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Paper No. 9
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AMNEAL PHARMACEUTICALS LLC.,
Petitioner,

v.

PURDUE PHARMA L.P.,
THE P.F. LABORATORIES, INC., and
PURDUE PHARMACEUTICALS L.P.
Patent Owners.

Case IPR2016-01413
Patent 9,034,376 B2

Before MICHAEL P. TIERNEY, LORA M. GREEN, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges.*

PAULRAJ, *Administrative Patent Judge.*

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

I. INTRODUCTION

Amneal Pharmaceuticals LLC ("Petitioner") filed a Petition (Paper 1, "Pet."), requesting institution of an *inter partes* review of claims 1–13 and 16–19 of U.S. Patent No. 9,034,376 B2 (Ex. 1001, "the '376 patent"). Purdue Pharma L.P., The P.F. Laboratories, Inc., and Purdue Pharmaceuticals L.P.. (collectively, "Patent Owner") timely filed a Preliminary Response (Paper 7, "Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Upon consideration of the Petition and the Preliminary Response, and for the reasons explained below, we determine that Petitioner has shown that there is a reasonable likelihood that it would prevail with respect to at least one of the challenged claims. We thus institute an *inter partes* review of claims 1–13 and 16–19 of the '376 patent.

A. Related Proceedings

The '376 Patent is asserted in two civil actions pending in the United States District Court for the District of Delaware captioned *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, 15-831, filed September 17, 2015 (Ex.1002) and *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, 15-1152, filed December 15, 2015 (Ex.1003). Pet. 1; Paper 5, 1. A related patent, U.S. Patent No. 8,337,888 ("the '888 patent"), was the subject of a district court proceeding in the Southern District of New York captioned *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, No. 13-3372 ("the SDNY Litigation") (Ex.1005). Pet. 1–2. The Federal Circuit upheld

the invalidity of the claims of the ’888 patent on April 8, 2016 (Ex. 1006). *Id.*

Additionally, in IPR2016-01412, Petitioner filed a separate Petition challenging the same claims of the ’376 patent on other grounds. Pet. 2; Paper 5, 1. Petitioner previously filed petitions in IPR2016-01027 and IPR2016-01028 seeking cancellation of claim 1 of U.S. Patent No. 9,060,976, which is another member of the same patent family. *Id.*

B. The ’376 Patent (Ex. 1001)

The ’376 patent issued on May 19, 2015, with Curtis Wright, Benjamin Oshlack, and Christopher Breder as the listed co-inventors. Ex. 1001. The ’376 patent is a continuation of application number 13/349,449, which issued as the ’888 patent. *Id.*

The ’376 patent notes that opioid analgesics may sometimes be subject to abuse. *Id.* at 1:21. According to the ’376 patent, the opioid analgesic may be more potent when administered parenterally as compared to the same dose administered orally. *Id.* at 1:22–224. The ’376 patent discloses that “[o]pioid antagonists have been combined with certain opioid agonists in order to deter the parenteral abuse of opioid agonists,” but states that there is still a need of opioid dosage forms that are less subject to abuse. *Id.* at 1:36–38, 2:13–15. Thus, the ’376 patent discloses “oral dosage forms . . . comprising an opioid analgesic; and an aversive agent or agents as a component(s) of the dosage form helps to prevent injection, inhalation, and/or oral abuse by decreasing the ‘attractiveness’ of the dosage form to a potential abuser.” *Id.* at 2:46–51.

According to the ’376 patent:

> In certain embodiments of the present invention, the dosage form comprises an aversive agent such as a gelling agent to discourage an abuser from tampering with the dosage form and thereafter inhaling, injecting, and/or swallowing the tampered dosage form. Preferably, the gelling agent is released when the dosage form is tampered with and provides a gel-like quality to the tampered dosage form which slows the absorption of the opioid analgesic such that an abuser is less likely to obtain a rapid "high". In certain preferred embodiments, when the dosage form is tampered with and exposed to a small amount (e.g., less than about 10 ml) of an aqueous liquid (e.g., water), the dosage form will be unsuitable for injection and/or inhalation. Upon the addition of the aqueous liquid, the tampered dosage form preferably becomes thick and viscous, rendering it unsuitable for injection.

Id. at 3:1–15. Moreover, the '376 patent defines the term "unsuitable for injection" "to mean one would have substantial difficulty injecting the dosage form (e.g., due to pain upon administration or difficulty pushing the dosage form through a syringe) due to the viscosity imparted on the dosage form, thereby reducing the potential for abuse of the opioid analgesics in the dosage form." *Id.* at 3:15–22.

