Case IPR2016-01413
Patent No. 9,034,376
Petition for *Inter Partes* Review
Attorney Docket No. AMNEAL 7.1R-004

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

Patent No. 9,034,376 to Wright *et al.*
Issue Date: May 19, 2015
Title: PHARMACEUTICAL FORMULATION CONTAINING GELLING AGENT

Inter Partes Review No. IPR2016-01413

PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,034,376

Mail Stop: Patent Board
Patent Trial and Appeal Board
U.S. Patent And Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

CASES

STATUTES, RULES & OTHER AUTHORITIES

PETITIONER'S EXHIBIT LIST

Exhibit #	Reference
1001	U.S. Patent No. 9,034,376 ("the '376 Patent")
1002	Complaint, *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, 15 cv 831, filed Sept. 17, 2015
1003	Complaint, *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, 15-1152, filed Dec. 15, 2015
1004	U.S. Patent No. 8,337,888 ("the '888 Patent)
1005	Purdue Pharma L.P. *et al. v. Amneal Pharmaceuticals LLC*, No. 13-3372 (S.D.N.Y. Apr. 8, 2015) Finding of Facts and Conclusion of Law ("SDNY Decision")
1006	*Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, No. 2015-1654 (Fed. Cir. Apr. 8, 2016) Order ("Federal Circuit Decision")
1007	Declaration of Dr. Anthony Palmieri ("Palmieri Declaration")
1008	*Curriculum Vitae* of Anthony Palmieri, Ph.D
1009	U.S. Patent No. 5,508,042 ("Oshlack")
1010	U.S. Patent No. 4,070,494 ("Hoffmeister")
1011	International Publication No. WO 99/32120 ("Palermo")
1012	*The Handbook of Pharmaceutical Excipients* 252-255, 399-400, 655 (3rd ed. 2000)
1013	U.S. Provisional Patent Application No. 60/287,509 ("Joshi Provisional")
1014	U.S. Patent Publication No. 2002/0187192 ("Joshi")
1015	International Publication No. WO 95/20947 ("Bastin")
1016	OxyContin, *Physicians' Desk Reference* 2569-74 (53rd ed. 1999) ("PDR")
1017	*Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, Nos. 2014-1306, 1307 (Fed. Cir. Feb. 1, 2016)
1018	Department of Justice, *Information Bulletin*: *OxyContin Diversion and Abuse* (Jan. 2001)
1019	Barry Meier, *U.S. Asks Painkiller Maker To Help Curb Wide Abuse*, The New York Times (May 1, 2001)
1020	Brief of Plaintiffs-Appellants in *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, No. 2015-1654 (Fed. Cir. Aug. 12, 2015)

Exhibit #	Reference
1021	Reply Brief of Plaintiffs-Appellants in *Purdue Pharma L.P. et al. v. Amneal Pharmaceuticals LLC*, No. 2015-1654 (Fed. Cir. Dec. 23, 2015)
1022	U.S. Patent No. 5,273,758 ("Royce")
1023	Serial No. 13/349,449, Originally Filed Specification, Jan. 12, 2012
1024	International Publication No. WO 97/49384 ("McGinity")
1025	Serial No. 10/214,412, Originally Filed Specification, Aug. 6, 2002
1026	U.S. Provisional Patent Application No. 60/310,534
1027	Serial No. 14/460,134, Preliminary Amendment, Aug. 14, 2014
1028	Serial No. 14/460,134, Office Action, Oct. 2, 2014
1029	Serial No. 14/460,134, Amendment and Response, Jan. 2, 2015
1030	Serial No. 14/460,134, Notice of Allowance, Mar. 23, 2015
1031	Serial No. 14/460,134, Request for Continued Examination, Apr. 9, 2015
1032	Serial No. 14/460,134, Second Notice of Allowability, Apr. 17, 2015
1033	*Oral Dosage Forms*, II (94) Remington: The Science and Practice of Pharmacy 1666-69 (19th ed. 1995)
1034	CRC Handbook of Chemistry and Physics F-56 (59th ed. 1978)
1035	*Opioid bill passes, but there's little money to act on its wish list*, Politics & Government (July 13, 2016), *available at* http://www.newsobserver.com/news/politics-government/article89403007.html (last visited July 14, 2016)

Pursuant to 35 U.S.C. §§ 311-319 and 37 C.F.R. § 42, Amneal Pharmaceuticals LLC ("Amneal" or "Petitioner") petitions for *Inter Partes* Review ("IPR") seeking cancellation of claims 1-13 and 16-19 of U.S. Patent No. 9,034,376 ("the '376 Patent") (Ex.1001).

I. MANDATORY NOTICES (37 C.F.R. § 42.8(a)(1))

A. Notice Of Each Real Party-In-Interest (37 C.F.R. § 42.8(b)(1))

The real party-in-interest for Petitioner is Amneal Pharmaceuticals LLC.

The '376 Patent is assigned on its face to Purdue Pharma L.P., The P.F. Laboratories, Inc., and Purdue Pharmaceuticals L.P. (collectively "Purdue" or "Patent Owners").

B. Notice Of Related Matters (37 C.F.R. § 42.8(b)(2))

Purdue has asserted the '376 Patent against Amneal 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). This petition is timely filed under 35 U.S.C. § 315(b).

Claims of U.S. Patent No. 8,337,888 ("the '888 Patent") (Ex.1004), the great-grandparent to the '376 Patent through a string of continuations, were asserted against Amneal 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. 13-3372 ("the SDNY Litigation") (Ex.1005). The Federal Circuit upheld the invalidity of those claims on April 8, 2016. (Ex.1006.)

Petitioner has also filed a second IPR bearing case number IPR2016-01412 seeking cancellation of these same claims on other grounds. Petitioner previously filed IPR Nos. IPR2016-01027 and IPR2016-01028 seeking cancellation of claim 1 of U.S. Patent No. 9,060,976, which is another member of this patent family.

C. Designation Of Lead And Backup Counsel (37 C.F.R. § 42.8(b)(3))

Lead Counsel:	**Backup Counsel:**
Tedd W. Van Buskirk (Reg. No. 46,282) tvanbuskirk@lernerdavid.com litigation@lernerdavid.com Postal and Hand-Delivery Address 600 South Avenue West Westfield, NJ 07090 Telephone: 908.654.5000 Fax: 908.654.7866	Nichole M. Valeyko (Reg. No. 55,832) nvaleyko@lernerdavid.com litigation@lernerdavid.com Postal and Hand-Delivery Address 600 South Avenue West Westfield, NJ 07090 Telephone: 908.654.5000 Fax: 908.654.7866

D. Notice Of Service Information (37 C.F.R. § 42.8(b)(4))

Please address all correspondence to the lead and backup counsel at the address shown above. Petitioner consents to electronic service by e-mail at the above-listed e-mail addresses.

E. Grounds For Standing (37 C.F.R. § 42.104(a))

Petitioner certifies that (1) the '376 Patent is available for IPR and (2) Petitioner is not barred or estopped from requesting IPR of the '376 Patent on

the grounds identified herein. The fee for this petition has been paid. The Office is hereby authorized to charge any fee deficiencies, or credit any overpayments, to Deposit Account No. 12-1095 in connection with this petition.

II. STATEMENT OF PRECISE RELIEF REQUESTED (37 C.F.R. § 42.22(a))

For the reasons set forth herein, the information presented establishes a reasonable likelihood that Amneal will prevail with respect to at least one of the claims challenged in this petition. Accordingly, Petitioner requests institution of an IPR and cancellation of claims 1-13 and 16-19 of the '376 Patent. The text of the challenged claims is included in the claim charts herein.

III. IDENTIFICATION OF THE CHALLENGE (37 C.F.R. § 104(b))

IPR of claims 1-13 and 16-19 of the '376 Patent is requested on the ground for unpatentability listed below. Pursuant to 37 C.F.R. § 42.6(d), a copy of each of the references is filed herewith. This petition is accompanied by the declaration of technical expert Anthony Palmieri III, Ph.D. (Ex.1007) and his *Curriculum Vitae* (Ex.1008), setting forth his definition of a person of ordinary skill in the art ("POSA") and explaining what the art would have conveyed to the POSA at the time of the invention. Dr. Palmieri is an expert in the fields of pharmaceutics, dosage form design, sustained release delivery systems, and dissolution, among others. (Ex.1007¶¶3-13.)

References	Basis
Ground 1 — Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of PDR (Ex.1016)	§ 103

The challenged claims of the '376 Patent are unpatentable over U.S. Patent No. 5,273,758 to Royce *et al*. ("Royce") (Ex.1022) in view of International Publication No. WO 97/49384 to McGinity *et al*. ("McGinity") (Ex.1024), U.S. Patent No. 4,070,494 to Hoffmeister *et al.* ("Hoffmeister") (Ex.1010), U.S. Patent Publication No. 2002/0187192 to Joshi *et al*. ("Joshi") (Ex.1014), and the *Physicians' Desk Reference* (53rd ed.1999) ("the PDR") (Ex.1016).

Royce teaches sustained release pharmaceutical formulations using polyethylene oxide ("PEO") in a tablet matrix for a variety of drugs, including analgesics. (Ex.1022 Abstract; 4:52-53.) Royce recognized that different amounts of varying molecular weight grades of PEO can have a significant impact on release rate and viscosity. Royce also taught that PEO could be formulated with hydroxypropylmethylcellulose ("HPMC") and exemplifies controlled release dosage forms including both. (*Id*. 5:49-6:5 (Example 2).) Royce does not teach abuse deterrence. But (1) the art merely explains that what Royce was already using would impart abuse deterrence; (2) merely discovering latent properties of

something that was otherwise obvious cannot confer patentability and confirming this in the prior art should not require separate motivation; and (3) motivation has been judicially recognized — there was ample motivation to seek out abuse deterrence technology. (Ex.1005, at 29, 51-52.)

McGinity teaches a POSA that analgesics can be formulated in an extended release PEO matrix and that analgesics would be understood to include oxycodone. (Ex.1024 Abstract, 8:20.) The PDR would also make clear that an oxycodone formulation, such as OxyContin®, is an opioid analgesic delivering known amounts of oxycodone HCl, which was susceptible of abuse, in a controlled release format. (Ex.1016, at 2569.)

