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 IPR2016-01027
Patent No. 9,060,976

PATENT OWNERS' NOTICE OF APPEAL

Office of the General Counsel
Patent and Trademark Office
Madison East
10B20 600 Dulany Street
Alexandria, VA 22314

Notice is hereby given, pursuant to 37 C.F.R. § 90.2(a), that Patent Owners Purdue L.P., The P.F. Laboratories, Inc. and Purdue Pharmaceuticals L.P. (collectively, "Purdue") appeal under 35 U.S.C. §§ 141 and 142 to the United States Court of Appeals for the Federal Circuit from the Final Written Decision entered on November 8, 2017 (Paper No. 48) (the "Final Written Decision"), and all underlying orders, decisions, rulings, and opinions. A copy of the Final Written Decision is attached.

In accordance with 37 C.F.R. § 90.2(a)(3)(ii), Purdue further indicates that the issues on appeal are: (1) the correctness of the determination that claim 1 of U.S. Patent No. 9,060,976 is unpatentable, and any finding or determination supporting or related to those issues, as well as all other issues decided adversely to Purdue in any orders, decisions, rulings, and opinions; and (2) whether the Patent and Trademark Office may constitutionally void patents consistent with Article III and the Seventh Amendment of the United States Constitution.

Copies of this Notice of Appeal are being filed simultaneously with the Director, the Board, and the Clerk of the United States Court of Appeals for the Federal Circuit, along with the filing fee to the Federal Circuit.

Dated: December 4, 2017

Respectfully submitted,

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CERTIFICATE OF FILING

I hereby certify that, in addition to being filed electronically through the Patent Trial and Appeal Board's E2E, the foregoing "Patent Owners' Notice of Appeal" was filed by on this 4th day of December, 2017, with the Director of the United States Patent and Trademark Office, by hand delivery at the following address:

Office of the General Counsel
Patent and Trademark Office
Madison East
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CERTIFICATE OF FILING

I hereby certify that a true and correct copy of the foregoing "Patent Owners' Notice of Appeal," along with the required $500 filing fee, was filed electronically by CM/ECF on this 4th day of December, 2017, with the United States Court of Appeals for the Federal Circuit, and that a paper copy of the foregoing "Patent Owners' Notice of Appeal" was hand-delivered to the Federal Circuit's Clerk's Office at the following address:

United States Court of Appeals for the Federal Circuit
717 Madison Place, N.W., Suite 401
Washington, D.C. 20439

EXHIBIT A

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Paper No. 48
Entered: November 8, 2017

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 Owner.

Case IPR2016-01027
Patent 9,060,976 B2

Before LORA M. GREEN, CHRISTOPHER G. PAULRAJ, and JACQUELINE T. HARLOW, *Administrative Patent Judges*.

PAULRAJ, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
Determining That Claim 1 Has Been Shown To Be Unpatentable
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. INTRODUCTION

Amneal Pharmaceuticals LLC ("Petitioner") filed a Petition requesting an *inter partes* review of claim 1 of U.S. Patent No. 9,060,976 B2 (Ex. 1001, "the '976 patent"). Paper 2 ("Pet."). The P.F. Laboratories, Inc., Purdue Pharma L.P., and Purdue Pharmaceuticals L.P. (collectively, "Patent Owner") filed a Preliminary Response to the Petition. Paper 9 ("Prelim. Resp."). We determined that the information presented in the Petition demonstrated that there was a reasonable likelihood that Petitioner would prevail in challenging claim 1 as unpatentable under 35 U.S.C. § 103(a). Pursuant to 35 U.S.C. § 314, the Board instituted trial on November 9, 2016, as to that claim of the '976 patent. Paper 13 ("Institution Decision" or "Inst. Dec.").

Following our institution, Patent Owner filed a Response to the Petition (Paper 17, "PO Resp.") and Petitioner filed a Reply to Patent Owner's Response (Paper 20, "Reply"). Pursuant to our authorization, Patent Owner also filed a Sur-Reply (Paper 40, "PO Sur-Reply"). An oral hearing was held on August 2, 2017. The transcript of the hearing has been entered into the record. Paper 47 ("Tr.").

We have jurisdiction under 35 U.S.C. § 6. This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. Based on the record before us, we conclude that Petitioner has demonstrated by a preponderance of the evidence that claim 1 of the '976 patent is unpatentable as obvious.

A. Related Proceedings

The '976 patent is asserted against Petitioner 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-cv-831, filed September 17, 2015 (Ex. 1007), and *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, 15-cv-1152, filed December 15, 2015 (Ex. 1008). Pet. 1.

Furthermore, the claims of U.S. Patent No. 8,337,888 B2 (Ex. 1002, the '888 patent), of which the '976 patent is a continuation (Ex. 1001), were also asserted against Petitioner, and were held invalid in a district court proceeding in the Southern District of New York captioned *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, No. 13-cv-3372 ("the SDNY Litigation"). The Federal Circuit upheld the invalidity of those claims on April 8, 2016. Ex. 1004.

Additionally, Petitioner filed a second Petition challenging the validity of claim 1 of the '976 patent. *See* Case IPR2016-01028, Paper 1. IPR2016-01028 is being decided concurrently with the instant proceeding.

B. The '976 Patent (Ex. 1001)

The '976 patent issued on June 23, 2015, with Curtis Wright, Benjamin Oshlack, and Christopher Breder as the listed co-inventors. Ex. 1001. The '976 patent is a continuation of application number 13/349,449, which issued as the '888 patent. *Id.* The '976 patent claims priority to a non-provisional application (No. 10/214,412) filed August 6, 2002 and a provisional application (No. 60/310.534) filed August 6, 2001. *Id.*

The '976 patent relates generally to a controlled release formulation of oxycodone, which has been marketed by Patent Owner under the tradename "OxyContin." *Id.* at 1:46–48. As noted in the SDNY Litigation, OxyContin, which was originally approved in 1995, has been at the center of

the current national opioid abuse epidemic, and Patent Owner stopped selling the original formulation in 2010 because it was susceptible to tampering and abuse. Ex. 1003, 28–29. The invention claimed in the '976 patent stems from Patent Owner's efforts to develop an abuse-deterrent alternative to the original formulation.

In this respect, the '976 patent notes that "[o]pioid analgesics are sometimes the subject of abuse." Ex. 1001, 1:17. According to the '976 patent, the opioid analgesic may be more potent when injected after mixing with a suitable vehicle, or when crushed and administered orally or nasally. *Id.* at 1:18–29. The '976 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 1:32–34, 2:9–11.

Thus, the '976 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 2:42–47. The '976 patent defines "aversive agent" as "a bittering agent, an irritant, a gelling agent, or combinations thereof." *Id.* at 4:12–14.

According to the '976 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 2:64–3:11. Moreover, upon contact with the mucous membranes of the nasal passages the gelling agent may also become a gel, which sticks to the nasal passage, minimizing absorption of the opioid. *Id.* at 3:25–30.

The '976 teaches as to the gelling agent:

> In certain embodiments of the present invention wherein the dosage form includes an aversive agent comprising a gelling agent, various gelling agents can be employed including, for example and without limitation, sugars or sugar derived alcohols, such as mannitol, sorbitol, and the like, starch and starch derivatives, cellulose derivatives, such as microcrystalline cellulose, sodium cahoxymethyl cellulose, methylcellulose, ethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, and hydroxypropyl methylcellulose, attapulgites, bentonites, dextrins, alginates, carrageenan, gum tragacanth, gum acacia, guar gum, xanthan gum, pectin, gelatin, kaolin, lecithin, magnesium aluminum silicate, the carbomers and carbopols, polyvinylpyrrolidone, polyethylene glycol [PEG], *polyethylene oxide* [PEO], polyvinyl alcohol, silicon dioxide, surfactants, mixed surfactant/wetting agent systems, emulsifiers, other polymeric materials, and mixtures thereof, etc. In certain preferred embodiments, the gelling agent is xanthan gum. In other preferred embodiments, the gelling agent of the present invention is pectin.