The '376 teaches identifies hydroxypropyl methylcellulose (HPMC) and polyethylene oxide (PEO) among the possible gelling agents that may be employed. *Id.* at 6:46–62. The '376 patent also teaches that the dosage form employing the aversive agents may be "controlled release" oral dosage form that "provides effective pain relief for at least 12 hours, or at least about 24 hours when orally administered to a human patient." *Id.* at 3:44–50.

C. District Court Proceeding Involving the '888 Patent (the SDNY Litigation)

According to the district court in the SDNY Litigation, the '888 patent relates to "a controlled release oral dosage form containing oxycodone that forms a gel when dissolved in an aqueous liquid," wherein the "gelling properties . . . enable it to resist abuse by injection, snorting, and oral ingestion." Ex. 1005, 1. Claim 1 of the '888 patent is reproduced below:

> 1. A controlled release oral dosage form comprising:
>
> from about 2.5 mg to about 320 mg oxycodone or a pharmaceutically acceptable salt thereof; and
>
> a gelling agent comprising polyethylene oxide in an effective amount to impart a viscosity of at least about 10 cP when the dosage form is subjected to tampering by dissolution in from about 0.5 to about 10 ml of an aqueous liquid;
>
> the dosage form providing a therapeutic effect for at least about 12 hours when orally administered to a human patient.

Ex. 1004, 40:22–32.

The district court concluded that the '888 patent was invalid as obvious. Ex. 1005, 40. Specifically, the district court found that the prior art teaches that gelling agents prevent potential abuse (*id.* at 41), and that the prior art teaches that PEO acts both as an agent to control the rate of release in sustained release dosage forms and as a gelling agent (*id.* at 43).

The Court of Appeals for the Federal Circuit, our reviewing court, affirmed the decision of the district court in a short per curium order. Ex. 1006. Specifically, the Federal Circuit held:

> The judgment of the United States District Court for the Southern District of New York is affirmed on the ground that the court did not err in concluding that the asserted claims of U.S. Patent No. 8,337,888 would have been obvious.

Id. at 2.

D. Illustrative Claim

Petitioner challenges claims 1–13 and 16–19 of the '376 patent. Independent claim 1 is illustrative, and is reproduced below:

> 1. A controlled release oral solid dosage form comprising:
>
> a controlled release matrix comprising a mixture of (i) from 2.5 mg to 320 mg oxycodone or a pharmaceutically acceptable salt thereof; and
>
> (ii) a gelling agent comprising polyethylene oxide and hydroxypropylmethylcellulose, the gelling agent in an effective amount to impart a viscosity of at least 10 cP when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid;
>
> the controlled release matrix providing a therapeutic effect for at least 12 hours when orally administered to a human patient.

Independent claims 18 and 19 also recite controlled release oral dosage form with the same ingredients recited in claim 1, but require the gelling agent in an effective amount to impart a viscosity either "unsuitable for parenteral administration" (claim 18) or "unsuitable to pull into an insulin syringe" (claim 19) when the dosage form is subject to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid, and further require that the oral dosage form "does not comprise a semipermeable wall."

D. The Asserted Ground of Unpatentability

Petitioner challenges the patentability of the claims of the '376 patent based on the following ground:

References	Basis	Claims challenged
Royce,[1] McGinity,[2] Hoffmeister,[3] Joshi,[4] and PDR[5]	§ 103(a)	1–13 and 16–19

Petitioner further relies upon the declaration of Anthony Palmieri III, Ph.D. (Ex. 1007) ("Palmieri Decl.").

II. ANALYSIS

A. Claim Construction

We interpret claims using the "broadest reasonable construction in light of the specification of the patent in which [they] appear[]." 37 C.F.R. § 42.100(b); *see also Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under the broadest reasonable construction standard, claim terms are generally given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc*., 504 F.3d 1249, 1257 (Fed. Cir. 2007). "Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition." *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004). "Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity,

[1] Royce, U.S. Patent 5,273,758, issued Dec. 28, 1993 (Ex. 1022) ("Royce").
[2] McGinity et al, WO 97/49384, published Dec. 31, 1997 (Ex. 1024) ("McGinity").
[3] Hoffmeister et al., U.S. Patent 4,070,494, issued Jan. 24, 1978 (Ex. 1010) ("Hoffmeister").
[4] Joshi et al., Pub. No. US 2002/0187192 A1, published Dec. 12, 2002 (Ex. 1014) ("Joshi").
[5] OxyContin entry in Physicians' Desk Reference, 2569–74 (53d ed., 1999) (Ex. 1016)("PDR").

deliberateness, and precision." *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

At this stage of the proceeding, we determine that no explicit construction of any claim term is necessary to determine whether to institute a trial in this case. *See 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 Analysis

1. Content of the Prior Art

Petitioner relies upon the following prior art in its challenges.

a. Royce (Ex. 1022)

Royce discloses the use of a polyethylene oxide (PEO) as a binder matrix in a sustained release dosage form, and notes that "the [PEO] has an adjustable rate control effect on the release of the medicament from the dosage form." Ex. 1022, Abstract.