Motivated to seek abuse deterrence, a POSA would note Hoffmeister (Ex.1010), which shows that as far back as the mid-1970s the art already contemplated achieving abuse deterrence by using gelling agents including HPMC.

And Joshi identifies PEO, the primary component of Royce, as a preferred gelling agent for providing abuse deterrence. (Ex.1014 ¶¶[0014], [0021].) A POSA would know from Royce and McGinity that controlled release dosage forms for oxycodone could be produced using a matrix of PEO and HPMC, and Hoffmeister and Joshi would teach a POSA that both of these materials are gelling agents that can impart abuse deterrence. Because Hoffmeister and Joshi merely explain the known properties of the combination of materials already in use in Royce, a POSA

would have motivation to combine these references and would have a reasonable expectation of success.

As discussed in more depth herein, the challenged claims are, for all intents and purposes, the same as the claims of the '888 Patent that were found invalid in the SDNY Litigation. The only meaningful difference is the addition of HPMC as a second gelling agent. But HPMC, like PEO, was well known at the time to provide both controlled release and abuse deterrence. Adding a second known element to do exactly what it was known and expected to do cannot render patentable an otherwise unpatentable formulation.

The SDNY Litigation also recognized the existing motivation to seek out abuse deterrent technology. Indeed, Judge Stein observed, "the Oxycontin abuse crisis — which was publicly known by early 2001 — provided motivation to produce an abuse-deterrent oxycodone formulation. In particular, persons of skill in the art would have been motivated to invent controlled release oxycodone tablets that resist injection, snorting, and oral ingestion, the known methods of abuse." (Ex.1005, at 51-52.)

Accordingly, Petitioner requests IPR of claims 1-13 and 16-19 of the '376 Patent.

IV. BACKGROUND

A. Oxycodone Abuse

Oxycodone hydrochloride is a very well-known opioid analgesic that was developed in 1917. (Ex.1007 ¶14.) As of 1999, the *Physicians' Desk Reference* ("PDR") listed 18 different formulations of oxycodone hydrochloride, in the form of tablets, capsules, caplets, and oral solutions. (Exs.1016, at 126; 1007 ¶14.) Original OxyContin®, Purdue's oral, controlled-release oxycodone, was approved in 1995 and originally available as 10, 20, 40, and 80mg tablets. (Exs.1018, at 2; 1007 ¶14.) A 160mg tablet was released in 2000. (Exs.1018, at 2; 1007 ¶14.) OxyContin distinguished itself from other short acting oxycodone formulations, such as Percocet®, by acting over 12 hours. (Exs.1018, at 2; 1007 ¶14.) As immediate release oxycodone formulations included only 5mg of oxycodone or less, and one controlled-release OxyContin contained as much as 160mg, OxyContin became an extremely attractive choice for "both abusers and legitimate users." (Exs.1018, at 2; 1007 ¶14.)

By 2001, OxyContin® abuse was becoming a nationwide concern. (*See* Exs.1018, at 2; 1019, at 1-2; 1007 ¶15.) Then existing oxycodone extended release tablets could easily be crushed into a powder, or their extended release coatings dissolved, usurping its extended release properties. The full dose would then be immediately available. (*See* Exs.1018, at 2; 1019, at 1-2; 1007 ¶15.)

The '376 Patent describes using gelling agents to prevent traditional methods of abuse while, at the same time, providing controlled release of the drug if not abused. When tampered with, the gelling agent will gel and thicken liquid it is exposed to — either by dissolution for intravenous injection or in an abuser's nasal passages if snorted. When taken orally and used properly, these dosage forms will slowly release the drug in the digestive tract. (Ex.1007 ¶16.)

Sustained release oxycodone formulations were in fact already known in the prior art, including Purdue's original formulation of OxyContin®. (Exs.1016, at 2569; 1007 ¶16.) Abuse resistant formulations for oxycodone were known as well. (Ex.1007 ¶16.) And both PEO and HPMC were well known as matrix materials used in dosage forms to provide controlled release and/or abuse deterrence. (*Id.* ¶¶17-19.)

Purdue did nothing more than combine familiar, well-known elements of the prior art in an entirely obvious manner. Indeed, as noted above, the Federal Circuit has already upheld the obviousness of using PEO as a gelling agent to provide both controlled release and abuse deterrence. Merely adding HPMC does nothing to change the outcome — adding a second gelling agent with the same known properties to take advantage of those known properties cannot make the claims patentable.

B. The SDNY Litigation And Federal Circuit Affirmance

In 2013, Purdue asserted the '888 Patent, the great-grandparent of the '376 Patent, against Petitioner Amneal and a number of other ANDA applicants in the SDNY Litigation. After a five-day bench trial, Judge Stein issued a detailed, 63-page ruling holding invalid all asserted claims of the '888 Patent. (Ex.1005, at 51-55.) That decision was summarily affirmed in its entirety by the Federal Circuit three days after oral argument. (Ex.1006.)

The district court found that the prior art (including Joshi (Ex.1014), Hoffmeister (Ex.1010), McGinity (Ex.1024), and Royce (Ex.1022)) taught the use of gelling agents to both deter abuse (Ex.1005, at 41-43) and provide extended release (*id.* 43-45). Specifically, the district court held that "[s]everal prior art patents or patent applications teach that gelling agents reduce the abuse potential of pharmaceutical formulations." (*Id.* 41.)

The district court also found specifically that "[s]everal prior art references teach that PEO has rate controlling properties that may be employed in sustained release dosage forms." (*Id*. 43.) And ultimately, the court held that it was obvious to apply this solution to the problem of oxycodone abuse. (*Id*. 45-47, 52-53.)

As shown in the claim chart below, claim 1 of both the '888 and '376 Patents is virtually identical.[1]

US 9,034,376	**US 8,337,888**
1.A controlled release oral solid dosage form comprising: a controlled release **matrix** comprising a mixture of	1.A controlled release oral dosage form comprising:
(i) from 2.5 mg to 320 mg oxycodone or a pharmaceutically acceptable salt thereof; and	from about 2.5 mg to about 320 mg oxycodone or a pharmaceutically acceptable salt thereof; and
(ii) a gelling agent comprising polyethylene oxide and **hydroxypropylmethylcellulose**,	a gelling agent comprising polyethylene oxide
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;	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 10ml of an aqueous liquid;
the controlled release matrix providing a therapeutic effect for at least 12 hours when orally administered to a human	the dosage form providing a therapeutic effect for at least about 12 hours when orally administered to a human patient.

[1]Claim 1 of the '888 Patent was not asserted in the SDNY Litigation. But the additional limitations found in the asserted dependent claims (5, 6, 23, 24) are analogous to those found in dependent claims of the '376 Patent (8, 9, 12, 13).

US 9,034,376	**US 8,337,888**
patient.	

But for reciting a "matrix" and the addition of a second, well-known polymer gelling agent (HPMC) having recognized controlled release and abuse deterrence properties, used by Purdue to take advantage of those known properties, these claims are effectively the same. Merely adding HPMC to the invalidated claims of the '888 Patent cannot alter the outcome of the SDNY Litigation.

In the SDNY Litigation, and in particular during its appeal, Purdue argued that one reference, Bastin (Ex.1015), taught away and would inform a POSA that using a gelling agent for controlling release would destroy its abuse deterrence (Exs.1020, at 8, 21-22, 30, 38, 40-41; 1021, at 2, 9-12, 20, 23). But its position was a serious overreach — one not accepted by the SDNY (Ex.1005, at 46-47), and one summarily dismissed by the Federal Circuit (Ex.1006). A POSA would see Bastin as an encouragement or affirmation, not a teaching away. (Ex.1007 ¶25.)

Any assertion of teaching away based on Bastin would be particularly inappropriate here since Royce (Ex.1022), the primary reference, actually exemplifies a mixture of PEO and HPMC, as claimed, in a single layer dosage form — obviously Royce would not be deterred by Purdue's arguments based on Bastin — even if Purdue was correct, which is not the case. Bastin cannot teach a POSA not to do something that the art was in fact already doing. (Ex.1007 ¶26.)

V. THE '376 PATENT

A. The Family History Of The '376 Patent

The '376 Patent issued on May 19, 2015, from U.S. Application Ser. No. 14/460,134 filed on August 14, 2014 (Ex.1001). The '376 Patent states on its face that it is a continuation of several earlier family members, including the '888 Patent (Ex.1004). All of these prior family members also claim the benefit of U.S. Provisional Application No. 60/310,534, filed August 6, 2001 ("the Provisional Application") (Ex.1026). Accordingly, the earliest possible effective filing date for the '376 Patent is August 6, 2001.

B. The Specification Of The '376 Patent

The specification of the '376 Patent discloses several sustained release oral dosage form strategies for delivering a drug susceptible to abuse along with known pharmaceutically acceptable excipients and a gelling agent capable of imparting sustained release. In some embodiments, an abuser seeking to circumvent the sustained release features to achieve an immediate "high" by dissolving a tablet in a liquid to be injected intravenously was thwarted by the gelling action of a polymer that caused the drug-containing liquid to thicken so it couldn't be injected through a needle. (Ex.1001, at 3:9-22.) Similarly, if the abuser seeks to crush the tablet and snort the crushed powder nasally, the gelling agent will mix with mucous and thicken in the nasal passages, thereby defeating that route of

administration. (*Id*. 3:28-39.) In other embodiments, an aversive agent used caused a bitter flavor or irritation. (*Id*. 2:52-67.) The specification lists PEO and HPMC as gelling agents, but never discusses their use together. Other pertinent aspects of the specification are discussed in the context of claim construction.

C. The Pertinent Prosecution History Of The '376 Patent

The prosecution history for the '376 Patent is rather brief. The application was filed with a preliminary amendment that canceled original claims 1-40 and added new claims 41-70. Independent claim 41 (which ultimately issued as claim 1) required a gelling agent that includes PEO and HPMC and imparts a viscosity of at least 10cp when the dosage form is subjected to tampering by dissolution in an aqueous liquid. (Ex.1027, at 3.)