Id. at 6:45–63 (emphasis added).

The '976 patent teaches further:

> A gelling agent may be added to the formulation in a ratio of gelling agent to opioid agonist of from about 1:40 to about 40:1 by weight, preferably from about 1:1 to about 30:1 by weight, and more preferably from about 2:1 to about 10:1 by weight of the opioid agonist. In certain alternative embodiments, the

> gelling agent may be present in a ratio to the opioid agonist of from about 1:15 to about 15:1, preferably in a ratio of from about 1:8 to about 8:1, and more preferably from about 1:3 to about 3:1 by weight of the opioid agonist.

Id. at 7:12–20.

The '976 patent teaches:

> The opioid analgesic formulation in combination with one or more aversive agents can be formulated as an immediate release formulation or controlled release oral formulation in any suitable tablet, coated tablet or multiparticulate formulation known to those skilled in the art. The controlled release dosage form may include a controlled release material which is incorporated into a matrix along with the opioid analgesic. In addition, the aversive agent may be separate from the matrix, or incorporated into the matrix.

Id. at 12:29–37.

According to the '976 patent, the matrix may contain suitable quantities of other materials, such as lubricants "that are conventional in the pharmaceutical art." *Id.* at 16:18–21. The '976 patent teaches that "[e]xamples of lubricants include but are not limited to magnesium stearate, sodium stearate, stearic acid, calcium stearate, magnesium oleate, oleic acid, potassium oleate, caprylic acid, sodium stearyl fumarate, and magnesium palmitate." *Id.* at 25:34–37

C. District Court Proceeding Involving the '888 patent

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. 1003, 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. 1002, 40:22–32.

The district court concluded that the '888 patent was invalid as obvious. Ex. 1003, 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. 1004. 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. Challenged Claim

Petitioner challenges claim 1, the only claim of the '976 patent, which is reproduced below:

> 1. An extended release abuse deterrent dosage form comprising:
>
> a. a core matrix comprising a blended mixture of:
>
> (a) PEO having a molecular weight of from about 300,000 daltons to about 5,000,000 daltons;

(b) magnesium stearate; and

(c) oxycodone or a pharmaceutically acceptable salt thereof;

wherein the core matrix is heated to melt at least a portion of the PEO included in the core matrix during preparation of the dosage form; and

b. PEG applied onto the core matrix;

wherein the dosage form provides extended release of the drug.

Ex. 1001, 40:35–48.

E. Instituted Ground of Unpatentability

The only patentability challenge at issue in this proceeding is the obviousness of claim 1 under 35 U.S.C. § 103 based on McGinity,[1] Joshi,[2] and Palermo[3].

Petitioner relies on the Declarations of Anthony Palmieri III, Ph.D. (Ex. 1009), Robert J. Timko, Ph.D. (Ex. 1040), and Thomas D. Vander Veen (Ex. 1042) to support its Petition and Reply.

Patent Owner relies on the Declarations of Stephen Byrn, Ph.D. (Ex. 2007; Ex. 2096), Benjamin Oshlack (Ex. 2097), Curtis Wright IV, M.D., M.P.H. (Ex. 2098), and Eric M. Gaier, Ph.D. (Ex. 2041) to support its Response and Sur-Reply.

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[1] McGinity et al, WO 97/49384, published Dec. 31, 1997 (Ex. 1013) ("McGinity").

[2] Joshi et al., Pub. No. US 2002/0187192 A1, published Dec. 12, 2002 (Ex. 1014) ("Joshi").

[3] Palermo et al, WO 99/32120, published Jul. 1, 1999 (Ex. 1011) ("Palermo").

II. DISCUSSION

A. Level of Skill in the Art

Petitioner contends that a person of ordinary skill in the art for the '976 patent would have "a degree in one or more fields of medicine, chemical engineering, chemistry, pharmaceutical science, polymer chemistry, pharmaceutics, pharmaceutical technology, pharmacokinetics, and/or pharmacology, and/or a number of years of industry training or experience in one or more of those fields." Pet. 24 (citing Ex.1009 ¶ 17). Patent Owner agrees with Petitioner's proposed level of skill in the art. PO Resp. 26. We, therefore, apply that skill level in our analysis, with the understanding that the level of skill is also reflected in the prior art of record. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

B. 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 the broadest reasonable construction standard, claim terms are presumed to have their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

Petitioner and Patent Owner have offered constructions for the following claim terms: "extended release," "abuse deterrent," "core matrix comprising a blended mixture," "core matrix is heated to melt at least a

portion of the PEO included in the core matrix during preparation of the dosage form," and "PEG applied onto the core matrix." Pet. 25–29; PO Resp. 27–32. For purposes of our Institution Decision, we construed the terms "extended release," "abuse deterrent," and "PEG applied onto the core matrix." Inst. Dec. 8–11. We have considered anew those claim constructions in this Final Written Decision based on the full record in this proceeding. In addition, in view of the arguments presented, we asked the parties during the oral hearing whether they were in agreement as to the construction to be given to the terms "core matrix" and "wherein the core matrix is heated to melt at least a portion of the PEO included in the core matrix during preparation of the dosage form." Tr. 30:20–32:19. In response, the parties sent an email to the Board memorializing their agreed-upon constructions for those terms. Ex. 3001.

On the present record, we determine that the following 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)).

i. "extended release"

Petitioner contends that the term "extended release" does not appear in the Specification, but rather the Specification uses the terms "sustained release" and "controlled release." Pet. 25. The Specification, Petitioner asserts, defines "sustained release" as "release of the opioid analgesic from the oral dosage form at a rate such that blood (*e.g.*, plasma) concentrations (levels) are maintained within the therapeutic range but below toxic levels

over an extended period of time." *Id.* at 25–26 (quoting Ex.1001, 4:56–60). Petitioner asserts further that although the Specification provides examples of 12 to 24 hours, it "does not suggest that such a period of release defines the concept." *Id.* at 26 (citing Ex. 1001, 4:61–62). Thus, Petitioner argues that "the broadest reasonable interpretation of extended release is the above phrase wherein 'over an extended period of time' means a period of time other than that of an immediate release of the opioid analgesic." *Id.* (citing Ex. 1009 ¶ 23).

Patent Owner responds that Petitioner's definition is "incomplete as it fails to provide a time period over which the drug must be maintained within the therapeutic window." PO Resp. 27. Patent Owner contends that Petitioner's "expert could not specify how to determine what release would have been 'longer than that of an immediate release of the opioid analgesic.'" *Id.* (citing Ex. 2099, 169:16–173:15). As such, Patent Owner requests the Board to adopt the exemplary teaching in the patent specification and incorporate a requirement that extended release must be "from about 12 to about 24 hours." *Id.* at 28 (citing Ex. 1001, 4:61).

The Specification teaches the following:

> The term "sustained release" is defined for purposes of the present invention as the release of the opioid analgesic from the oral dosage form at such a rate that blood (e.g., plasma) concentrations (levels) are maintained within the therapeutic range but below toxic levels over an extended period of time, e.g., from about 12 to about 24 hours as compared to an immediate release product. Preferably the sustained release is sufficient to provide a twice-a-day or a once-a-day formulation.

Ex. 1001, 4:56–64. The use of "e.g." in the above definition for "sustained release" plainly indicates that a 12 to about 24 hour time period is exemplary. Thus, we decline to limit the claim term as Patent Owner would

have us do. Rather, we construe "extended release" as "release of the opioid analgesic from the oral dosage form at a rate such that blood (*e.g.*, plasma) concentrations (levels) are maintained within the therapeutic range but below toxic levels over a period of time longer than that of an immediate release of the opioid analgesic."

ii. "abuse deterrent"

Petitioner contends that the claim term "abuse deterrent" appears only in the preamble, and, thus, should not be limiting. Pet. 26. Specifically, Petitioner asserts "the preamble term 'abuse deterrent' should be nonlimiting because the claim body describes a structurally complete pharmaceutical dosage form and does not attribute abuse deterrence to any particular element." *Id.* (citing Ex. 1009 ¶ 24).