Royce teaches that PEO is "a water soluble resin which is available . . . in several grades which vary in viscosity profile when dissolved in water." *Id.* at 2:68–3:2. According to Royce, the "[m]olecular weights [of PEO] range from about 100,000 to about 6,000,000, corresponding to a viscosity range of under about 200 cps for a 5% aqueous solution of the lower molecular weight polymers to over about 6,200 cps for a 1% solution of the higher molecular weight polymers." *Id.* at 3:3–8. For example, a 5% aqueous solution of Polyox® WSR (with an average molecular weight of about 200,000) is measured to have a viscosity of about 65 to 115 cps, and a

1% aqueous solution of Polyox® WSR 303 (with an average molecular weight of about 5,000,000 to 6,000,000) was measured to have a viscosity of 7,200 to 10,000 cps. *Id.* at 3:14–23.

In addition to PEO, Royce discloses that "[o]ther optional components of the compositions of the invention include various binders, . . . such as hydroxypropyl methylcellulose." *Id.* at 3:50–53. The active drugs that can be delivered according to Royce's dosage form include, *inter alia*, "analgesics." *Id.* at 4:44–53. Royce discloses that the "[t]ablets of the invention provide a gradual, controlled release of the medicament over an extended period of time." *Id.* at 5:44–46. Figure 1 of Royce is a chart that discloses the cumulative amount of medicament dispensed over an extended period of time (18 hours). *Id.* at 5:41–43.

In Example 2, Royce discloses formulations of placebo tablets prepared "by mixing 98.7 mg of polyethylene oxide having a molecular weight of (a) about 200,000 (Polyox®. N80) or (b) about 6,000,000 (Polyox® 303), with 11.0 mg. of hydroxypropyl methylcellulose (Pharmocoat 606)." *Id.* at 5:49–53. Royce teaches that the use of "higher molecular weight polyethylene-oxide-based tablets do not disintegrate under standard testing procedures, indicating suitability as a sustained release form." *Id.* at 6:2–5.

b. McGinity (Ex. 1024)

McGinity discloses pharmaceutical formulations in which the formulation has been prepared "by hot-melt extrusion of mixtures containing high molecular weight PEO and a therapeutic compound for use in controlled release drug delivery." Ex. 1024, 1:8–12. According to McGinity, "[i]t [had] not been appreciated that a high molecular weight PEO

based therapeutic compound containing composition can be hot melt extruded without significant degradation or decomposition of either the PEO or therapeutic compound." *Id.* at 2:15–17.

McGinity teaches that the PEO may have an average molecular weight of from about 1,000,000 to 10,000,000, with the PEO not exceeding 99.99% by weight of the formulation. *Id.* at 5:2–4, 11–12. The formulation of McGinity may also contain a plasticizer, wherein the plasticizer may be a low molecular weight PEO having a molecular weight less than 500,000. *Id.* at 6:4–27.

With respect to the therapeutic compound, McGinity teaches that the structure of that compound is not critical, as long as it can diffuse from the formulation upon exposure to a biological fluid. *Id.* at 7:20–24. McGinity specifically teaches that the therapeutic compound may be "analgesics such as aspirin, acetaminophen, deflunisal and the like." *Id.* at 8:18–20.

c. Hoffmeister (Ex. 1010)

Hoffmeister teaches the incorporation of a non-toxic gelable material in pharmaceutical compositions in order to inhibit the aqueous extraction of the medicinal agents for parenteral abuse. Ex. 101, Abstract. Hoffmeister notes that "many analgesics" can cause physical and psychic dependence, and therefore be abused by people who are dependent on opiate-like substances. *Id.* at 1:29–38. In order to address this problem, Hoffmeister teaches:

> a method of inhibiting the water extractability from an enteral pharmaceutical composition of a medicinal agent having a high abuse potential which comprises incorporating in said composition, a nontoxic, aqueously gelable material, said gelable material being present in said composition in a quantity at least sufficient to form a gel with substantially no residual filterable

> liquid when combined with that volume of water otherwise necessary to dissolve all of said medicinal agent.