The Examiner issued a nonfinal office action on October 2, 2014, which rejected all of claims 41-70 for lack of written description (Ex.1028, at 4), and as obvious over WO 93/10765 to Oshlack, US 2003/0054027 to Unger, and US 6,245,357 to Edgren (*id*. at 5).

Applicants responded on January 2, 2015, by canceling claims 56-61, amending claims 41-44 and 62-70, and adding new claims 71-74. (Ex.1029, at 7.) The only pertinent revisions to the claims were the addition of a requirement that the dosage form be "solid" and that the mixture of oxycodone and the gelling agent

be in the form of a "controlled release matrix." New claims 71, 73, and 74 correspond to allowed claims 16, 18, and 19, and exclude a semipermeable wall.

Applicants argued that Unger does not teach a solid oral dosage form and only teaches a delivery system for delivering opioid peptides in a controlled-release manner, thus a POSA would not be motivated to combine with Oshlack or Edgren. (*Id*. at 8-13.) Applicants also argued that Edgren is directed to a dosage form that includes a semipermeable wall and thus does not read upon the "controlled release matrix" of the amended claims. (*Id*. at 11.) In regard to the viscosity limitation, Applicants argued that since Oshlack did not teach a viscosity of 10cp, the Examiner did not establish a *prima facie* case of obviousness. (*Id*. at 13.)

The Examiner issued a Notice of Allowability on March 23, 2015. (Ex.1030.) The Examiner stated:

> The prior art does not teach or suggest the claimed invention as a controlled release solid dosage form comprising a drug susceptible for abuse (*here as oxycodone*) that comprises a gelling agent as a combination of *polyethylene oxide* and *hydroxypropyl methylcellulose* to impart the viscosity unsuitable for injections or nasal administrations when the dosage form is subjected to tampering by dissolution and to provide a therapeutic effect of 12 hours when said dosage form is orally administered to a human patient.

(*Id.* at 4-5.)

Purdue paid the issue fee on March 26, 2015, and then filed a petition on April 9, 2015, to withdraw the application from issue. Purdue then submitted an RCE and an IDS (Ex.1031) to identify the SDNY Decision (Ex.1005), issued the day before, holding invalid the asserted claims of the '888 Patent. Despite this submission, the PTO issued a second Notice of Allowability one week later. (Ex.1032.) The second Notice of Allowability included an Examiner Initiated Interview Summary detailing the Examiner's opinion on why the SDNY Decision was not applicable to the allowed claims. (*Id.*) The Examiner did not comment on McGinity, Joshi, or Royce, and only mentioned two references specifically: Hoffmeister and Shaw. The Examiner then generally opined that the prior art "does not teach or suggest employing a gelling agent comprising a combination of PEO and HPMC to impart a viscosity of at least 10cP." (Ex.1032, at 4.)

The allowance was issued long before the Federal Circuit's affirmation of the SDNY Decision. Petitioner respectfully submits that the Examiner's opinion cannot be squared with the art and combinations discussed herein.

Purdue paid the issue fee on April 29, 2105, and the '376 Patent issued on May 19, 2015. (Ex.1001.)

VI. PERSON OF SKILL IN THE ART

Factors relevant to determining the level of skill in the art include: the educational level of the inventors, the types of problems encountered in the art, prior art solutions to those problems, the rapidity with which innovations are made, the sophistication of the technology, and the educational level of active workers in the field. *Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1373, 1376 (Fed. Cir. 2012).

As explained in the Palmieri Declaration, a POSA has 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. (Ex.1007 ¶¶31-34.) Dr. Palmieri bases this opinion on his own knowledge, experience, and reading in the fields of pharmaceutical science, his teaching of students and graduate students, his interaction with those practicing drug product formulation, and on the fact that this definition was stipulated to by the parties in the SDNY Litigation and as used by Judge Stein in his opinion holding invalid the asserted claims of the ’888 Patent. (Exs.1005, at 14, 40; 1007 ¶34.)

VII. CLAIM CONSTRUCTION[2]

In IPR, a claim term is given its "broadest reasonable construction in light of the specification." 37 C.F.R. § 42.100(b); *see also Cuozzo Speed Techs., LLC v. Lee*, 579 U.S. ___ (2016).

A. "Gelling Agent In An Effective Amount To Impart A Viscosity"

Claim 1 recites "gelling agent in an effective amount to impart a viscosity of at least 10cp," claim 18 recites "gelling agent in an effective amount to impart a viscosity unsuitable for parenteral administration," and claim 19 recites "gelling agent in an effective amount to impart a viscosity unsuitable to pull into an insulin syringe." (Ex.1001 cls.1, 18, 19.) The specification does not define what constitutes an "effective amount." But whether defined numerically (cl.1) or functionally (cls.18, 19) all address the same thing in the context of the specification — the amount needed to provide a viscosity that would provide abuse deterrence. (Ex.1007 ¶¶36-37.)

The broadest reasonable interpretation of "an effective amount to impart a viscosity of at least 10cp" is including enough gelling agent to impart a viscosity of at least 10cp. It is noted that 10cp is the minimum amount of viscosity and there is no upper end to the range. In the context of the claimed invention, 10cp must be

[2]None of the claim terms discussed herein was the subject of the court's interpretation in the SDNY Litigation.

considered viscous enough to provide abuse deterrence to one who tampers with the dosage form and dissolves it in up to 10ml of an aqueous liquid, reducing the chance that it will be injected or inhaled. (Ex.1007 ¶38.)

Independent claim 18 requires "a viscosity unsuitable for parenteral administration," and claim 19 requires "an effective amount to impart a viscosity unsuitable to pull into an insulin syringe." Both mean, albeit recited functionally, at least 10cp. According to the specification, "parenterally" means "injections." (Ex.1001, at 5:6-9.) The term "unsuitable" is not expressly defined by the specification. However, the term "unsuitable for injection" is defined as "to mean that 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 analgesic from the dosage form." (*Id*. 3:15-20.) "Unsuitable for injection" does not require injections be "impossible," merely that it presents difficulty. (Ex.1007 ¶¶39-40.)

The specification also demonstrates that a viscosity of between 10-60cp is considered "thick" and hard to pull into a syringe. (*Id.* 32:8-24, Table 3.) Thus the specification teaches that a viscosity of at least 10cp is difficult to pull into a syringe or administered parenterally and thus the broadest reasonable interpretation

of "unsuitable for parenteral administration" and "unsuitable to pull into an insulin syringe" is a gelling agent that imparts a viscosity of at least 10cp. (Ex.1007 ¶41.)

B. "Subjected To Tampering"

Claims 1-6, 9, 12, 13, and 18-19 recite "subjected to tampering." The term "subjected to tampering" is not explicitly defined in the specification. However, the term "tampered dosage form" is defined as "the dosage form has been manipulated by mechanical, thermal, and/or chemical means which changes the physical properties of the dosage form . . . The tampering can be, e.g., by means of crushing, shearing, grinding, chewing, dissolution in a solvent, heating, (e.g., greater than about 45° C.), or any combination thereof." (Exs.1001, at 4:18-28, 1007 ¶42.)

Based on the specification and language of the claims, the broadest reasonable interpretation of "subject to tampering" is that the dosage form is that the physical properties of the dosage form are changed by mechanical, thermal, and/or chemical means to speed release of the active ingredient. (Ex. 1007 ¶43.)

VIII. THERE IS A REASONABLE LIKELIHOOD THAT AT LEAST ONE CLAIM OF THE '376 PATENT IS UNPATENTABLE

As Petitioner explains below, claims 1-13 and 16-19 of the '376 Patent are invalid as obvious over Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of PDR (Ex.1016).

The obviousness inquiry is one of law based on four factual predicates: (1) "the scope and content of the prior art," (2) "[the] differences between the prior art and the claims at issue," (3) "the level of ordinary skill in the pertinent art," and (4) "secondary considerations" such as "commercial success, long felt but unsolved needs, failure of others, etc." *KSR Int'l Co. v. Teleflex Inc.,* 550 U.S. 398, 406 (2007) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966)); 35 U.S.C. § 103(a). *KSR* reaffirmed that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, 550 U.S. at 416. The Supreme Court also instructed that "any need or problem known in the field of endeavor at the time of [the] invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *Id.* at 420. "Common sense teaches, however, that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* Finally, the Court held that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill [in the art] has good reason to pursue the known options within his or her technical grasp." *Id.* at 421.

A "[m]otivation to combine may be found in many different places and forms." *Par Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1197 (Fed. Cir. 2014). Thus, for example, a challenger is not limited to the same motivation that the patentee had. *See id.* (citing *Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1369 (Fed. Cir. 2012)). The Federal Circuit has recognized that inherency may supply a missing claim limitation in an obviousness analysis. *See, e.g.*, *Santarus, Inc. v. Par Pharm., Inc.,* 694 F.3d 1344, 1354 (Fed. Cir. 2012) (holding "an obvious formulation cannot become nonobvious simply by administering it to a patient and claiming the resulting serum concentrations. . . . To hold otherwise would allow any formulation — no matter how obvious — to become patentable merely by testing and claiming an inherent property.").

Secondary considerations, which in any event are Patent Owner's burden, weigh against any finding of unobviousness, especially here where the Patent Owner has admitted that the '376 Patent does not cover its commercial products.

A. Ground 1: Claims 1-13 And 16-19 Are Obvious Over Royce (Ex.1022) In View Of McGinity (Ex.1024), Hoffmeister (Ex.1010), Joshi (Ex.1014), And Further In View Of PDR (Ex.1016)

Ground 1 is based generally on art considered and relied upon in the SDNY Litigation. When it invalidated the claims of the '888 Patent, the district court found that the prior art taught that gelling agents reduce abuse potential citing,

inter alia, Hoffmeister and Joshi. (Ex.1005, at 41-43.) The court also found that the prior art taught that PEO functions as both a rate controlling agent and a gelling agent relying on, *inter alia,* Royce and McGinity.[3] (*Id.* 43-44.)

The court acknowledged that many of the references it relied on did not specifically teach oxycodone. But noting that the APIs involved all had abuse potential and, for example, Hoffmeister's teachings of using a gelling agent to reduce parenteral abuse, the court found this difference "not especially significant." (*Id.* 44-45.) The court also acknowledged that the art did not teach the specific viscosities claimed. (*Id.* 45.) This was also not enough to impart patentability.