Patent Owner responds that "abuse deterrent" in the preamble should be limiting, as it "describes a fundamental characteristic of the claimed invention that informs [a skilled artisan] as to the structure required by the claim." PO Resp. 28 (quoting *Deere & Co. v. Bush Hog, LLC*, 703 F.3d 1349, 1358 (Fed. Cir. 2012). According to Patent Owner, the "abuse deterrent" language imparts a functional limitation on the amount of the PEO gelling agent that must be present to practice the invention. *Id.* at 29 (citing Ex. 2096 ¶¶ 89–93). Additionally, Patent Owner contends that "the phrase 'extended release abuse deterrent dosage form' is limiting because it provides an antecedent basis for the term 'the dosage form' that appears elsewhere in the claim." *Id.* (citing *Electro Sci. Indus., Inc. v. Dynamic Details, Inc.*, 307 F.3d 1343, 1348 (Fed. Cir. 2002)). Patent Owner also contends that that the specification and prosecution history confirm that abuse deterrence is the "raison d'etre" or "fundamental characteristic of the

claimed invention." *Id.* at 30–31 (citing Ex. 1001, 1:1–2, 1:15–31, 2:9–11, 2:15–47, 2:64–3:36, 7:4–34;. Ex. 1030, 5; Ex. 1032, 7; Ex. 1036, 7).

We are unpersuaded by Patent Owner's arguments. Claim 1 is drawn to a dosage form—a composition. Patent Owner does not point out how the recitation of "abuse deterrent" in the preamble modifies the structurally complete dosage form recited in the body of claim 1. *See Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) ("[A] preamble is not limiting 'where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention.'") (quoting *Rowe v. Dror*, 112 F.3d 473, 478 (Fed.Cir.1997)). We conclude, therefore, that the term "abuse deterrent" is a goal of the invention, that is, it is merely a statement of intended use that is not entitled to patentable weight.

iii. "PEG applied onto the core matrix"

Petitioner argues that the ordinary artisan "would understand this term to mean the [polyethylene glycol, 'PEG'] is placed on or in contact with the core matrix," which "can occur before, during, or after the core matrix is heated." Pet. 29 (citing Ex.1009 ¶ 28).

Patent Owner contends that the broadest reasonable construction of this claim term is "PEG coating the core matrix." PO Resp. 27. According to Patent Owner, Petitioner's construction of "in contact" with the core matrix suggests that the PEG may be contained within the core matrix. *Id.*

We agree with Patent Owner that the broadest reasonable construction of "PEG applied onto the core matrix" is a "PEG coating of the core matrix." Petitioner's proposed construction would read "applied *onto* the core matrix" (emphasis added) out of the claim, which we decline to do. *See Bicon, Inc.*

v. Straumann Co., 441 F.3d 945, 951 (Fed. Cir. 2006) (noting that claim language "should not [be] treated as meaningless").

iv. "core matrix"

The parties agree that the broadest reasonable construction of "core matrix" is "a blended mixture having: (a) PEO having a molecular weight of from about 300,000 to about 5,000,000 daltons, (b) magnesium stearate, and (c) oxycodone or a pharmaceutically acceptable salt of oxycodone." Ex. 3001. We adopt that agreed-upon construction for purposes of this Decision.

v. "wherein the core matrix is heated to melt at least a portion of the PEO included in the core matrix during preparation of the dosage form"

The parties agree that the broadest reasonable construction for "wherein the core matrix is heated to melt at least a portion of the PEO included in the core matrix during preparation of the dosage form"[4] is:

> heating the blended mixture having (a) PEO having a molecular weight of from about 300,000 to about 5,000,000 daltons, (b) magnesium stearate, and (c) oxycodone or a pharmaceutically acceptable salt of oxycodone, during preparation of the dosage form sufficient to melt at least part of the PEO. *Heating occurs at any time during* or after preparation of the blended mixture of PEO, magnesium stearate, and oxycodone.

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[4] Although this phrase would appear to be a "product-by-process" limitation, neither Patent Owner nor Petitioner have argued that it should not be considered in our patentability analysis. *See* Tr. 17:9–18:2 (Petitioner's counsel acknowledging that Petitioner has not stated the position that the limitation is a product-by-process limitation); *but see Amgen Inc. v. F. Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1370 n 14, (Fed. Cir. 2009) ("Because validity is determined based on the requirements of patentability, a patent is invalid if a product made by the process recited in a product-by-process claim is anticipated by or obvious from prior art products, even if those prior art products are made by different processes.").

Ex. 3001 (emphasis added).

Notwithstanding the parties' apparent agreement that heating may occur "at any time during" preparation of the blended mixture of PEO, magnesium stearate, and oxycodone, there nevertheless continues to be a dispute about whether this claim limitation requires all three components of the blended mixture (i.e., PEO, magnesium stearate, and oxycodone) to be heated together only *after* the core matrix is formed. For example, Petitioner asserts in its Reply that "[t]he claim does not require heating or high-shear mixing of" magnesium stearate. Reply 9. Patent Owner, in its Sur-Reply, contends that "[t]his interpretation of claim 1 flies in the face of the plain and ordinary meaning of the claim and all of the other evidence in these proceedings." PO Sur-Reply 6. In support, Patent Owner points out that Petitioner's original expert, Dr. Palmieri, explained at his deposition that "the claim takes the core mixture of the three ingredients [i.e., PEO, oxycodone, and magnesium stearate] and then heats it." *Id.* (citing Ex. 2099, 197:4–7, 199:20–200:5). Patent Owner further points out that Petitioner's other expert, Dr. Timko, also agreed at his deposition, confirming that "in order to practice claim 1. . . you have to mix PEO, magnesium stearate, and oxycodone together before you heat it" and that "if I heat something and I don't have the magnesium stearate in it, I have not heated the core matrix." *Id.* (citing Ex. 2147, 35:2–5, 37:2–6).

The specification of the '976 patent does not indicate that the magnesium stearate should be added to the core matrix during the heating/ melt-extrusion step. Rather, it states that "[t]he preparation of a suitable melt-extruded matrix according to the present invention may, for example, include the steps of blending the opioid analgesic and at least one aversive

agent, together with a sustained release material and preferably a binder material to obtain a homogeneous mixture," and "[t]he homogenous mixture is then heated to a temperature sufficient to at least soften the mixture sufficiently to extrude the same." Ex. 1001, 17:4–11. As such, the melt extrusion process described in the specification only indicates that the opioid analgesic, an aversive agent (to deter abuse), and the sustained release material are heated together. Although the specification further states that lubricants, such as magnesium stearate, "may be used during the manufacture of the dosage form to prevent sticking to die wall or punch faces," this statement also does not suggest that the lubricant must necessarily be added during the heating/melt-extrusion step. *Id.* at 25:31–35.

Furthermore, during prosecution, the Applicants for the '976 patent stated the following:

> Applicants respectfully submit that the element "*wherein the core matrix is heated to melt at least a portion of the PEO included in the core matrix during preparation of the dosage form*" does encompass the core matrix prepared by melt extrusion or melt-granulation but is not limited as such. Applicants further respectfully submit that the element does encompass heating during preparation of the core matrix but is not limited as such as the claim recites "*during preparation of the dosage form*." Thus the claim also encompasses heating, e.g., after preparation of the core matrix; or e.g., before or after PEG is applied onto the core matrix.

Ex. 2009, 2 (Applicants' communication in response to Examiner's Reasons for Allowance). As set forth above by Applicants through its use of "e.g.," heating after preparation of the core matrix is only one example of when the dosage form may be heated. As such, Applicants plainly indicated during prosecution that heating can occur at *any* point during preparation of the

dosage form, which would include before all the required components are incorporated into the core matrix.

