsson teach an injection vehicle that meets the claimed viscosity limitation. Moreover, the record regarding secondary considerations is incomplete. We, therefore, determine that it would be premature to reach any conclusion regarding secondary considerations. Any final decision will be based on the full record developed during the trial, including any evidence of secondary considerations.

III. CONCLUSION

For the foregoing reasons, we are persuaded that the Petition establishes a reasonable likelihood that Petitioner would prevail in showing

that claims 1–13 and 17–23 of the '976 patent is unpatentable under 35 U.S.C. §103(a).

Our determinations at this stage of the proceeding are based on the evidentiary record developed thus far. This decision to institute trial is not a final decision as to patentability of the claim for which *inter partes* review is instituted. Our final decision will be based on the full record developed during trial.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that pursuant to 35 U.S.C. §314(a), an *inter partes* review is hereby instituted on the following grounds:

Claims 1–13, 22, and 23 are rendered obvious by the combination of Johnson and Kino; and

Claims 1–3, 6–9, 12, 13, and 17–23 are rendered obvious by the combination of Gustafsson, Ramstack, and the Handbook.

FURTHER ORDERED that no other proposed grounds of unpatentability are authorized; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this Decision.

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