Having found that a strong motivation existed for seeking abuse deterrence (*id.* 51-52), the court found that a POSA would have turned first to prior art that addresses abuse deterrent formulations and, citing, *inter alia,* Hoffmeister and Joshi, would have concluded that gelling agents frustrate the extraction and injectability of dissolved dosage forms. Bastin, a reference Purdue unsuccessfully advocated was a teaching away, was also relied on by the district court for its teaching that a gelling agent could provide abuse deterrence in a controlled release

[3]The '963 Patent referenced by the court in the SDNY Litigation is the U.S. equivalent of McGinity. (Ex.1024.)

system. The court also noted that, *inter alia,* McGinity provided a strong starting point for producing a gel-forming controlled release oxycodone dosage form. (*See generally* Ex.1005, at 51-54.)

The 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. That issue was not before the court. But 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)).

Instead of using a single polymeric gelling material known to have controlled release and abuse resistant properties as was claimed in the '888 Patent, here Purdue claimed using two polymeric gelling materials both known to impart those properties. Absent unexpected results — none of which has been shown — the claims of the '376 Patent are obvious for all the reasons given by the district court and summarily affirmed by the Federal Circuit.

1. <u>The Scope And Content Of The Prior Art</u>

Royce issued on December 28, 1993, and was of record in the '376 Patent but was not discussed during its prosecution. Royce qualifies as prior art under 35 U.S.C. § 102(b). Royce (Ex.1022) relates to a dosage form for, *inter alia*, analgesics (Exs.1022, at 4:52-53; 1007 ¶¶44, 73) that can provide extended release

from a PEO-based matrix (Exs.1022, at 2:64-3:49; 5:9-6:5; 1007 ¶¶44, 73). Royce taught that drug release will vary with the grade and amount of PEO used, which will also vary the viscosity profile when dissolved in water. Royce provides several illustrations of how viscosity can vary by adjusting the molecular weight and amount of PEO used. (Exs.1022, at 2:67-3:8, 3:14-23, 3:31-49; 1007 ¶¶44, 73.) For example, Royce explains that a one percent aqueous solution of 5-6 million average molecular weight PEO (Polyox® WSR 303) has a viscosity of 7200 to 10,000cP. (Exs.1022, at 3:19-23; 1007 ¶¶44, 73.) A higher percentage (5%) of a lower molecular weight PEO (WSR *N*-80 having an average molecular weight of about 200,000) provided a viscosity of about 65-115cp. (Ex.1022, at 3:14-18.) Other optional matrix components can include, *inter alia,* HPMC. (Ex.1022, at 3:52-53.) Indeed an extended release tablet containing both PEO and HPMC is exemplified in Example 2. (Exs.1022, at 5:48-6:5; 1007 ¶¶44, 73.)

McGinity published on December 31, 1997, as WO 97/49384. (Ex.1024.) Accordingly, McGinity qualifies as prior art under 35 U.S.C. § 102(b). Purdue did not argue to the contrary in the SDNY Litigation. (*See* Ex.1005, at 37.) McGinity was of record but was never discussed by the Examiner during prosecution.

McGinity is directed to hot-melt extrudable pharmaceutical matrix formulations that include a therapeutic compound and a high molecular weight PEO. (Exs.1024 Abstract, 1:9-12; 1007 ¶¶46, 74.) The matrix may be formed from

a blended mixture of a therapeutic compound and the PEO. (Exs.1024, at 8:6-7, 18:15-30, Example 3; 1007 ¶¶46, 74.) The PEO can have an average molecular weight of between about 1,000,000 to about 10,000,000. (Exs.1024, at 5:1-4; 1007 ¶¶46, 74.)

McGinity teaches that the therapeutic compound may be "analgesics . . . and the like." (Exs.1024, at 8:20; 1007 ¶¶47, 75.) 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. (Exs.1005, at 37; 1007 ¶¶47, 75.) This was affirmed, twice. (Exs.1006, 1017.) In particular, the court noted that it had "previously found that [McGinity] discloses controlled-release dosage forms containing oxycodone." (Ex. 1005, at 37.) The Federal Circuit upheld that finding:

> The McGinity reference explicitly notes the use of its process with analgesics to treat pain, and the words "such as" and the residual clause "and the like" demonstrate that the application discloses a broader group of analgesics than just those listed. Moreover, the record showed that opioids are a major class of analgesics and that oxycodone was one of the most widely prescribed analgesics at the time. The district court also noted that the McGinity reference is directed to sustained-release dosage forms and credited expert testimony that the only analgesics on the market in a sustained-release form at the time were opioids. The district court's assessment is persuasive and not clearly erroneous.

(Ex.1017, at 20 (footnotes omitted).) And the Federal Circuit recently affirmed the court's invalidity decision as to the parent '888 Patent, relying on this same construction. (Exs.1006; 1007 ¶¶47, 75.) Accordingly, McGinity teaches that the therapeutic agent may be controlled release oxycodone or oxycodone hydrochloride. (Exs.1024 ¶¶43, 67; 1007 ¶¶47, 75.) The PDR (Ex.1016) also shows that oxycodone is an opioid analgesic susceptible of abuse that is provided in a controlled release format (Exs.1016, at 2572; 1007 ¶¶66, 75). The PDR (Ex.1016) teaches that OxyContin is controlled release oxycodone hydrochloride, which is available in 10mg, 20mg, 40mg, and 80mg tablet strengths (Exs.1016, at 2569; 1007 ¶¶66, 75).

Hoffmeister (Ex.1010) issued on January 24, 1978, was of record and discussed, albeit briefly, in the second notice of allowance issued in the '376 Patent. Hoffmeister qualifies as prior art under 35 U.S.C. § 102(b). Hoffmeister discloses the use of gelling agents to increase viscosity of a liquid to provide abuse deterrence. (Exs.1010 Abstract; 1007 ¶¶50, 76.) Hoffmeister taught inhibiting the water extractability of a pharmaceutical composition of a medicinal agent having high abuse potential, which comprises incorporating in said composition a nontoxic, aqueously gelable material in an amount sufficient to form a gel when combined with that volume of water otherwise necessary to dissolve all of said medicinal agent. (Exs.1010, at 1:66-2:8; 1007 ¶¶50, 76). Hoffmeister does

not mention oxycodone, but many of the discussed compounds are opioids. (Exs.1010, at 1:31-36; 1007 ¶¶50, 76.)

HPMC is specifically identified as an example of a suitable gelling agent and, indeed, its use is exemplified. (Exs.1010, at 2:20-21 ("methylhydroxypropylcellulose")[4], Example 4, at 6:21-35; 1007 ¶¶51, 77.) The amount of gellable material in the dosage forms of Hoffmeister can range from about 5 to about 40% by weight of the medicament. (Exs.1010, at 2:44-48; 1007 ¶¶51, 77) "Mixtures of two or more gel-producing substances can be used if desired." (Exs.1010, 2:23-24; 1007 ¶¶51, 77.)

When testing for its gelling effect and abuse deterrence, the dosage forms of Hoffmeister were coarsely crushed and placed in 10ml of water to compare the amount of active which could be extracted from the tablets with and without 4000cp methylcellulose. (*Id.* 3:1-64, Table 1; Ex.1007 ¶78.) A POSA would therefore conclude that 10ml was an amount "sufficient to form a gel," "when combined with that volume of water otherwise necessary to dissolve all of said medicinal agent." (Exs.1010, at 2:3-8; 1007 ¶78; *see also* 1005, at 41-42, 44.)

[4]Methyhydroxypropylcellulose is a synonym for HPMC, also known as hydroxymethylpropylcellulose. (Ex.1012, at 252.)

As noted by Hoffmeister, the results for Table 1 show that extractability can be "severely inhibited or completely prevented by adding a water gelable material, such as methylcellulose." (Exs.1010, 3:58-62; 1007 ¶79.)

Joshi was also mentioned by the court in this connection. Joshi is a patent application published on December 12, 2002 (Ex.1014), which claims priority to a provisional application (U.S. 60/287,509) filed on April 30, 2001 ("Joshi Provisional") (Ex.1013). Purdue has acknowledged that Joshi and the Joshi Provisional are "largely identical." (Ex.1020, at 23.) Moreover, as explained by Dr. Palmieri, the relevant disclosures of the provisional application and the nonprovisional application are the same. (Ex.1007 ¶52.) Joshi qualifies as prior art under 35 U.S.C. § 102(e). Purdue did not argue to the contrary in the SDNY Litigation (*see* Ex.1005, at 42) or on appeal. Joshi was not of record and was not considered by the Examiner in connection with this claim.

Joshi is directed to a pharmaceutical composition that reduces or eliminates the drug abuse potential of central nervous stimulants, such as Ritalin®. (Exs.1014 Abstract; 1007 ¶53.) Joshi teaches that drug abuse is a serious issue and that it is desirable to provide compositions that eliminate drug abuse without decreasing the effectiveness of the drug. (Exs.1014 ¶¶[0001], [0005], [0007]; 1007 ¶53.) In making its case for the need for abuse resistance, Joshi cites to WO 97/33566, which describes an abuse-deterrent dosage form containing an opioid composition.

(Exs.1014 ¶[0006]; 1007 ¶53.) Joshi's citation to WO 97/33566 suggests a recognition of the desirability of abuse deterrent dosage forms for use with opioids, including oxycodone. (Ex.1007 ¶53.)

Joshi teaches that PEO is one of three preferred gel-forming polymers useful in reducing the nasal absorption and injectability of the drug — the very sort of abuse discussed in the '376 Patent. (Exs.1014 ¶¶[0008], [0009], [0021]; 1007 ¶¶54, 80.) The court made similar factual findings with regard to Joshi in a section of its opinion entitled, "*The prior art teaches that gelling agents reduce abuse potential*." (*See* Ex.1005, at 41-43.) Joshi also identified HPMC as a gelling agent and notes that a plurality of gelling agents can be used. (Ex.1014 ¶¶[0014]-[0015]; 1007 ¶ 81.) Joshi also exemplifies ratios of gelling agent to drug of from about 4:1 to about 1:3.34. (Exs.1014 ¶[0036], [0038], [0040], Examples 1-3; 1007 ¶80.) And, in testing the ability of the formulations to gel to establish abuse deterrence, Joshi crushed the tablets of Examples 1-3, placed them in 1ml of water, and stirred for one minute. In each case, "[g]el formation occurs." (Exs.1014 ¶¶[0042]-[0044]; 1007 ¶80.)