Given the parties' agreement, as well as the clear statements made in the specification and during prosecution, we give little weight to the expert testimony cited by Patent Owner to support a contrary interpretation. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1318 (Fed. Cir. 2005) (*en banc*) ("[A] court should discount any expert testimony 'that is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history, in other words, with the written record of the patent.'") (quoting *Key Pharms. v. Hercon Labs. Corp.*, 161 F.3d 709, 716 (Fed. Cir. 1998)).

Accordingly, we adopt the parties' agreed-upon construction with the further clarification, consistent with the parties' construction, that the heating step can occur before the magnesium stearate is included in the core matrix.

C. Prior Art Relied Upon

Petitioner relies upon the following prior art teachings for its patentability challenge in this proceeding:

i. Overview of McGinity (Ex. 1013)

McGinity discloses pharmaceutical formulations in which the formulation has been prepared "by hot-melt extrusion of mixtures containing high molecular weight [polyethylene oxide ('PEO')] and a therapeutic compound for use in controlled release drug delivery." Ex. 1013, 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.

ii. Overview of 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.

iii. Overview of Palermo (Ex. 1011)

Palermo discloses an opioid oral dosage form that is less subject to potential parenteral or oral abuse. Ex. 1011, 6:1–9. The potential for abuse is reduced by "combining an analgesically effective amount of an opioid agonist together with an opioid antagonist into an oral dosage form." *Id.* at 6:10–16. The opioid may be oxycodone hydrochloride, with the antagonist being naltrexone hydrochloride. *Id.* at 6:25–28.

Palermo discloses further that the dosage form may be a sustained release formulation, which may be accomplished by incorporating a sustained release carrier into the matrix containing the opioid and its antagonist, as well as using a sustained release coating. *Id.* at 8:1–6. Specifically, Palermo teaches that the "tablets may be uncoated or they may be coated by known techniques for elegance or to delay release of the active ingredients." *Id.* at 18:3–5.

Palermo teaches that in preferred embodiments the substrate, that is the matrix particle, is coated with a hydrophobic material. *Id.* at 22:6–9. According to Palermo, the inclusion of a plasticizer in the aqueous dispersion of the hydrophobic material used in the coating will improve the physical properties of the sustained release coating. *Id.* at 24:25–29. An

example of a plasticizer that may improve the elasticity of acrylic films that comprise the hydrophobic coating includes polyethylene glycol ("PEG"). *Id.* at 25:11–17.

Palermo also discloses the use of melt-granulation or melt-extrusion techniques to form sustained release matrices. *Id.* at 32:11–12. Palermo teaches that sustained release dosage form formed by melt-extrusion may be coated with a sustained release coating, such as those discussed above. *Id*. at 34:25–27.

D. Obviousness over McGinity, Joshi, and Palermo

Petitioner asserts that claim 1 is rendered obvious by the combination of McGinity, Joshi, and Palermo. Pet. 40–55. Petitioner presents a claim chart for claim 1. *Id.* at 52–55. Patent Owner contends that Petitioner has not established a reasonable likelihood that claim 1 is rendered obvious by the combination of references relied upon by Petitioner. Prelim. Resp. 20–24, 39–55.

Petitioner relies on McGinity for teaching "hot-melt extrudable pharmaceutical formulations that include a therapeutic compound and a high molecular weight PEO." Pet. 42 (citing Ex. 1013, Abstract, 1:9–12; Ex. 1009 ¶¶ 42, 66). Petitioner notes that McGinity teaches that the matrix may be a blended mixture of the PEO and a therapeutic compound, and teaches also that the PEO may have "an average molecular weight of between about 1,000,000 to about 10,000,000, a range that overlaps with much of the 300,000 to 5,000,000 range claimed in the '976 Patent." *Id.* (citing Ex. 1013, 5:1–4, 8:6–7, 18:15–30 (Example 3); Ex. 1009 ¶¶ 42, 43, 66, 68). Petitioner notes further that McGinity teaches that other formulation components, such as lubricants, may be added to the dosage form, and may

be included in the PEO and active ingredient in the extruder. *Id.* at 43 (citing Ex. 1013, 9:33–10:2, 11:18–21, 13:26–30; Ex. 1009 ¶¶ 43–45, 66, 68, 69).

As to the use of oxycodone, Petitioner contends:

> McGinity teaches that the therapeutic agent may be "analgesics . . . and the like." (Exs.1013, at 8:20; 1009 ¶¶ 43, 67.) As discussed . . . above, the court in the SDNY Litigation held that in the context of abuse-prone drugs, McGinity's disclosure of "analgesics . . . and the like" includes controlled release oxycodone. (Ex.1003, at 37.) This was affirmed, twice. (Exs. 1004, 1017.) Accordingly, McGinity teaches that the therapeutic agent may be controlled release oxycodone. (Ex. 1009 ¶ 43, 67.) But even were this not the case, oxycodone is one of the preferred drugs formulated in Palermo. (Exs. 1011, at 7:5-6; 1009 ¶ 35, 72.)

Id.

According to Petitioner, Joshi "is directed to a pharmaceutical composition that reduces or eliminates the drug abuse potential of central nervous stimulants, such as Ritalin®." *Id.* at 44 (citing Ex. 1014, Abstract). Petitioner notes that in discussing the need to prevent potential drug abuse, Joshi points to WO 97/33566, which, Petitioner asserts, discusses "an abuse-deterrent dosage form containing an opioid." *Id.* (citing Ex. 1014 ¶ 6; Ex. 1009 ¶ 54). Petitioner further relies on Joshi for teaching that PEO, the same gel forming polymer of McGinity, when combined with the drug, reduces the ability to absorb the drug nasally and also reduces its injectability, and teaches also that the gel forming polymer may have a molecular weight of from about 70,000 to 2,000,000, which also overlaps with the range required by challenged claim 1. *Id.* at 44–45 (citing Ex. 1014 ¶¶ 8, 21, 22; Ex. 1009 ¶¶ 55, 70).

As to Palermo, Petitioner argues that the reference "teaches a method for preventing abuse of sustained release dosage forms." *Id.* at 45 (citing Ex. 1011, Abstract, 8:1–2; Ex. 1009 ¶¶ 56–57). Petitioner also relies on Palermo for teaching "a matrix that may include gelling agents or a hydrophilic material capable of providing extended release and capable of melting or softening." *Id.* at 45–46 (citing Ex. 1011, 6:31, 28:21–22; Ex. 1009 ¶¶ 56, 57). According to Petitioner, "PEO is a hydrophilic material and a well-known gelling agent." *Id.* at 46 (citing Ex. 1009 ¶¶ 46–52). Petitioner further relies on Palermo for its teaching that the matrix may contain oxycodone and magnesium stearate, and may be formed by melt-granulation or melt-extrusion techniques. *Id.* (citing Ex. 1011, 31:13–14, 32:10–21; Ex. 1009 ¶¶ 57, 72). In addition, Petitioner depends on Palermo for teaching that "the matrix may be coated for protection or to regulate the release of materials, and that the coatings may include well-known plasticizers," such as PEG. *Id.* (citing Ex. 1011, 18:3–5, 21:18–22:17, 25:13–15; Ex. 1009 ¶¶ 57, 73).

Petitioner acknowledges that McGinity is silent as to the use of its dosage form to deter abuse, but contends that "Joshi teaches that it was known that opioids were susceptible to abuse and that abuse deterrence of drugs was desirable." *Id.* at 47 (citing Ex. 1014 ¶¶ 1, 5, 6). Moreover, Petitioner asserts that the ordinary artisan would have been aware "of the growing concern for oxycodone abuse." *Id.* (citing Ex. 1018; Ex. 1019; Ex. 1009 ¶¶ 29, 31, 74). Petitioner contends further that the "fact that both the McGinity and Joshi references teach very similar compositions using high molecular weight PEO gelling agents within the claimed range would only serve to reinforce a reasonable expectation that what McGinity was already

doing would impart some measure of abuse resistance identified by Joshi," as well as provide a reason to combine the references. *Id.* at 48 (citing Ex. 1009 ¶¶ 70, 75, 77).