Id. at 1:67–2:8.

Hoffmeister teaches that "[e]xamples of suitably aqueously gelable materials include . . . methylhydroxypropylcellulose [i.e., HPMC]," and that "[m]ixtures of two or more gel-producing substances can be used if desired." *Id.* at 2:18–24. The formulation of Example 5 in Hoffmeister includes HPMC. *Id.* at 6:21. Hoffmeister also teaches that the concentration of the gelable material can range from about 5 to about 40% by weight of the medicament. *Id.* at 2:44–48.

In Table 1, Hoffmeister summarizes the results of a solubility test on propiram tablets with and without added 4,000 cp methylcellulose used as a gelable material. *Id.* at cols. 3–4 (Table 1). The amount of distilled water used for the extraction was either 10 ml or 20 ml. *Id.* Royce states that "[t]he results summarized in Table 1 clearly show that the extractability with water of the active compound, which in itself is readily water-soluble, can be severely inhibited or completely prevented by adding a water gelable material, such as a methylcellulose," and the "[t]he potential for abuse of these preparations is thus substantially reduced." *Id.* at 3:58–64.

d. Joshi (Ex. 1014)

Joshi is drawn to a pharmaceutical composition that reduces drug abuse, wherein the composition comprises a central nervous system stimulant and a gel forming polymer. Ex. 1014 ¶ 1. According to Joshi, adding a gel forming polymer to the composition "reduces or eliminates potential drug abuse by swelling in the presence of moisture which is, for example, present in the dermis layer of skin and mucous membrane, and thus, prevents nasal absorption and injectability of the drug." *Id.* ¶ 9.

Joshi teaches that PEO is a preferred gel forming polymer, and that the polymer may have a molecular weight "from about 70,000 to about 2,000,000." *Id.* ¶¶ 21–22. The gel forming polymer is from about 2 to about 40 weight percent of the composition. *Id.* ¶ 23. The tablets are prepared, for example, by forcing the solid ingredients through a mesh, blending the solid ingredients, and compressing them into a tablet. *Id.* ¶ 37. Joshi teaches also that additional agents that are commonly used to prepare oral pharmaceutical dosage forms may also be used, such as enteric coatings. *Id.* ¶ 26.

Joshi references WO 97/33566 in its "Background of the Invention," which teaches an opioid composition that deters abuse, wherein an opioid antagonist is incorporated into the system to reduce the effect of the opioid. *Id.* ¶ 6.

e. PDR (Ex. 1016)

PDR teaches that "OxyContin® (oxycodone hydrochloride controlled-release) tablets are an opioid analgesic supplied in 10 mg, 20 mg, 40 mg, and 80 mg tablet strengths for oral administration." Ex. 1016, 2569. PDR teaches that a study comparing 10 mg of OxyContin every 12 hours to 5 mg of immediate-release oxycodone every 6 hours shows that the two treatments were equivalent with respect to both the extent of absorption (AUC) and peak plasma concentration (C_{max}) and similar for C_{min} (trough) concentrations. *Id.* at 2570. PDR also teaches that patients should be advised that OxyContin is a potential drug of abuse. *Id.* at 2572.

2. Obviousness over Royce, McGinity, Hoffmeister, Joshi, and PDR

Petitioner asserts that claims 1–13 and 16–19 are rendered obvious by the combination of Royce, McGinity, Hoffmeister, Joshi, and PDR. Pet. 21–

41. Petitioner presents a claim chart for each of the challenged claims. *Id.* at 41–53. Petitioner contends that the challenge presented in its Petition "is based generally on art considered and relied upon in the SDNY Litigation." *Id.* at 21. Petitioner states that "[t]he most significant difference between the invalidated claims of the ''888 Patent and those challenged here is the addition of HPMC as a gelling agent with PEO." *Id.* at 23. Petitioner, however, also notes that "the very art the court relied on included HPMC, not only identifying it as a gelling agent that could be used for abuse deterrence (*see* Hoffmeister (Ex.1010)), but also describing combinations of HPMC and PEO in a controlled release dosage form (*see* Royce (Ex.1022))." *Id.*

Petitioner acknowledges that Royce does not teach oxycodone or a salt thereof in an amount of 2.5 mg to 320 mg as claimed, but points to McGinity's disclosure of dosage form of "analgesics . . . and the like." Pet. 31. The district court in the SDNY Litigation found that in the context of abuse-prone drugs, McGinity's disclosure of "analgesics . . . and the like" includes controlled release oxycodone. Exs.1005, 37. This determination was upheld by the Federal Circuit. Ex. 1017, 20. Petitioner also points to PDR's teaching that oxycodone HCL is an analgesic provided in doses of 10mg, 20mg, 40 mg, and 80 mg in an extended release format. *Id.* at 31–32 (citing Ex. 1016, 2569; Ex. 1007 ¶ 87). Petitioner contends that "[t]he mere substitution of one analgesic for another is not an invention and providing oxycodone in amounts that were known per se would be obvious," and, thus, "[i]t would be obvious to use the claimed amount of oxycodone HCl as the analgesic in Royce." *Id.* at 32.