Looking at this art together, as courts have ruled a POSA would be motivated to do (Ex.1005, at 51-52), a POSA would know from their general knowledge and from Joshi and Hoffmeister that the PEO used in Royce's Example 2 and in McGinity to provide controlled release, as well as HPMC used in

Royce Example 2, are both gelling agents that can also be used to provide abuse deterrence. Hoffmeister makes this clear for HPMC (Exs.1010, at 2:9-24; 1007 ¶83), and Joshi does so for PEO (Exs.1014 ¶[0021]; 1007 ¶83). Joshi would also reconfirm Hoffmeister's teaching of HPMC as a gelling agent for abuse deterrence. (Exs.1014 ¶[0015]; 1007 ¶83.)

Moreover, while Hoffmeister specifically identified and exemplified HPMC for use as a gelling agent to impart abuse deterrence of opioid analgesics (Ex.1010, at 2:20-21, Example 4, 6:21), Hoffmeister's list of gellable materials is not exclusive. As PEO was a known gelling agent, Hoffmeister would also suggest PEO's use and abuse deterrence properties as well. (Ex.1007 ¶84.) This combined teaching results in controlled release dosage forms capable of providing abuse deterrence. And both suggest the possibility of using a plurality of gelling agents.

While both Royce and Hoffmeister contemplate analgesics and, indeed, Hoffmeister is specifically concerned with opioid drugs liable to be abused, neither reference discloses oxycodone *per se.* The court was not troubled by this. (Ex.1005, at 44-45.) McGinity has been interpreted to disclose controlled release opioid analgesics to a POSA by the U.S. District Court for the Southern District of New York and has been affirmed twice. (Exs.1006, 1017.) The PDR would also make clear that analgesics likely to be abused included oxycodone. Indeed, as

noted in the background, oxycodone was a very well-known target. (Exs.1016, at 2572; 1007 ¶85.)

2. The Differences Between The Claimed Invention And The Prior Art

As further established in Claim Chart 1 below, there are few differences — and none that is meaningful — between the combination of Royce, McGinity, Hoffmeister, Joshi and the PDR, and claims 1-13 and 16-19 of the '376 Patent.

a. Claims 1, 16, 18, And 19

Independent claims 1, 18, and 19 require an abuse deterrent controlled release oral dosage form including a controlled release matrix comprising a mixture of 2.5-320mg oxycodone or a pharmaceutically acceptable salt and the gelling agents PEO and HPMC. These claims also require an amount of these gelling agents to provide a certain viscosity, recited numerically or functionally, be achieved when the dosage form is abused and placed in a small amount of aqueous liquid. (Ex.1007 ¶86.)

Royce does not teach oxycodone or a salt thereof in an amount of from 2.5mg to 320mg as claimed. (*Id.* ¶87.) Royce does, however, teach delivering an analgesic. McGinity discloses dosage forms including "analgesics . . . and the like" which, as discussed above, have been interpreted to teach oxycodone HCl. The PDR also shows that oxycodone HCl is an analgesic provided in doses of 10mg,

20mg, 40mg, and 80mg in an extended release format. (Exs.1016, at 2569; 1007 ¶87.) These amounts fall within the range claimed. (Ex.1007 ¶87.) The mere substitution of one analgesic for another is not an invention and providing oxycodone in amounts that were known *per se* would be obvious. It would be obvious to use the claimed amount of oxycodone HCl as the analgesic in Royce. (*Id.*)

The independent claims also require the use of PEO and HPMC as gelling agents. Royce teaches a formulation that includes both PEO and HPMC as claimed. (Ex.1022, at 3:31-54; 5:47-6:5, Example 2.) And Hoffmeister and Joshi would confirm that both are known gelling agents. (Exs.1010, at 2:18-25; 1014 ¶¶[0015], [0019], [0020]; 1007 ¶88.) The claims further require a therapeutic effect for at least 12 hours. Royce teaches providing a controlled release for a period of 18 hours. (Ex.1022, at 5:10-46, Example 1, Fig.1.) And McGinity teaches a controlled release oxycodone, which provided relief for 12 hours. (Ex.1011; PDR 2570.) These aspects of the independent claims are also obvious. (Ex.1007 ¶88.)

Claim 1 requires that the amount of gelling agent used be sufficient to provide a viscosity of at least 10cP when the dosage form is subject to tampering by dissolution in from 0.5 to 10ml of an aqueous liquid. Independent claim 18 functionally states that the amount of gelling agent will impart a viscosity that is

unsuitable for parenteral administration under the same conditions. Independent claim 19 alters the theme by requiring that the amount be unsuitable to pull into an insulin syringe. (Ex.1007 ¶89.)

Hoffmeister teaches that HPMC may be used as a gelling agent to provide abuse deterrent formulations for delivering analgesics. (Ex.1010, at 1:66-2:8, 2:18-24.) Here, Hoffmeister would teach a POSA that what Royce was already doing — namely using HPMC in a sustained release of analgesic formulation — would provide abuse-deterrence. Indeed, Hoffmeister specifically identified and exemplified HPMC for use as a gelling agent to impart abuse deterrence of opioid analgesics. (Exs.1010, at 2:20-21, Example 4, 6:21; 1007 ¶90.)

Hoffmeister does not expressly teach PEO. But as noted earlier, Hoffmeister's list of gellable materials is not exclusive. Since PEO was also a known gelling agent, Hoffmeister would suggest to a POSA that PEO could provide abuse deterrence as well. (Ex.1007 ¶91.) And that teaching would be seconded by Joshi's teaching that PEO is a particularly preferred gelling agent for imparting abuse deterrence. (Ex.1014 ¶¶[0008], [0009], [0021].) Indeed, Joshi also identifies HPMC as a gelling agent that can be used for abuse deterrence, albeit not one of its preferred gelling agents. (*Id.*¶[0015].) Thus POSAs would understand

that both of the gelling agents exemplified in Example 2 of Royce (Ex.1022, at 5:47-6:5) could provide abuse deterrence.

As for the amount of gelling agents used to provide the specific claimed viscosity sufficient to provide this deterrence, Royce teaches that various viscosities can be obtained by using different amounts of PEO. (Ex.1007 ¶92.) Using specific examples, Royce described a 5% solution of Polyox® WSR *N*-80, a particular grade of PEO having an average molecular weight of about 200,000cps, which had a viscosity in the range of 65-115cps, and a 1% solution of Polyox® WSR 303 having an average molecular weight of 5,000,000-6,000,000, which had a viscosity in the range of 7200 to 10,000cps. (Exs.1022, at 3:14-23; 1007 ¶92.) Thus, Royce teaches the use of amounts of PEO that would provide the claimed viscosity.

A POSA would also appreciate that the viscosity of solutions can vary with the amount of PEO and/or HPMC and their grade/molecular weight. (Ex.1007 ¶93.) It would be obvious to a POSA that virtually any of the claimed viscosities, whether expressed numerically or functionally, could be obtained by routine experimentation. (*Id.*)

The viscosities exemplified in Royce are all greater than 10cP (cl.1) and meet the recitation of claim 1. A POSA would also have reason to think that a

solution with a viscosity of, for example, 65-115cPs (5% solution of Polyox® WSR *N*-80) would be unsuitable for parenteral administration (cl.18) and would be unsuitable to be pulled into an insulin syringe (cl.19), if abused and dissolved in 1-10mls of an aqueous solution. For comparative purposes, olive oil at 20°C has a viscosity of 84.0cP. (Exs.1034, at F-56; 1007 ¶94.) It would be difficult to inject olive oil. And Royce also teaches using a 1% solution of Polyox® WSR 303, which provides a viscosity at 7200 or more (Exs.1022, at 3:19-23; 1007 ¶94), almost ten times as viscous as olive oil. Moreover, as interpreted, these functional recitations require a minimum viscosity of 10cp (10cp viscosity is "unsuitable" for parenteral use or being drawn into an insulin syringe), which is also met by the combined teachings here. (Ex. 1007 ¶94.)

Ample motivation exists for this combination. Royce already teaches a formulation containing both PEO and HPMC; there need not be additional motivation to combine the two polymers. (Ex.1007 ¶¶95-96.) As for a reason to seek to make the dosage forms of Royce more abuse resistant, Hoffmeister and Joshi would inform POSAs that what Royce was doing already would provide this additional benefit. (*Id*.) Merely recognizing an additional benefit of what was already being done does not confer patentability. *In re Baxter Travenol Labs*., 952 F.2d 388, 392 (Fed. Cir. 1991) ("Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention.").

To the extent additional motive is deemed necessary, the district court observed that the known public crisis of opioid abuse would have provided a motivation for a POSA to seek out technology that resists the known methods of abuse. (Ex.1005, at 51-52; *KSR*, 550 U.S. 420 (any need or problem can be the source of motivation.) The court also specifically found that POSAs so motivated would have looked to prior art abuse deterrent formulations citing, *inter alia*, Hoffmeister and Joshi. (Ex.1005, at 52.) And given these combined teachings, a POSA would have a reasonable expectation of success in being able to optimize the formulation to provide the desired viscosity if abused, and the desired controlled release if not. (Ex. 1007 ¶96.)

As to the volume (0.5-10ml in an aqueous solution) used for testing the viscosity in claims 1, 18, and 19, Hoffmeister makes clear its objectives, which include preventing abuse by creating a gelled solution when an abused dosage form is dissolved in water. (Ex.1007 ¶97.) And it made clear that it contemplated dissolution in only a modest volume of an aqueous liquid. (Ex.1010, at 3:35 Table 1 (10ml).) Hoffmeister also noted that its objective was to create dosage forms that would gel "when combined with that volume of water otherwise necessary to dissolve all of said medicinal agent." (*Id.* 2:6-8.) Joshi did its testing in 1ml of water. (Exs.1014 ¶¶[0042]-[0043]; 1007 ¶97.)