As to the requirement of claim 1 that the drug is oxycodone, Petitioner contends that, although McGinity does not specifically mention oxycodone, "the court in the SDNY Litigation has already found that McGinity's teaching of an analgesic and the like was sufficient to render oxycodone obvious," which was "affirmed by the Federal Circuit, *twice*." *Id.* at 49 (citing Ex.1003, 37; Ex.1017, 19–20; Ex. 1004). Moreover, Petitioner contends that Palermo specifically teaches that "an opioid can be formulated in a hot-melt extruded matrix using polymers which can include a hydrophilic material that can be melted or softened by heat would provide a reasonable expectation that an opioid, including oxycodone specifically, could be formulated in the fashion disclosed in McGinity." *Id.* at 50 (citing Ex. 1011, 7:6; Ex. 1009 ¶¶ 57, 72, 75).

Patent Owner has made several arguments as to why claim 1 is not proven obvious based on the teachings of McGinity, Joshi, and Palermo.

Patent Owner argues that a skilled artisan would not have consulted McGinity to tackle the problem of abuse deterrence. PO Resp. 34–38. In particular, Patent Owner contends that McGinity's hot-melt extrusion (HME) process was "a new, developing, and investigational technique to pharmaceutical scientists," and the skilled artisan would not have looked to that technology for answers regarding the oxycodone abuse problem. *Id.* at 35 (citing Ex. 2096 ¶ 100; Ex. 2115, 27); *see also id.* at 16 ("At the time of the invention, HME was a relatively new technique in the pharmaceutical industry that was not particularly well understood.") (citing Ex. 2096 ¶ 59).

Patent Owner also contends that drug release from a HME formulation is pH-dependent and can be accelerated in the acidic environment of the human stomach, and the skilled artisan would therefore have been concerned with overdosage ("dose dumping") if oxycodone is used in such a formulation. *Id.* at 35 (citing Ex. 2096 ¶ 102; Ex. 2113, 247). Additionally, Patent Owner contends that the skilled artisan would have tried to avoid using McGinity's HME process because it could cause stability problems with the active ingredient and thermal degradation of the PEO. *Id.* at 36 (citing Ex. 1013, 8; Ex. 2031, 2014-15; Ex. 2096 ¶¶ 21–25, 101, 103; Ex. 2131, 196–97). Patent Owner also argues that McGinity does not provide any information on any oxycodone formulation, and that the inclusion of oxycodone would be incompatible with magnesium stearate. *Id.* at 20 (citing Ex. 2130, 669, Ex. 2132, 306; Ex. 2096 ¶ 75). Patent Owner further argues that McGinity does not disclose the use of magnesium stearate in its HME process, and, on the contrary, teaches that excipients like binders, lubricants, and glidants are not required to facilitate processing. *Id.* at 21 (citing Ex. 2096 ¶ 77; Ex. 2113, 241). Rather than looking to McGinity as the starting point, Patent Owner contends that the skilled artisan's "lead formulation" would have been original OxyContin. *Id.* at 37.

We are unpersuaded by these arguments. As an initial matter, we reject Patent Owner's argument that the skilled artisan would have only started with the original OxyContin formulation in arriving at the claimed invention. Rather, under the correct obviousness analysis, "any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *KSR, Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420

(2007); *see also Galderma Labs., L.P. v. Tolmar, Inc.*, 737 F.3d 731, 737 (Fed. Cir. 2013) ("Nothing in the statute or our case law requires [the challenger] to prove obviousness by starting with a prior art commercial embodiment and then providing motivation to alter that commercial embodiment."). We, therefore, consider McGinity as an appropriate starting point in the obviousness analysis.

We also find no basis on the record of this proceeding to deviate from prior court findings that McGinity's disclosure of "analgesics such as aspirin, acetaminophen, deflunisal and the like" (Ex.1013, at 8:20) includes controlled release oxycodone. Ex. 1003, 37; Ex. 1017, 20; Ex. 1009 ¶ 43 (Petitioner's expert agreeing that "McGinity at least suggests a therapeutic agent that may be oxycodone"). Patent Owner does not dispute that oxycodone was one of the most widely prescribed analgesics by 2001. *See* Ex. 1017, 20 (finding that "opioids are a major class of analgesics and that oxycodone was one of the most widely prescribed analgesics at the time"). Insofar as McGinity encompasses an oxycodone formulation, the problem of oxycodone abuse was well-recognized by the time the priority applications for the '976 patent were filed, thereby providing the motivation to arrive at abuse-deterrent formulations. *See* Ex. 1018 (Justice Department bulletin dated January 2001 indicating that oxycodone abuse "is a major problem"). As such, McGinity need not discuss the problem of abuse deterrence specifically in order to render the claimed formulation obvious when combined with Joshi and Palermo.

We find that the skilled artisan would not have had significant concerns about utilizing McGinity's HME process to arrive at the claimed formulation. Indeed, the '976 patent itself states that "[a] sustained-release

matrix can also be prepared by, e.g., . . . melt-extrusion techniques." Ex. 1001, 16:49–50. Palermo also discloses that an abuse deterrent, sustained release opioid dosage form may be made using a melt-extrusion process. Ex. 1011, 32:10—35:23. As such, we find that the claimed formulation may be made using a HME process. With respect to any concerns about instability or thermal degradation, McGinity indicates that "[t]he one-step process presented as part of the invention also provides therapeutic formulations with *minimal degradation* of either the therapeutic compound or the PEO. Ex. 1013, 4:29–31 (emphasis added). Furthermore, Petitioner's expert, Dr. Timko, testified that the skilled artisan "would not be concerned with adding oxycodone to a PEO-containing HME knowing that oxycodone melts at 218–220°C and decomposes at 270–272°C, both of which are well above PEO's melting point of 60-75°C." Ex. 1040 ¶ 37 (citing Ex.1070, 1194; Ex. 1012, 399). Additionally, we find that the skilled artisan would not be concerned about pH-dependent drug release in a HME formulation. The basis for Patent Owner's pH-dependency argument is a publication by Zhang (with McGinity as a co-author), but that publication does not suggest that tablets prepared by a HME technique could not be administered in the acidic environment of the stomach. PO Resp. 18–19 (citing Ex. 2113, 247). To the contrary, Zhang teaches that "the hot-melt extrusion technique was demonstrated to be a viable method for the preparation of sustained-release tablets." Ex. 2113, 249. As explained by Dr. Timko, a skilled artisan reading Zhang would have known how to compensate for any acceleration of drug release. Ex. 1040 ¶¶ 70–71. For example, the skilled artisan could have chosen to use an appropriate grade/molecular weight of PEO, mitigate

the impact of an acidic environment by using buffers, and/or use coatings to assist in extending the release of the drug. *Id.*

We find that the skilled artisan would also not be concerned about combining magnesium stearate with oxycodone in McGinity's HME process. Indeed, we note that McGinity expressly lists magnesium stearate as a lubricant that may be included in its solid unit dosage forms. Ex. 1013, 13:26–29. Likewise, Palermo and Joshi also teach the inclusion of magnesium stearate in a pharmaceutical dosage form. Ex. 1011, 18:3 (identifying "lubricating agents such as magnesium stearate" for use in an opioid dosage form); Ex. 1014 ¶ 30 ("Examples of lubricants that can be used in the compositions of the invention include but are not limited to stearic acids and its salts such as Mg, Al or Ca stearate."). In accordance with the parties' stipulated claim construction, and for the reasons discussed above, there is no requirement that all three components of the blended mixture (PEO, magnesium stearate, and oxycodone) must be heated together. Ex. 3001. Therefore, consistent with both the prior art's teachings and the '976 patent, a skilled artisan would have known that magnesium stearate could be added as a lubricant in the final mixing step just before tableting, i.e., *after* the PEO is melted during the HME process. Ex. 1040 ¶ 38.