Petitioner further asserts that "Royce teaches a formulation that includes both PEO and HPMC as claimed," and "Hoffmeister and Joshi would confirm that both are known gelling agents." *Id.* (citing Ex.1022, 3:31–54, 5:47–6:5, Example 2; Ex. 1010, 2:18–25; 1014, ¶¶ 15, 19, 20; 1007 ¶ 88). With respect to the claim requirement of providing a therapeutic effect for at least 12 hours, Petitioner also relies upon Royce as teaching a controlled release for a period of 18 hours, and McGinity as teaching a controlled release oxycodone, which provides relief for 12 hours. *Id.* (citing Ex. 1022, 5:10–46, Example 1, Fig. 1; Ex. 1016, 2570).

With respect to the requirement that the gelling agent is used in an effective amount to impart a viscosity that would provide abuse deterrence, as recited in independent claims 1, 18, and 19, Petitioner relies upon Royce's teaching that various viscosities can be obtained by using different amounts of PEO, which can range from 65–115 cps for lower molecular weight PEO and 7200 to 10,000 cps for higher molecular weight PEO. *Id.* at 34 (citing Ex. 1022, 3:14–23; Ex. 1007 ¶ 92). Petitioner also asserts that the skilled artisan would "appreciate that the viscosity of solutions can vary with the amount of PEO and/or HPMC and their grade/molecular weight," and, thus, obtaining the claimed viscosities, whether expressed numerically or functionally, could be obtained by routine experimentation. *Id.* (citing Ex. 1007 ¶ 93). Petitioner relies upon a similar optimization rationale with respect to the more specific viscosities recited in dependent claims 2–6. *Id.* at 38–39.

With respect to the volume of liquid used for dissolving the dosage form in order to determine the viscosity of the gelling agent, Petitioner relies upon Hoffmeister's teaching that 10 ml of distilled water was used for

extraction and Joshi's teaching that 1 ml of water was used for testing. *Id.* at 36 (citing Ex. 1010, 3:35; Ex. 1014, ¶¶ 42–43). Petitioner relies upon the same teachings of Hoffmeister and Joshi to allege the obviousness of dependent claims 8 (specifying that the aqueous liquid is water), 9 (specifying dissolution in 1 to 3 ml of aqueous liquid), and 12 (specifying tampering by dissolution in the aqueous liquid after crushing). *Id.* at 38–39. With respect to claim 13 (specifying tampering by dissolution in the aqueous liquid after heating at greater than 45 °C), Petitioner contends that a skilled artisan "would appreciate that viscosity measurements are dependent on the temperature at which the viscosity is taken," and that "[o]btaining a viscosity of greater than 120cp at 45 degrees would be a matter of routine experimentation and optimization." *Id.* at 40–41.

With respect to the ratio of gelling agent to drug recited in dependent claim 7 (40:1 to 1:40), Petitioner relies upon Royce's teaching that the amount of medicament can range from 0.01 to 95 wt% while the amount of PEO can vary from 5 to 99.99 wt%, which overlaps the claimed range. *Id.* (citing Ex. 1022, 2:37–42; Ex. 1007 ¶ 102). Petitioner also relies upon amount of gelling material taught by Hoffmeister (e.g., 5–40% by weight relative to medicament) and the ratios exemplified by Joshi (i.e., 4:1 to about 1:3.34). *Id.* at 39–40 (citing Ex. 1010, 2:44–46, 56–61; Ex. 1014 ¶¶ 36, 38, 40; Ex. 1007 ¶ 102). Based on these teachings, Petitioner contends that the claimed range is obvious.

With respect to the requirement in dependent claim 10 specifying the salt oxycodone hydrochloride and the further requirement in dependent claim 11 specifying a dosage of 10–80 mg of that salt, Petitioner relies upon the teaching in PDR that OxyContin® satisfies those requirements, and on

that basis asserts it would have been obvious to use oxycodone within the recited dosage amount range as the active ingredient of the formulation. *Id.* at 40 (citing Ex. 1016, 2569; Ex. 1007 ¶ 103).