Therefore, it would be obvious to a POSA that the viscosity target would be based on an amount of liquid that would be relevant to an abuser and that this would be from about 1 to about 10mL. (Ex.1007 ¶97.)

Claims 18 and 19 (as well as claim 16, which depends directly from claim 1) contain a further negative limitation; namely, that the dosage form not include a semipermeable wall. A POSA would understand this requirement to preclude the dosage form from being an osmotic device. (Exs.1001, at 24:37-46 (Applicants' teaching in the "Osmotic Dosage Forms" section of the '376 Patent of an embodiment that includes "a substantially homogenous core . . . surrounded by a semipermeable wall having a passageway (as defined above) for the release of the opioid analgesic, and the one or more aversive agents."); 1007 ¶98.) None of the references used in this ground describe dosage forms including a semipermeable wall. Thus they teach a POSA to create dosage forms without a semipermeable wall. (Ex. 1007 ¶98.)

It therefore would be obvious to use an amount of PEO and HPMC sufficient to meet the requirements of claims 1, 18, and 19 as gelling agents to provide a sustained release formulation of oxycodone in an amount falling within 2.5 to 320mg. And a POSA would have an expectation that doing so would provide abuse deterrence. It would be obvious, in view of these references, to produce dosage forms with the claimed viscosity and without a semipermeable

wall as recited in claims 16, 18, and 19. Accordingly, claims 1, 16, 18, and 19 are obvious.

b. Claims 2-6, 8-9, And 12

Claims 2-6 each depend from claim 1 and require sufficient gelling agent to impart a viscosity of at least: 60cP (cl.2); 120cP (cl.3); 375cP (cl.4); or 2000cP (cl.5) or within the range of 120 to 5000cP (cl.6) when the dosage form is subject to tampering by dissolution in from 0.5 to 10ml of an aqueous liquid. Claim 8 depends from claim 3 and specifies that the aqueous liquid is water. Claim 9 also depends from claim 3 and narrows the amount of aqueous liquid that the viscosity increase occurs by dissolution in from 1 to 3ml. Claim 12 depends from claim 3 and specifies that the tampering involves crushing.

It would be routine for a POSA to vary the amount and grade of HPMC and/or PEO so as to achieve viscosity over a wide range encompassed by the claims given the volumes necessary. (Ex.1007 ¶100.) As noted above, Royce teaches that the viscosity of solutions can vary with the amount of PEO and its molecular weight (5 wt% of 200,000MW PEO=65-115cP and 1% solution of 6,000,000 PEO=7200-10,000cP. (Ex.1022, at 3:19-23.) The viscosity of the 1% solution is 7200-10,000cps, which falls within the viscosity ranges of claims 2-5. The full range of viscosities exemplified by Royce (65-10,000cps) would bracket the range of viscosity in claim 6 and would render that obvious as well.

Hoffmeister also used an alkylcellulose which provided a 4000cp viscosity, which also falls within the ranges of claims 2-6. (Ex. 1010, 3:34-57, Table 1.) Finally, Joshi described a range of gelling agent of 2-40% and range of molecular weights of 70,000-2,000,000. (Ex.1014 ¶¶[0022]-[0023].) Given what Royce teaches, this would render obvious the claimed ranges as well, so claims 2-6 are obvious. (Ex.1007 ¶100.)

The testing undertaken by Hoffmeister was in 10ml of water and Joshi was in 1ml water, which meets the recitations of claims 8 and 9. (Ex.1007 ¶101.) And Hoffmeister and Joshi crushed their tablets when testing to simulate abuse as recited in claim 12. (Exs.1010, at 3:20-25; 1014 ¶¶[0042]-[0044].) Thus claim 12 is obvious as well. (Ex.1007 ¶101.)

c. Claims 7, 10, And 11

Claim 7 depends from claim 3 and requires a 40:1 to 1:40 ratio of gelling agent to drug. Royce teaches 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. (Exs.1022, at 2:37-42; 1007 ¶102.) Hoffmeister teaches that the amount of HPMC would be from about 5-40% by weight relative to the amount of medicament. (Exs.1010, at 2:44-46; 1007 ¶102.) It also teaches that the amount of gelable material should be at least equal to the amount of medicinal agent (Exs.1010, at 2:56-61, 1007 ¶102), which is a 1:1 ratio. Joshi exemplifies ratios of

4:1 to about 1:3.34 (Exs.1014 ¶¶[0036], [0038], [0040]; 1007 ¶102). Thus the claimed range is obvious. (Ex. 1007 ¶102.)

Claim 10 depends from claim 3 and specifies the salt oxycodone hydrochloride. It would be obvious to use a salt of oxycodone based on the PDR, which teaches oxycodone HCl. (Exs.1016, at 2569; 1007 ¶103.) Claim 11 depends from claim 10 and specifies between 10-80mg of that salt. Again, the amount administered according to the PDR falls into this range. (Exs.1016, at 2569; 1007 ¶103.) The claims are obvious. (Ex. 1007 ¶103.)

d. Claim 13

Claim 13 also depends from claim 3 and requires that the claimed viscosity is obtained when the dosage form is subjected to tampering by dissolution in an aqueous liquid when heated to greater than 45°C. It is not clear if the claim is referring to measuring viscosity when the resulting viscous liquid is heated or after it is cooled. Moreover, only a minimum temperature is stated, not a maximum. Claim 13 thus literally reads on measuring viscosity when the dosage form is tampered with at ***any*** temperature above 45°C. Thus, it is difficult to be sure what the goal of the claim truly is. That aside, a POSA would appreciate that viscosity measurements are dependent on the temperature at which the viscosity is taken. (Ex.1007 ¶104.) It is also obvious, for the reasons discussed herein, to adjust the viscosity over a wide range. Obtaining a viscosity of greater than 120cp at 45

degrees would be a matter of routine experimentation and optimization. (*Id*.) Thus, the claim is obvious over the same sort of optimization discussed previously in connection with claims 1-6, 18, and 19. (*Id.*)

e. Claim 17

Claim 17 requires a film coating. The tablets tested in Hoffmeister included a lacquer coating that had to be peeled off so the testing could be performed. (Exs.1010, at 3:20-21; 1007 ¶105.) Joshi also taught use of enteric coating materials. (Ex.1014 ¶[0026].) A POSA would recognize this as a film coating. (Ex.1007 ¶105.) Claim 17 is therefore obvious. (*Id.*)

3. Claims 1-13 And 16-19 Are Obvious

Royce in view of McGinity, Hoffmeister, Joshi, and the PDR therefore teaches or suggest every limitation of claims 1-13 and 16-19 of the ’376 Patent. Any minor differences would have been obvious. As is clear from the above discussion, Claim Chart 1 below, and the supporting declaration of Dr. Palmieri, the challenged claims are obvious.

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
1. A controlled release oral solid dosage form comprising:	Ex.1022, at 5:44-46 (“tablets of the invention provide a gradual, controlled release of the medicament over an extended period of time.”) Ex.1007 ¶¶44, 73, 88

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
a controlled release matrix comprising a mixture of	Ex.1022, at 2:34-36 ("dosage forms may be prepared from compositions comprising polyethylene oxide as a binder-matrix."); *id.* 2:43-48 ("adjustable rate controlling effect") Ex.1007 ¶¶22, 44, 73
(i) from 2.5 mg to 320 mg oxycodone or a pharmaceutically acceptable salt thereof; and	Ex.1022, at 4:52-53 ("analgesics"); 2:41-42 ("The therapeutic medicament may comprise from about 0.01 to about 95 wt. % of such compositions.") Ex.1024, at 8:20 ("analgesics…and the like") Ex.1010, at 1:14-57 ("analgesics…potential for abuse") Ex.1016, at 2569 ("OxyContin® (oxycodone hydrochloride controlled-release) tablets are an opioid analgesic supplied in 10 mg, 20 mg, 40 mg, and 80 mg tablet strengths....") Ex.1007 ¶¶16, 44, 47, 66, 73, 75, 76, 82, 87, 103
(ii) a gelling agent comprising polyethylene oxide and hydroxypropylmethylcellulose,	Ex.1022, at 2:64-3:49 ("polyethylene oxide"); *id.* at 5:8-6:5, Examples 1, 2 (PEO and HPMC) Ex.1024, at 2:27 ("poly(ethylene oxide)") Ex.1010, at 2:18-24 ("gelable materials...methylhydroxypropylcellulose...Mixtures of two or more gel-producing substances") Ex.1014 ¶[0014] ("gel forming polymers"), ¶[0015] ("hydroxypropylmethylcellulose"), ¶[0019] ("polyethylene oxide") Ex.1007 ¶¶54, 55, 73, 74, 76-77, 80, 83, 88, 90, 91

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
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;	Ex.1022, at 2:67-3:49 (1% aqueous solution of Polyox WSR 303 (MW 6,000,000)...has a viscosity of 7200 to 10,000cps) Ex.1010, at 3:1-63, Table 1 ("added 4,000 cp methylcellulose"); 3:20-23 ("lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed"); Table 1 (10ml of distilled water was used for the extraction) Ex.1014 ¶[0022] (MW 70,000-2,000,000), ¶[0023] ("about 2 to 40 weight percent"); Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶¶44, 73, 78, 92, 94
the controlled release matrix providing a therapeutic effect for at least 12 hours when orally administered to a human patient.	Ex.1022, at 2:34-36 ("dosage forms may be prepared from compositions comprising polyethylene oxide as a binder-matrix."); *id.* 2:43-48 ("adjustable rate controlling effect"); *id*. 4:25-32 ("humans"); *id*. 5:44-46 ("provide a gradual, controlled release of the medicament over an extended period of time."); *id.* 5:9-46 (Example 1, Fig.1). Ex.1016, at 2570 ("OxyContin tablets are designed to provide controlled delivery of oxycodone over 12 hours.") Ex.1007 ¶¶22, 44, 66, 73, 88

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
2.The controlled release oral solid dosage form of claim 1, wherein the gelling agent is in an effective amount to impart a viscosity of at least 60 cP when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid.	Ex.1022, at 2:67-3:49 ("a 5% aqueous solution [of Polyox WSR *N*80 (MW 200,000)] has a viscosity...of...65 to 115cps"); Example 2 ((tablets prepared including Polyox® N80 (molecular weight about 200,000) and hydroxypropyl methylcellulose (Pharmocoat 606).) Ex.1010, at 3:1-63, Table 1 ("added 4,000 cp methylcellulose"); 3:20-23 ("lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed"); Table 1 (10ml of distilled water was used for the extraction) Ex.1014 ¶[0022] (MW 70,000-2,000,000), ¶[0023] ("about 2 to 40 weight percent"); Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶¶44, 73, 78, 80, 99-101
3.The controlled release oral solid dosage form of claim 1, wherein the gelling agent is in an effective amount to impart a viscosity of at least 120 cP when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid.	