Moreover, even if we were to construe the claims as requiring heating of the core sometime during the preparation of the dosage form after the PEO, magnesium stearate, and oxycodone have all been combined, the prior art of record would also render that step of forming the claimed dosage form obvious. As noted above, McGinity specifically teaches that magnesium stearate may be included as a lubricant in its solid unit dosage forms. Ex.

1013, 13:7–12, 13:26–29. In particular, McGinity teaches that "[a]dditional components that would not significantly prohibit the hot-melt extrusion process may be added to the formulation prior to hot melt extrusion." *Id.* at 13:7–12. In discussing solid dosage forms on that same page, McGinity teaches that "the compounds can be combined with conventional carriers, for example . . . lubricants, such as stearic acid or magnesium stearate." *Id.* at 13:26–29.

We acknowledge that Dr. Byrn testifies that there is no suggestion "that magnesium Stearate should be used in the hot-melt extrusion process." Ex. 2096 ¶ 76. In addition, Patent Owner and Dr. Byrn rely upon prior art teaching that the negative effects of magnesium stearate on tablet strength or dissolution are known to increase with prolonged mixing or with high intensity mixing, and that blending times with magnesium stearate should be carefully controlled. PO Resp. 25–26 (citing Ex. 2096 ¶¶ 106–110; Ex. 2132, 306–07; Ex. 2133, 127, 130). Patent Owner asserts, however, that "one of the well-known characteristics of [HME] is that it subjects the matrix excipients to intense mixing and agitation, causing suspended drug particles to be dispersed within the rate controlling polymer 'at the molecular level.'" *Id.* at 39.

As argued by Patent Owner (PO Sur-Reply 3), Petitioner's expert, Dr. Timko, acknowledges that "formulators are taught to wait until the very end of the mixing step to add magnesium stearate, and to limit the mixing time and intensity when that ingredient is present." Ex. 1040 ¶ 45. Dr. Timko testifies further, however:

> Nothing in McGinity or Palermo or in the '976 Patent regarding the use of magnesium stearate is outside the standard practice of an experienced formulator. More to the point, the

> '976 Patent's recitation of how much magnesium stearate to use and when to use it in the formulation process is no different than that taught by McGinity, Palermo, Oshlack, Remington, and countless other prior art references. How Dr. Byrn can allege that these well-known issues would dissuade the POSA from using magnesium stearate --- perhaps the most common tableting lubricant --- escapes me.

Id. ¶ 48. We also recognize, as argued by Patent Owner (PO Sur-Reply 5), that Dr. Timko testifies:

> Purdue *assumes* that McGinity would add the magnesium stearate to the [hot melt extrusion] exposing it to higher temperatures, prolonged and/or high shear mixing, etc. But this is a false assumption. Nothing in McGinity suggests adding the magnesium stearate to the HME. It is simply added to the extruded PEO and oxycodone to form a blend before being tableted into a core and coated.

Id. ¶ 42.

We agree with Dr. Timko that, consistent with McGinity and the '976 patent, the ordinary artisan would have understood how to add magnesium stearate to a combination of PEO and oxycodone in forming the claimed dosage form. *See* Ex. 1040 ¶ 47. We disagree, however, with Dr. Timko (Ex. 1040 ¶ 42) that McGinity itself does not suggest the use of magnesium stearate in HME. Indeed, Petitioner's counsel took a different position during oral argument. *See e.g.* Tr. 23:22–24:6 (counsel for Petitioner responding that McGinity suggests heating the core matrix comprising all three components). As noted above, McGinity teaches that "[a]dditional components that would not significantly prohibit the hot-melt extrusion process may be added to the formulation prior to hot-melt extrusion," and on the same page identifies magnesium stearate as a lubricant that may be included in the dosage form. *See* Ex. 1013, 13:7–30. Thus, when that page

of McGinity is read as a whole, we conclude that the implication is that McGinity suggests the use of magnesium stearate in its HME process.

As to the possible problems with the use of magnesium stearate identified by Patent Owner, McGinity teaches that the temperature only need be above room temperature, but is generally 60º C to about 160º C. *Id.* at 11:8–13. McGinity specifically notes that "[i]t is important to select an operating temperature range that will minimize the degradation or decomposition of the therapeutic compound during processing." *Id.* at 11:10–11. McGinity teaches:

> The hot-melt extrusion process is generally described as follows. An effective amount of a powdered therapeutic compound is mixed with a high molecular weight PEO, and in some embodiments, with a plasticizer such as PEG. Other components may be added in the various embodiments of the invention. In some embodiments, the therapeutic compound:PEO ratio is generally about 0.01 :about 99.99 to about 20:about 80% wt. depending on the desired release profile, the pharmacological activity and toxicity of the therapeutic compound and other such considerations. The mixture is then placed in the extruder hopper and passed through the heated area of the extruder at a temperature which will melt or soften the PEO and/or plasticizer, if present, to form a matrix throughout which the therapeutic compound is dispersed. The molten or softened mixture then exits via a die, or other such element, at which time, the mixture (now called the extrudate) begins to harden. Since the extrudate is still warm or hot upon exiting the die, it may be easily shaped, molded, chopped, ground, molded, spheronized into beads, cut into strands, tableted or otherwise processed to the desired physical form.

Id. at 11:18–32.

According to McGinity:

> Many conditions may be varied during the extrusion process to arrive at a particularly advantageous formulation. Such conditions include, by way of example, formulation

> composition, feed rate, operating temperature, extruder screw RPM, residence time, die configuration, heating zone length and extruder torque and/or pressure. Methods for the optimization of such conditions are known to the skilled artisan.

Id. at 12:7–12.

Thus, in view of the teachings of McGinity, the skilled artisan would understand that different variables could be optimized to achieve the claimed composition, such as the amount of magnesium stearate, the feed rate, the rotation rate of the screw, and the residence time of the composition in the extruder. In addition, Patent Owner does not point us to any disclosure in McGinity that explicitly states that magnesium stearate should *not* be added during the HME process. In that regard, we note that claim 1 does not require any particular concentration of magnesium stearate, and only requires that a portion of the PEO be melted.

We find further that the teachings of McGinity comport with those of the specification of the '976 patent. The '976 patent teaches that the "opioid analgesic formulation in combination with one or more aversive agents can be formulated as an immediate release formulation or controlled release oral formulation in any suitable tablet, coated tablet or multiparticulate formulation known to those skilled in the art." Ex. 1001, 12:29–33. In addition, the '976 patent teaches that the sustained-release matrix may be prepared by melt-granulation or melt-extrusion techniques, referencing U.S. Patent No. 4,861,598 (Ex. 1037). Ex. 1001, 16:49–59. That is, the '976 patent does not specifically teach melt-granulation or melt-extrusion techniques, but relies on the teachings of the prior art in that regard. In addition, the '976 patent teaches that when the opioid and the aversive agent, such as the gelling material, are being formulated into a tablet, the agents may be combined with "one or more inert, non-toxic pharmaceutical," such

as "excipients which are suitable for the manufacture of tablets," for example, "lubricating agents such as magnesium stearate." *Id.* at 12:1–9.

Thus, the specification of the '976 supports our conclusion that the claimed compositions may be prepared using known, conventional techniques. We note in that regard that the specification does not exemplify production of the claimed formulation. *See* Tr. 43:22–44:2 (counsel for Patent Owner, Mr. Larosa, acknowledging that the specification does not exemplify a formulation with the ingredients required by claim 1). And again, like McGinity, the specification of the '976 patent does not disclose that a conventional lubricant, such as magnesium stearate, should not be added before melt-granulation or melt-extrusion. Thus, even if we were to construe the claims as requiring heating the oxycodone, magnesium stearate, and PEO together to melt a portion of the PEO, we determine that process is rendered obvious by the prior art.