With respect to the requirement in dependent claim 16 that the dosage form is "without a semipermeable wall" (also recited in independent claims 18 and 19), Petitioner asserts that the skilled artisan would understand this to preclude the dosage form from being an osmotic device. *Id.* at 37 (citing Ex. 1001, 24:37–46; Ex. 1007 ¶ 98). Petitioner contends that none of the references relied upon in the Petition include a semipermeable wall, thereby satisfying this requirement. *Id.*

With respect to the requirement in dependent claim 17 that the dosage form further comprise a film coat, Petitioner asserts that Hoffmeister and Joshi teach the use of coatings, which renders this claim obvious. *Id.* at 41 (citing Ex. 1010, 3:20–21; Ex. 1014 ¶ 26; Ex. 1007 ¶ 105).

We have considered the arguments and evidence presented by Patent Owner in its Preliminary Response. As an initial matter, we note that Patent Owner relies heavily upon the Declaration of Stephen Byrn, Ph.D. to support its arguments. Ex. 2001 ("Byrn Decl."). Although Dr. Byrn disagrees with Petitioner's Declarant, Dr. Palmieri, on many issues of fact, our rules provide that "a genuine issue of material fact created by such testimonial evidence will be viewed in the light most favorable to the petitioner solely for purposes of deciding whether to institute an *inter partes* review." 37 C.F.R. 42.108(c). Accordingly, we resolve any disputed factual issues in the parties' Declarations in Petitioner's favor at this stage.

Patent Owner argues that the Petition does not explain why the skilled artisan would look to the references cited in the Petition in the first place.

Prelim. Resp. 38–43. More specifically, Patent Owner contends that that the problem confronting the skilled artisan at the time of the '376 patent would have been the abuse of original OxyContin®, and the skilled artisan would not have considered Royce or McGinity, both of which are directed to controlling release using PEO, a completely different agent from that successfully used in original OxyContin® for achieving extended release. *Id.* at 39–40. Similarly, Patent Owner argues that the skilled artisan would have started with original OxyContin® and attempted to add abuse deterrence. *Id.* at 43–47. Patent Owner further argues that the skilled artisan "developing an extended-release oxycodone formulation would not have looked to Hoffmeister or Joshi because both relate only to immediate-release dosage forms." *Id.* at 42.

We are not persuaded by these arguments on the current record. The challenged claims are broadly directed to conferring abuse deterrence on sustained release formulations of oxycodone generally, rather than only a specific improvement upon the previously-existing OxyContin® formulation. For instance, the other ingredients besides oxycodone HCl included the original OxyContin formulation are not recited in the claims of the '376 patent. Prelim. Resp. 45 (citing Ex. 2025, Table 7). As such, we determine that the record at this stage supports a conclusion that the skilled artisan would have considered Royce and McGinity, which discuss sustained release formulations that could have been used for analgesics (and which would have been understood to include oxycodone as found in the SDNY Litigation). The record at this stage also supports a conclusion that the skilled artisan would have looked to Joyce and Hoffmeister, as the use of a gelling agent to address the problem of oxycodone abuse would have been

considered relevant regardless of whether the drug was contained in a sustained-release or immediate-release formulation. *See In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004) (a prior art reference may be considered in an obviousness analysis if the "art is from the same field of endeavor, regardless of the problem addressed" or if it "is reasonably pertinent to the particular problem with which the inventor is involved").

Patent Owner also argues that there has been no showing of why the skilled artisan would have come up with the specific combination of two gelling agents. Prelim. Resp. 47–52. Patent Owner contends that the use of gelling agents would have an "unpredictable influence" of the drug's release profile and could "trap" the drug, and "[i]t is especially not predictable how a combination of two structurally different polymers would influence viscosity." *Id.* at 50. We are unpersuaded based on the current record, as we find that Royce teaches the use of both PEO and HPMC in a single formulation. Ex. 1022, 5:49–53. As such, we determine that no further reason is required to come up with the specific combination of gelling agents when both ingredients are already taught by Royce's formulation, albeit for a different purpose. Although Royce does not recognize that the PEO and HPMC polymers may serve as gelling agents that impart abuse deterrence, the skilled artisan need not have recognized that property of those components in order to render the claims obvious. *See Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, 424 F.3d 1293, 1323 (Fed. Cir. 2005) ("One of ordinary skill in the art need not see the identical problem addressed in a prior art reference to be motivated to apply its teachings."). In addition, as noted above, Hoffmeister and Joshi teach that PEO and HPMC both may be used as abuse-deterrent gelling agents. Moreover, the