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
4.The controlled release oral solid dosage form of claim 1, wherein the gelling agent is in an effective amount to impart a viscosity of at least 375 cP when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid.	
5.The controlled release oral solid dosage form of claim 1, wherein the gelling agent is in an effective amount to impart a viscosity of at least 2,000 cP when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid.	

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
6.The controlled release oral solid dosage form of claim 1, wherein the gelling agent is in an effective amount to impart a viscosity from 120 cP to 5,000 cP when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid.	Ex.1022, at 2:67-3:49 ("a 5% aqueous solution [of Polyox WSR N80 (MW 200,000)] has a viscosity of…65 to 115cps...a 1% aqueous solution [of Polyox WSR 303 (MW 6,000,000)]...has a viscosity of 7200 to 10,000cps"); Example 2 (tablets prepared including Polyox® N80 (molecular weight about 200,000) or Polyox® 303(molecular weight about 6,000,000) and hydroxypropyl methylcellulose (Pharmocoat 606).) Ex.1010, at 3:1-63, Table 1 ("added 4,000 cp methylcellulose"); 3:20-23 ("lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed"); Table 1 (10ml of distilled water was used for the extraction) Ex.1014 ¶[0022] (MW 70,000-2,000,000), ¶[0023] ("about 2 to 40 weight percent"); Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶¶44, 73, 78, 80, 99-101
7.The controlled release oral solid dosage form of claim 3, wherein the ratio of gelling agent to oxycodone or pharmaceutically acceptable salt thereof is from 1:40 to about 40:1.	Ex.1022 cl.2 ("wherein the composition comprises 0.01 to 95 wt.% medicament."); *id.* cl.3 (wherein the composition comprises 5 to 99.99 wt.% polyethylene oxide.") Ex.1010, at 2:56-61 ("gelable...at least equal to that of the medicinal agent") Ex.1014 ¶[0036], Example 1 (POLYOX: di-methylphenidate is 4:1), Example 2 (PEG:di-methylphenidate is 3:10), Example 3 (CARBOPOL: di-methylphenidate 2.5:1.) Ex.1007 ¶102

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
8.The controlled release oral solid dosage form of claim 3, wherein the aqueous liquid is water.	Ex.1014 ¶¶[0042]-[0044], Examples 4-6 (The formulations of Examples 1-3 were added to 1ml of water.) Ex.1007 ¶¶44, 78, 80, 99-101
9.The controlled release oral solid dosage form of claim 3, wherein the viscosity is imparted when the dosage form is subjected to tampering by dissolution in 1 to 3 ml of aqueous liquid.	Ex.1014 ¶¶[0042]-[0044], Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶¶44, 78, 80, 99-101
10.The controlled release oral solid dosage form of 3, wherein the oxycodone or pharmaceutically acceptable salt thereof comprises oxycodone hydrochloride.	Ex.1022, at 4:52-53 ("analgesics"); *id.* 2:41-42 ("The therapeutic medication may comprise from about 0.01 to about 95 wt. % of such compositions.") Ex.1024, at 8:20 ("analgesics...and the like") Ex.1010, at 1:14-57 ("analgesics...potential for abuse") Ex.1016, at 2569 ("oxycodone hydrochloride") Ex.1007 ¶¶16, 44, 47, 66, 73, 75, 76, 82, 87, 103
11.The controlled release oral solid dosage form of claim 10, comprising from 10 mg to 80 mg oxycodone hydrochloride.	Ex.1016, at 2569 ("tablets are an opioid analgesic supplied in 10mg, 20mg, 40mg, and 30mg tablet strengths") Ex.1007 ¶¶16, 44, 47, 66, 73, 75, 76, 82, 87, 103

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
12.The controlled release oral solid dosage form of claim 3, wherein the viscosity is obtained when the dosage form is subjected to tampering by dissolution in the aqueous liquid after crushing.	Ex.1010, at 3:20-22 ("The lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed") Ex.1014 ¶¶[0042]-[0044], Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶¶44, 78, 80, 99-101
13.The controlled release oral solid dosage form of claim 3, wherein the viscosity is obtained when the dosage form is subjected to tampering by dissolution in the aqueous liquid with heating at greater than 45°C.	Ex.1022, at 2:67-3:49 ("Molecular weights range from about 100,000 to about 6,000,000, corresponding to a viscosity range of under about 200 cps...to over about 6,200 cps", "a 5% aqueous solution [of Polyox WSR N80 (MW 200,000)] has a viscosity of…65 to 115cps...a 1% aqueous solution [of Polyox WSR 303 (MW 6,000,000)]...has a viscosity of 7200 to 10,000cps"); Example 2 ((tablets prepared including Polyox® N80 (molecular weight about 200,000) or Polyox® 303(molecular weight about 6,000,000) and hydroxypropyl methylcellulose (Pharmocoat 606).); *id*. 5:25-27 ("A dissolution medium comprising 900 mL of deaerated and distilled water is maintained at 37°± 0.5° C.") Ex.1010, at 3:1-63, Table 1 ("added 4,000 cp methylcellulose"); 3:20-23 ("lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed"); Table 1 (10ml of distilled water was used for the extraction) Ex.1014 ¶[0022] (70,000 to 2,000,000 MW"); *id*. ¶[0023] ("about 2 to 40 weight percent"); *id*. ¶¶[0042]-[0044], Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶104.

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
16.The controlled release oral solid dosage form of claim 1, without a semipermeable wall.	Ex.1007 ¶98.
17.The controlled release oral solid dosage form of claim 1, further comprising a film coat.	Ex.1010, at 3:20-22 ("The lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed") Ex.1014 ¶[0026] ("enteric coating agents") Ex.1007 ¶105
18.A controlled release oral solid dosage form comprising:	Ex.1022, at 5:44-46 ("tablets of the invention provide a gradual, controlled release of the medicament over an extended period of time.") Ex.1007 ¶¶44, 73, 88
a controlled release matrix comprising a mixture of	Ex.1022, at 2:34-36 ("dosage forms may be prepared from compositions comprising polyethylene oxide as a binder-matrix."); *id.* 2:43-48 ("adjustable rate controlling effect") Ex.1007 ¶¶22, 44, 73
(i) from 2.5 mg to 320 mg oxycodone or a pharmaceutically acceptable salt thereof; and	Ex.1022, at 4:52-53 ("analgesics"); 2:41-42 ("The therapeutic medicament may comprise from about 0.01 to about 95 wt. % of such compositions.") Ex.1024, at 8:20 ("analgesics…and the like") Ex.1010, at 1:14-57 ("analgesics…potential for abuse") Ex.1016, at 2569 ("OxyContin® (oxycodone hydrochloride controlled-release) tablets are an opioid analgesic supplied in 10 mg, 20 mg, 40 mg, and 80 mg tablet strengths....") Ex.1007 ¶¶16, 44, 47, 66, 73, 75, 76, 82, 87, 103

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
(ii) a gelling agent comprising polyethylene oxide and hydroxypropylmethylcellulose,	Ex.1022, at 2:64-3:49 ("polyethylene oxide"); *id*. at 5:8-6:5, Examples 1, 2 (PEO and HPMC) Ex.1024, at 2:27 ("poly(ethylene oxide)") Ex.1010, at 2:18-24 ("gelable materials...methylhydroxypropylcellulose...Mixtures of two or more gel-producing substances") Ex.1014 ¶[0014] ("gel forming polymers"), ¶[0015] ("hydroxypropylmethylcellulose"), ¶[0019] ("polyethylene oxide") Ex.1007 ¶¶54, 55, 73, 74, 76-77, 80, 83, 88, 90, 91
the gelling agent in an effective amount to impart a viscosity unsuitable for parenteral administration when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid;	Ex.1022, at 2:67-3:49 (1% aqueous solution of Polyox WSR 303 (MW 6,000,000)...has a viscosity of 7200 to 10,000cps) Ex.1010, at 3:1-63, Table 1 ("added 4,000 cp methylcellulose"); 3:20-23 ("lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed"); Table 1 (10ml of distilled water was used for the extraction) Ex.1014 ¶[0022] (MW 70,000-2,000,000), ¶[0023] ("about 2 to 40 weight percent"); Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶¶44, 73, 78, 92, 94
the oral solid dosage form does not comprise a semipermeable wall,	Ex.1007 ¶98

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
the controlled release matrix providing a therapeutic effect for at least 12 hours when orally administered to a human patient.	Ex.1022, at 2:34-36 ("dosage forms may be prepared from compositions comprising polyethylene oxide as a binder-matrix."); *id.* 2:43-48 ("adjustable rate controlling effect"); *id*. 4:25-32 ("humans"); *id*. 5:44-46 ("provide a gradual, controlled release of the medicament over an extended period of time."); *id.* 5:9-46 (Example 1, Fig.1). Ex.1016, at 2570 ("OxyContin tablets are designed to provide controlled delivery of oxycodone over 12 hours.") Ex.1007 ¶¶22, 44, 66, 73, 88
19.A controlled release oral solid dosage form comprising:	Ex.1022, at 5:44-46 ("tablets of the invention provide a gradual, controlled release of the medicament over an extended period of time.") Ex.1007 ¶¶44, 73, 88
a controlled release matrix comprising a mixture of	Ex.1022, at 2:34-36 ("dosage forms may be prepared from compositions comprising polyethylene oxide as a binder-matrix."); *id.* 2:43-48 ("adjustable rate controlling effect") Ex.1007 ¶¶22, 44, 73
(i) from 2.5 mg to 320 mg oxycodone or a pharmaceutically acceptable salt thereof; and	Ex.1022, at 4:52-53 ("analgesics"); 2:41-42 ("The therapeutic medicament may comprise from about 0.01 to about 95 wt. % of such compositions.") Ex.1024, at 8:20 ("analgesics…and the like") Ex.1010, at 1:14-57 ("analgesics…potential for abuse") Ex.1016, at 2569 ("OxyContin® (oxycodone hydrochloride controlled-release) tablets are an opioid analgesic supplied in 10 mg, 20 mg, 40 mg, and 80 mg tablet strengths....") Ex.1007 ¶¶16, 44, 47, 66, 73, 75, 76, 82, 87, 103