Furthermore, Patent Owner argues that other prior art of record taught away from using McGinity's HME process to combine oxycodone with magnesium stearate, and PEO. PO Resp. 38–43. In particular, Patent Owner asserts that Kibbe, HANDBOOK OF POLYMER EXCIPIENTS (3rd ed.) (2000) ("HPE-3rd") (Ex. 2132) indicates that magnesium stearate cannot be used in products containing "most alkaloidal salts," and that oxycodone hydrochloride is such an alkaloidal salt. PO Resp. 24–25, 38–39 (citing Ex. 2096 ¶ 105; Ex. 2130, 669; Ex. 2132, 305).

We are unpersuaded by Patent Owner's teaching away argument. Even though HPE-3rd suggests that magnesium stearate should not be used in products containing "most alkaloidal salts" (Ex. 2135, 588), other evidence of record indicates that there were numerous commercial products

combining magnesium stearate with alkaloidal salts known in the prior art. Ex. 1040 ¶ 39 (citing Ex. 1061, 936, 1473, 2253–4, 2808). In fact, mixing magnesium stearate and oxycodone hydrochloride was previously disclosed by one of the inventors of the '976 patent, and such a combination was used in the original OxyContin formulation. Ex. 1062, 6:5–11; Ex. 1016, 2569–70. As such, we do not find that the prior art taught away from combining magnesium stearate and oxycodone hydrochloride in the core of an extended-release formulation.

As an additional teaching away argument, Patent Owner relies on Bastin[5] as discouraging the use of gelling agents. PO Resp. 41. Patent Owner asserts that Bastin teaches a combination in which only 50% of the drug was released within two hours, and the remaining drug was "trapped in the tablet matrix" with no release after two hours, which would preclude an extended release. *Id.* (citing Ex. 1015, 5:29–36, 28:1–22). 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 42. Patent Owner relies also on the CPDD Paper[6] as teaching away from challenged claim 1 because, although it taught the inclusion of antagonists, it did not identify any additional

[5] Bastin et al., WO 95/20947, published August 10, 1995 ("Bastin") (Ex. 1015). Bastin is relied upon for one of Petitioner's patentability challenges in IPR2016-01028, and we discuss Bastin in further detail in our Final Written Decision for that proceeding.

[6] 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. 2012) ("CPDD Paper").

strategies such as the use of gelling agents to confer abuse deterrence in a drug formulation. *Id.* at 42–43.

Consistent with the district court determination in the SDNY Litigation, we determine that Bastin does not teach away from claim 1. 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 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. 1003, 46–47 (citations and footnote omitted).

The CPDD paper has a publication date of 2003 whereas the challenged patent claims a priority date as early as August 6, 2001. Thus, as noted by the district court, the CPDD Paper was not prior art to the '888 patent (Ex. 1003, 45 n.13), and is not prior art to the '976 patent, which is a continuation of '888 patent. As the CPDD paper was not available until 2003, two years after the time of invention, Patent Owner has not pointed to any evidence that the CPDD paper reflects the understanding of the ordinary artisan at the time of invention. Moreover, even if the CPDD paper were

considered, we find nothing in its disclosure that would have discouraged the skilled artisan from including a gelling agent at the time of invention. Patent Owner points out that the CPDD paper taught the use of opioid antagonists, but did not teach the use of gelling agents as a potential strategy to reduce abuse liability. Ex. 2012, 224. However, the fact that the CPDD paper taught alternative strategies for tackling the abuse problem is not a teaching away. *See In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004) ("The prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed.").

Patent Owner argues that Joshi and Palermo do not teach modifying McGinity in a way that practices the claimed invention. PO Resp. 43–44. In particular, Patent Owner contends that "Joshi does not describe a HME formulation, or any other manufacturing technique that involves the use of heat," provide any "guidance about how to modify the formulations described in McGinity for abuse deterrence," or address "any of the substantial concerns a POSA would have had regarding the use of magnesium stearate" in a HME oxycodone formulation. *Id.* at 43–44 (citing Ex. 2096 ¶¶ 112-113). With regard to Palermo, Patent Owner contends that the reference proposes the use of an opioid antagonist, which is "an entirely different way of deterring abuse than the '976 patent," and "Palermo also does not address any of the questions or concerns about using hot melt extrusion or magnesium stearate in the core of an oxycodone formulation." *Id.* at 44 (citing Ex. 2096 ¶ 114). Patent Owner also argues that Petitioner relies upon impermissible hindsight, and provides no evidence of motivation

to combine particular portions of the prior art in a way that practices the claimed invention. *Id.* at 44–48.

We are unpersuaded by these arguments. As discussed above, McGinity itself teaches or suggests all the components required for the claimed formulation, with the exception of the requirement of that PEG is "applied onto the core matrix" as a coating. Insofar as McGinity fails to disclose the use of a coating, Palermo provides the motivation to apply a PEG coating onto the core matrix taught by McGinity by teaching that opioid dosage forms "may optionally be coated with one or more materials suitable for the regulation of release or for the protection of the formulation." Ex. 1011, 21:18–19. Furthermore, although Palermo employed an antagonist, claim 1 is open-ended (by use the transitional phrase "comprising") and, therefore, does not preclude the use of an antagonist in the claimed formulation. As such, we find that the skilled artisan would have consulted Palermo's teachings in arriving at the claimed formulation. Moreover, although McGinity does not teach that the controlled-release formulation taught therein is abuse deterrent, we have construed "abuse deterrent" in the preamble of claim 1 as merely a statement of intended use that is not entitled to patentable weight. Regardless, Joshi confirms that the PEO within the molecular weight range taught by McGinity can serve as a gelling agent that confers abuse deterrence. Ex. 1014 ¶¶ 20–21.

Additionally, Patent Owner argues that the skilled artisan would not have had a reasonable expectation of successfully practicing the invention. PO Resp. 49–53. In particular, Patent Owner contends that the skilled artisan would understand that drug release from formulations controlled by

gelling agents was unpredictable. *Id.* at 49–50. As support, Patent Owner relies primarily upon the allowance of claims in later patent applications in the same family as the '976 patent. *Id.* We are not persuaded that the Examiner's allowance of different claims in other patents is sufficient evidence of unpredictability in the art with respect to claim 1 of the '976 patent. To the contrary, the prior art of record demonstrates that those skilled in the art would have known how to incorporate PEO within the claimed molecular weight range into a controlled release drug formulation. Ex. 1013; Ex. 1014.

Patent Owner further argues that "the prior art relied upon by Dr. Palmieri contains no data regarding release of oxycodone from any formulation," and "[n]o effort has been made by Dr. Palmieri to present any evidence upon which a POSA could have predicted whether the prior-art formulations could deliver therapeutically effective amounts of oxycodone hydrochloride over an extended period of time." PO Resp. 51–52. However, claim 1 of the'976 patent does not require any particular release profile for oxycodone. Rather, it only requires that "the dosage form provides extended release of the drug," and we have construed "extended release" to mean "release of the opioid analgesic from the oral dosage form at a rate such that blood (e.g., plasma) concentrations (levels) are maintained within the therapeutic range but below toxic levels over a period of time longer than that of an immediate release of the opioid analgesic." To the extent that any experimentation was required to arrive at the claimed "extended release" formulation, we find that such experimentation would have been routine to the skilled artisan. *See* Ex. 1040 ¶ 55. In this regard,

we note that the '976 patent itself provides no details or guidance as to how to achieve "extended release."