fact that Royce's Example 2 only discloses both PEO and HPMC in a placebo formulation does not negate obviousness, as the conclusion reached in Royce with respect to that example is that high molecular weight PEO-based tablets "do not disintegrate under standard testing procedures, indicating suitability as a sustained release dosage form." Ex. 1022, 6:2–5. Thus, even though the formulations of Example 2 only used a placebo, the record at this stage supports a conclusion that the skilled artisan would have understood that such a sustained release dosage form could be used to deliver an active drug, including an analgesic such as oxycodone. *Id.* at 4:44–53. The fact that the existing OxyContin® formulation provided a therapeutic effect for a 12 hour period would have motivated the skilled artisan to adjust the amounts of the ingredients used in Royce's formulation to provide a similar therapeutic effect. Ex. 1016, 2570.

We are also unpersuaded by Patent Owner's argument that the references cited in the Petition fail to disclose the claimed viscosity elements. Prelim. Resp. 57–59. With respect to claims 1 and 3–6, which recite specific numeric viscosities, Patent Owner argues that "the viscosity of a PEO or an alkylcellulose (or the molecular weight of a substance) is not the viscosity of a tampered dosage form, let alone the claimed dosage forms, which are not disclosed in Royce or any other of Amneal's references, alone or in combination. *Id.* at 58 (citing Ex. 2001 ¶ 41). With respect to claim 9, which recites that the viscosity is imparted when the dosage form is dissolved in 1 to 3 ml of aqueous liquid, Patent Owner argues that "Joshi does not even report viscosities . . . ; rather only molecular weights, and those molecular weights are of PEO, not a tampered oxycodone dosage form. *Id.* (citing Ex. 1007 ¶ 100; Ex. 2001 ¶55). With respect to claims 18

and 19, which recite the viscosity in functional terms, Patent Owner argues that Petitioner "failed to provide any basis for its position that the viscosity disclosures in the references will produce the claimed viscosities for the claimed dosage forms" and "does not explain how its references would have taught the effect of the claimed combination of gelling agents on viscosity." *Id.* at 59. However, as discussed above, Royce teaches that the viscosity profile of PEO when dissolved in water depends upon the molecular weight of the polymer, which can affect whether the formulation is suitable as a sustained release dosage form. Ex. 1022, 3:1–23, 6:2–5. Hoffmeister and Joshi both teach that the extractability of drug from water can be inhibited using a gelling agent. Ex. 1010, 3:58–62; Ex. 1014, ¶ 43. As such, the record supports a finding that a skilled artisan would have found it obvious to adjust the molecular weights of the PEO and HPMC polymers used in Royce's formulation in order to obtain a viscosity greater than 10 cp when dissolved in water so as to achieve both optimized sustained release and reduce the potential for abuse of the drug by making it unsuitable for injection.

Additionally, Patent Owner argues that the art taught away from using a gelling agent in an extended-release formulation to deter abuse. Prelim. Resp. 52–57. Patent Owner relies on Bastin[6] as discouraging the use of gelling agents. *Id.* at 52. Patent Owner asserts that Bastin teaches a combination in which only 50% of the drug was released within two hours, and suggests that the gelling agent should be reduced, but that reduction may result in limiting the abuse resistance potential of the tablet. *Id.* at 52–53

[6] Bastin et al., WO 95/20947, published August 10, 1995 (Ex. 1015) ("Bastin").

(citing Ex. 1015, 28:1–22, 5:29–362). According to Patent Owner, Bastin teaches, therefore, "that including amounts of gelling agents sufficient to resist abuse of extended-release products would disrupt the carefully calibrated release of drug—an attribute critical to extended-release formulations such as OxyContin®." *Id.* at 53 (citing Ex. 2001 ¶ 99). Thus, Bastin teaches an approach of layering the drug and active agent, essentially separating them, and focusing on an immediate release formulation. *Id.* (citing Ex. 1015, Abstract, 1:3–7, 5:21–27; Ex. 2001 ¶ 99)). Patent Owner asserts that "Bastin's teaching that combining abuse-deterrence and extended-release properties results in an 'inoperative' formulation teaches away from the '976 claim." *Id.* at 54.