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
(ii) a gelling agent comprising polyethylene oxide and hydroxypropylmethylcellulose,	Ex.1022, at 2:64-3:49 ("polyethylene oxide"); *id*. at 5:8-6:5, Examples 1, 2 (PEO and HPMC) Ex.1024, at 2:27 ("poly(ethylene oxide)") Ex.1010, at 2:18-24 ("gelable materials...methylhydroxypropylcellulose...Mixtures of two or more gel-producing substances") Ex.1014 ¶[0014] ("gel forming polymers"), ¶[0015] ("hydroxypropylmethylcellulose"), ¶[0019] ("polyethylene oxide") Ex.1007 ¶¶54, 55, 73, 74, 76-77, 80, 83, 88, 90, 91
the gelling agent in an effective amount to impart a viscosity unsuitable to pull into an insulin syringe when the dosage form is subjected to tampering by dissolution in from 0.5 to 10 ml of an aqueous liquid;	Ex.1022, at 2:67-3:49 (1% aqueous solution of Polyox WSR 303 (MW 6,000,000)...has a viscosity of 7200 to 10,000cps) Ex.1010, at 3:1-63, Table 1 ("added 4,000 cp methylcellulose"); 3:20-23 ("lacquer coatings were peeled off the tablets and the tablet cores were coarsely crushed"); Table 1 (10ml of distilled water was used for the extraction) Ex.1014 ¶[0022] (MW 70,000-2,000,000), ¶[0023] ("about 2 to 40 weight percent"); Examples 4-6 (After the formulations of Examples 1-3 were crushed and added to 1ml of water: "Gel formation occurs.") Ex.1007 ¶¶44, 73, 78, 92, 94
the oral solid dosage form does not comprise a semipermeable wall,	Ex.1007 ¶98

U.S. Patent No. 9,034,376 (Ex.1001), Claims 1-13 and 16-19	**Royce (Ex.1022) in view of McGinity (Ex.1024), Hoffmeister (Ex.1010) and Joshi (Ex.1014), and further in view of the PDR (Ex.1016)**
the controlled release matrix providing a therapeutic effect for at least 12 hours when orally administered to a human patient.	Ex.1022, at 2:34 36 ("dosage forms may be prepared from compositions comprising polyethylene oxide as a binder matrix."); id. 2:43 48 ("adjustable rate controlling effect"); id. 4:25 32 ("humans"); id. 5:44 46 ("provide a gradual, controlled release of the medicament over an extended period of time."); id. 5:9 46 (Example 1, Fig.1). Ex.1016, at 2570 ("OxyContin tablets are designed to provide controlled delivery of oxycodone over 12 hours.") Ex.1007 ¶¶22, 44, 66, 73, 88

IX. SECONDARY CONSIDERATIONS

It is Purdue's burden to establish secondary indicia of nonobviousness, if any. Of the several objective indicia of nonobviousness, such as commercial success, copying, long-felt but unmet need, skepticism, and industry acclaim, Purdue did not offer any such evidence during prosecution of the '376 Patent. Purdue should also be unsuccessful here in proving the existence of unexpected and superior results, or that there is a nexus between any secondary indicia, such as commercial success, and the claim of the '376 Patent.

"We have held on a number of occasions that evidence of commercial success alone is not sufficient to demonstrate nonobviousness of a claimed invention." *In re DBC*, 545 F.3d 1373, 1384 (Fed. Cir. 2008). "[T]he proponent must offer proof 'that the sales were a direct result of the unique characteristics of

the claimed invention — as opposed to other economic and commercial factors unrelated to the quality of the patented subject matter.'" *Id.*

To prove nexus, Purdue will have to establish that any commercial success it enjoyed was based on patentable features — features of its invention that were not disclosed in the prior art. *See Asyst Techs., Inc. v. Emtrak, Inc.*, 544 F.3d 1310, 1316 (Fed. Cir. 2008); *see also J.T. Eaton & Co. v. Atl. Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997).

As discussed in the SDNY Decision, the commercial success of Purdue's Reformulated OxyContin is meaningless unless it can be attributed to the claimed features of the '376 Patent. (Ex.1005, at 49.) *See Tokai Corp. v. Easton Enters., Inc.*, 632 F.3d 1358, 1369-70 (Fed. Cir. 2011). At trial, the court found that Purdue did not market OxyContin on the basis of its abuse-deterrent properties, and Purdue's marketing message remained centered around efficacy and the side effect profile. (Ex.1005, at 48.) At trial, Purdue did not present data on whether the demand for OxyContin increased or decreased based on its abuse-deterrent features, nor did Purdue raise the cost of the drug based on the "new" gelling properties. (*Id.*) Accordingly, the court found that "[t]his evidence strongly suggests that the commercial success of Reformulated OxyContin is not the result of the '888 Patent's claimed features but rather its bioequivalence to Original OxyContin." (*Id.*) The same analysis applies with respect to the '376 Patent.

Here, in particular, its strains credulity to claim commercial success considering that the '376 Patent is not even listed in the *Orange Book* and therefore, by Purdue's own admission, has no connection with its commercial product, OxyContin. Finally, as previously recognized by the Federal Circuit, market entry here was precluded by a complex regulatory scheme. Accordingly, any inference of nonobvious based on commercial success is "weak." *Merck & Co. v. Teva Pharms. USA*, 395 F.3d 1364, 1377 (Fed. Cir. 2005).

Moreover, while the court found that the gelling features allowed Purdue to achieve ***regulatory*** success from the FDA decision to withdraw approval of Original OxyContin and not accept or approve any ANDAs seeking to market a generic version of it, the court was "hesitant to equate regulatory success to commercial success when Purdue's own evidence shows that the '888 Patent would not be nearly as successful if consumers had the choice to reject Reformulated OxyContin in favor of a bioequivalent generic product not covered by the patent." (*Id*. at 48.) The court also found that Purdue's assertion of copying by Petitioner was not an indication of nonobviousness since "evidence of copying in the ANDA context is not probative of nonobviousness because a showing of bioequivalence is required for FDA approval." (*See id*. at 50 (citing *Bayer Healthcare Pharm., Inc. v. Watson Pharm., Inc.*, 713 F.3d 1369, 1377 (Fed. Cir. 2013)).)

In addition, the court found that the ’888 Patent did not fulfill a long-felt but unmet need, as the need for abuse-resistant oxycodone formulations did not arise until 2001, the same year that Purdue filed the Provisional Application from which the ’888 Patent and the ’376 Patent arose. (*See* Ex.1005, at 50.) The court found that “the very short period of time that elapsed between the recognition of the need for abuse deterrent oxycodone formulations and the invention that matured into the ’888 Patent simply does not indicate any long-felt need.” (*Id.* (citing *In re OxyContin Antitrust Litig.*, 994 F. Supp. 2d 367, 400-01, 428 (S.D.N.Y. 2014)).)

With respect to any alleged skepticism, the court found that although Purdue contended that there was concern that gelling agents could hinder the release of the API, that worry existed only with respect to immediate release dosage forms, and the prior art actually supported the idea that certain gelling agents were compatible with — and in fact advantageous to — controlled release formulations. (Ex.1005, at 51.)

Finally, to the extent Purdue argues any unexpected results and predicates them on OxyContin, there is both a lack of nexus to what is claimed as the ’376 Patent does not cover OxyContin and there is real reason to doubt whether OxyContin has actually accomplished any meaningful abuse resistance. (Ex. 1035.)

In affirming the court's invalidity decision, the Federal Circuit necessarily rejected any alleged evidence of secondary considerations. (*See* Ex.1006.)

X. CONCLUSION

For the foregoing reasons, Petitioner requests that *inter partes* review be instituted for claims 1-13 and 16-19 of the '376 Patent and that those claims be held unpatentable over each of the grounds discussed in Part VIII.

Respectfully submitted,

Dated: July 15, 2016

By: s/Tedd Van Buskirk/
Tedd W. Van Buskirk
Reg. No. 46,282

4576359_1.docx

CERTIFICATE OF COMPLIANCE
WITH TYPE-VOLUME LIMITATION

Pursuant to Rule 37 C.F.R. § 42.24(d), the undersigned hereby certifies that, based upon the word count of the word-processing system used to prepare this petition, the number of words in this petition is 12,078. Pursuant to 37 C.F.R. § 42.24(a), this word count does not include "a table of contents, a table of authorities, a certificate of service or word count, exhibits, appendix, or claim listing."

Dated: July 15, 2016 By: s/Tedd Van Buskirk/
Tedd W. Van Buskirk
Reg. No. 46,282

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing **PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,034,376**, together with all exhibits, Power of Attorney, and all other papers filed therewith, were served on July 15, 2016, as follows.

VIA FEDEX

Patent Docket Administrator
Lowenstein Sandler LLP
65 Livingston Avenue
Roseland, NJ 07068
Tel: 973.597.2500

Jack B. Blumenfeld, Esq.
Rodger D. Smith II, Esq.
MORRIS NICHOLS
ARSHT & TUNNELL LLP
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
Tel: 302.658.9200

John J. Normile, Esq.
Kelsey I. Nix, Esq.
Gasper I. LaRosa, Esq.
Sarah A. Geers, Esq.
JONES DAY
222 East 41st Street
New York, NY 10017
Tel: 212.326.3939

Dated: July 15, 2016

By: s/Tedd Van Buskirk/
Tedd W. Van Buskirk
Reg. No. 46,282

4576359_1.docx