E. Objective Indicia of Non-Obviousness

As objective indicia of non-obviousness, Patent Owner relies upon the commercial and regulatory success of its reformulated OxyContin formulation, which it contends practices the claim 1 of the '976 patent. PO Resp. 54–58. Patent Owner also contends that the initial skepticism, unexpected results, and subsequent acclaim associated with the abuse-deterrent formulation of OxyContin supports a conclusion of non-obviousness. *Id.* at 58–59. We have considered this objective indicia evidence as part of our obviousness analysis. *See Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1358 (Fed. Cir. 2013) ("[T]he Board should give the objective indicia its proper weight and place in the obviousness analysis, and not treat objective indicia of nonobviousness as an afterthought."); *Apple Inc. v. Int'l Trade Comm'n*, 725 F.3d 1356, 1365 (Fed. Cir. 2013) ("[O]bjective evidence of secondary considerations . . . must be considered before determining whether the claimed invention would have been obvious to one of skill in the art at the time of invention.").

i. Commercial/Regulatory Success

Patent Owner asserts that reformulated OxyContin has achieved tremendous commercial success since its launch in 2010, as evidenced by its sales exceeding $2 billion annually and over 5 million annual prescriptions written for the drug by physicians. PO Resp. 54 (citing Ex. 2041 ¶ 17). Patent Owner contends that reformulated OxyContin's commercial success is directly attributed to its abuse-deterrent properties. Ironically, despite touting the drug's significant sales and prescriptions, Patent Owner also

contends that "the typical nexus analysis does not apply here" because "the nature of the claimed invention is to reduce use (i.e., by abusers) and, thus, sales." *Id.* at 55. Patent Owner further contends that, "[g]iven the significant reduction in OxyContin® abuse, the fact that Purdue maintained relatively stable overall sales and prescriptions for OxyContin® after its 2010 launch . . . demonstrates that demand, sales and prescriptions for appropriate uses of OxyContin increased compared to original OxyContin®." *Id.* As further evidence of nexus, Patent Owner relies upon the sales of Opana ER, an abuse-deterrent, extended-release formulation of a different opioid (i.e., oxymorphone), as demonstrating that that "Opana®'s abuse-deterrent properties are a driving factor behind its success," and, thus, "at least a like percentage of OxyContin®'s success is due to its own abuse-deterrent features, including the patented gelling invention at issue here." *Id.* at 56.

Although we agree that reformulated OxyContin has been a commercial success, the evidence in the record does not establish a nexus between that commercial success and the claimed invention. As an initial matter, we note that Patent Owner's only evidence that reformulated OxyContin formulation practices claim 1 comes from the declaration of Patent Owner's expert Dr. Byrn that was submitted with Patent Owner's Preliminary Response. PO Resp. 54 (citing Ex. 2007 ¶¶ 145–150). Patent Owner and Dr. Byrn, however, have not shown that the reformulated OxyContin formulation is coextensive with claim 1. To the contrary, although claim 1 specifies that PEO included within the core matrix has a molecular weight of from about 300,000 daltons to about 5,000,000 daltons, Dr. Byrn only indicates that reformulated OxyContin includes PEO with an approximate molecular weight of 4,000,000 daltons. Ex. 2007 ¶ 147.

Accordingly, we decline to presume a nexus between reformulated OxyContin's commercial success and the claimed invention. *See SightSound Techs., LLC v. Apple Inc.*, 809 F.3d 1307, 1319 (Fed. Cir. 2015) ("If a product both 'embodies the claimed features' and is 'coextensive' with the claims at issue, 'a nexus is presumed.'") (citing *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1130 (Fed. Cir. 2000)).

Furthermore, Patent Owner has not pointed to any evidence showing that the sales or any reduction in abuse of reformulated OxyContin is attributable to the specific formulation claimed in the '976 patent. The district court in the SDNY Litigation found that, despite having launched the reformulated version of drug in 2010, Patent Owner did not market reformulated OxyContin on the basis of its abuse-deterrent properties prior to April 2013. Ex. 1003, 48. The district court concluded that "the commercial success of Reformulated OxyContin is not a result of the '888 Patent's claimed features but rather its bioequivalence to original OxyContin." *Id.* Having considered the expert declarations of Dr. Van Der Veen (Ex. 1042) and Dr. Gaier (Ex. 2041), we reach the same conclusion on this record with respect to the '976 patent, and find that any commercial success attributable to reformulated OxyContin is more likely due to the drug's well-established tradename and bioequivalence to the original formulation. *See, e.g.*, Ex. 2041 ¶ 28 (noting that Patent Owner's documents stated as early as 2011 that OxyContin was reformulated "to be bioequivalent to the original formulation and in an effort to make the tablet more difficult to manipulate for the purpose of intentional misuse and abuse," but Patent Owner did not market the abuse-deterrent properties of reformulated OxyContin until 2014) (citing Ex. 2084; Ex. 2085); Ex. 1042

¶¶ 37–39 (discussing bioequivalence). Finally, we are not persuaded that the commercial success of Opana, an entirely different drug involving a different opioid, is relevant in any meaningful way to the issue of nexus of the reformulated OxyContin to the claimed invention.

In addition to commercial success, Patent Owner argues that reformulated OxyContin achieved "regulatory success" in the form of an FDA decision prohibiting generics of the original OxyContin. PO Resp. 56–58. In the SDNY Litigation, the district court rejected a similar argument, noting that the court "is hesitant to equate regulatory success to commercial success." *See* Ex. 1003, 49; *see also AstraZeneca LP v. Breath Ltd.*, 603 F. App'x 999, 1003 (Fed. Cir. 2015) ("We also reject [patent owner's] attempt to equate regulatory compliance with evidence of nonobviousness."). We likewise decline to give weight to any regulatory success that Patent Owner may have achieved at the FDA in our obviousness determination.

ii. Initial Skepticism, Unexpected Results, and Subsequent Acclaim

Patent Owner also argues that the FDA was initially skeptical whether the '976 invention worked as claimed, and only after requiring more comprehensive testing of the formulation's abuse-deterrent properties did the FDA ultimately approve Patent Owner's New Drug Application (NDA) for reformulated OxyContin in 2010. PO Resp. 58. Patent Owner's arguments in this regard are similar to its "regulatory success" argument discussed above, and we find them unpersuasive for the same reason. Patent Owner has not shown that any skepticism, unexpected results, or acclaim was specifically due to the formulation claimed in the'976 patent.

F. Motions to Exclude

Patent Owner has filed a Motion to Exclude portions of Dr. Timko's Declaration (Ex. 1040 ¶¶ 23, 43, 49–52, 75–77 and 84), and Exhibits 1065, 1068, 1074, 1127. Paper 27. Petitioner has filed a Motion to Exclude Exhibits 2011, 2034, 2104, 2118, 2138, and 2139. Paper 31. Because we have not relied upon the evidence sought to be excluded in this Final Written Decision, we dismiss both Patent Owner's and Petitioner's Motions to Exclude as moot.

G. Motion to Seal

Patent Owner has filed a motion to seal Exhibits 2104–2108 on the basis that these exhibits contain confidential and non-public information pertaining to research and development efforts. Paper 16. Petitioner does not oppose the motion to seal. The standard for granting a motion to seal is "for good cause." 37 C.F.R. § 42.54. The party moving to seal bears the burden of proof of showing entitlement to the requested relief, and establishing that information sought to be sealed is confidential information. 37 C.F.R. § 42.20(c).

We agree that Exhibits 2104–2108 appear to contain confidential business information. We have not relied upon these Exhibits in this Final Written Decision. We, therefore, are persuaded that Patent Owner shows good cause for sealing Exhibits 2104–2108.

The parties also filed a Joint Motion for Entry of a Stipulated Protective Order. Paper 15. We grant the motion and enter the parties' Stipulated Protective Order.

III. CONCLUSION

Based on the evidence and arguments, Petitioner has demonstrated by a preponderance of the evidence that claim 1 of the ’976 patent is unpatentable under 35 U.S.C. § 103 as obvious over McGinity, Joshi, and Palermo.

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claim 1 of the’976 patent is held to be unpatentable;

FURTHER ORDERED that Patent Owner’s and Petitioner’s Motions to Exclude are *dismissed as moot*;

FURTHER ORDERED that the parties’ Joint Motion for Entry of a Stipulated Protective Order is *granted*;

FURTHER ORDERED that Patent Owner’s Motion to Seal Exhibits 2104–2108 is *granted*;

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

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), this is to certify that I caused to be served a true and correct copy of the foregoing "Patent Owners' Notice of Appeal" on this 4th day of December, 2017, by Priority Mail Express® to counsel for Petitioner at the following addresses:

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By: */s/ Gasper J. LaRosa*
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