Patent Owner relies also on the CPDD Paper[7] as teaching away from challenged claim 1. *Id.* at 55. Specifically, Patent Owner argues that paper taught the use of extended release formulations, such as original OxyContin, or the inclusion of antagonists, but does not suggest the use of gelling agents. *Id.*

We determine, consistent with the district court determination in the SDNY Litigation, that Bastin does not teach away from the challenged claims. Specifically, the portions of Bastin relied upon by Patent Owner relate to immediate release formulation, not extended release dosage forms. As stated by the district court:

> Placed in its proper context, Bastin provides very little support to Purdue. Bastin expressed concern about gelling

[7] James Zacny et al., *College on Problems of Drug Dependence Taskforce on Prescription Opioid Non-Medical Use and Abuse: Position Statement*, 69 DRUG AND ALCOHOL DEPENDENCE 215–232 (2003) (Ex. 2009) ("CPDD Paper").

> agents' effect on drug release only with respect to immediate release formulations, for which delay poses a serious problem. By drawing an explicit comparison between gelling agents and the swelling properties of rate controlling high molecular weight polymers Bastin in fact implies that gelling agents are well-suited to controlled release dosage forms. And although all of the gelling patents focus primarily on immediate release tablets, Bastin notes that its invention may include a sustained release coating or "materials known in the art intended for the modification of release characteristics of the drug." Although the '888 Patent may be the first patent to disclose in detail controlled release dosage forms that utilize gelling agents to deter abuse, the Court cannot find that the prior art taught away from such formulations.

Ex. 1005, 46–47 (citations and footnote omitted).

In addition, the CPDD paper has a publication date of 2003. Ex. 2009, 215. The challenged patent claims a priority date as early as August 6, 2001. Ex. 2001, Title Page. Thus, as noted by the district court, the CPDD Paper was not prior art to the '888 patent (Ex. 1005, 45 n.13), and is not prior art to the '376 patent, which is a continuation of '888 patent. Patent Owner, at this stage of the proceeding, does not point us to any evidence that the CPDD paper reflects the understanding of the ordinary artisan at the time of invention. Thus, as the paper was not available until 2003, two years after the time of invention, it could not have discouraged the ordinary artisan from including a gelling agent at the time of invention.

Accordingly, for the foregoing reasons, we determine that Petitioner has demonstrated a reasonable likelihood of prevailing with respect to its obviousness challenge of claims 1–13 and 16–19 based on the combination of Royce, McGinity, Hoffmeister, Joshi, and PDR.

C. 35 U.S.C. § 325(d)

Patent Owner also argues that Petitioner's challenge should be rejected because it was already considered and dismissed by the PTO. Prelim. Resp. 28–36. In particular, Patent Owner argues that the Examiner considered and addressed the SDNY decision during prosecution of the '376 patent, and that the issues presented in the SDNY Litigation are similar to the arguments set forth in the Petition. *Id.* Patent Owner also argues that the Examiner recognized, in allowing later applications in the same patent family, that the skilled artisan "would have avoided gelling agents based on their unpredictable behavior in pharmaceutical formulations." *Id.* at 55–57.

Denial of institution under § 325(d) is a matter of discretion. We are not persuaded that denial on that basis is an appropriate exercise of discretion here. Although the prior art considered in the SDNY Litigation overlap with those presented in the Petition, the obviousness of claims that required both PEO and HPMC in a sustained release formulation was not specifically at issue in that proceeding. Likewise, the fact that the Examiner may have allowed later applications in the same patent family, is not relevant to the specific patentability challenge presented in the Petition with regard to the '376 patent claims. The Petition presents additional arguments and evidence beyond what was already considered by the Examiner, including those presented in the Palmieri Declaration (Ex. 1007). Accordingly, we do not find that "the same or substantially the same prior art or arguments previously were presented to the Office." 35 U.S.C. § 325(d).

III. CONCLUSION

We conclude that Petitioner has established a reasonable likelihood of prevailing on its assertion that claims 1–13 and 16–19 of the '376 patent are unpatentable as obvious.

At this stage of the proceeding, the Board has not made a final determination as to the patentability of any challenged claim or the construction of any claim term. Thus, our view with regard to any conclusion reached in the foregoing could change upon consideration of Patent Owner's merits response and upon completion of the current record.

IV. ORDER

Accordingly, it is:

ORDERED that, pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted as to claims 1–13 and 16–19 of U.S. Patent No. 9,034,376 B2 based on the following ground of unpatentability:

A. Claims 1–13 and 16–19 under 35 U.S.C. § 103(a) as obvious over the combination of Royce, McGinity, Hoffmeister, Joshi, and PDR.

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(a), *inter partes* review of the '376 patent is hereby instituted commencing on the entry date of this Order, and 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.

FURTHER ORDERED that the trial is limited to the grounds of unpatentability listed above, and no other grounds of unpatentability are authorized for *inter partes* review.

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