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Paper 68
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ENDO PHARMACEUTICALS, INC.,
Petitioner,

v.

DEPOMED, INC.,
Patent Owner.

Case IPR2014-00652
Patent 6,723,340 B2

Before GRACE KARAFFA OBERMANN, GEORGIANNA W. BRADEN, and TINA E. HULSE, *Administrative Patent Judges*.

BRADEN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318 and 37 C.F.R. § 42.73

I. INTRODUCTION

We have jurisdiction to hear this *inter partes* review under 35 U.S.C. § 6(c). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73. For the reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1, 3–5, and 10–13 of U.S. Patent No. 6,723,340 B2 (Ex. 1001, "the '340 patent") are unpatentable. We also address the parties' Motions to Exclude.

A. Procedural History

Endo Pharmaceuticals, Inc. ("Petitioner") filed a Corrected Petition (Paper 5, "Pet.") to institute an *inter partes* review of claims 1–5 and 10–13 of the '340 patent pursuant to 35 U.S.C. § 311. Depomed, Inc. ("Patent Owner") filed a Preliminary Response (Paper 11, "Prelim. Resp."). Pursuant to 35 U.S.C. § 314(a), we instituted an *inter partes* review of claims 1, 3–5, and 10–13 on the following grounds alleged in the Petition.

Reference(s)	Basis	Claims challenged
Shell 1998 Publication[1]	§ 103	1, 3–5, and 10–13
Shell 1998 Publication and Papadimitriou[2]	§ 103	1, 3–5, and 10–13
Edgren[3] and Papadimitriou	§ 103	1, 3–5, and 10–13

Paper 12 ("Dec. to Inst."), 29.

[1] WO 1998/55107, PCT/US98/11302, issued Dec. 10, 1998 (Ex. 1003, "Shell 1998 Publication").
[2] Papadimitriou E., et. al., "*Swelling studies on mixtures of two hydrophilic excipients*," S.T.P. Pharma. Sciences Vol. 3, issue 3, pages 232–236 (Jun. 1993) (Ex. 1007, "Papadimitriou").
[3] U.S. Patent No. 4,871,548, issued Oct. 3, 1989 (Ex. 1006, "Edgren").

After institution of trial, Patent Owner filed a Patent Owner Response (Paper 25, "PO Resp."),[4] to which Petitioner filed a Reply (Paper 41, "Reply").

In addition, Petitioner filed a Motion to Exclude. Paper 51 ("Pet. Mot. Exclude"). Patent Owner filed an Opposition to Petitioner's Motion to Exclude (Paper 56, "PO Exclude Opp."), and Petitioner filed a Reply (Paper 58, "Pet. Exclude Reply"). Patent Owner also filed a Motion to Exclude. Paper 53 ("PO Mot. Exclude"). Petitioner filed an Opposition to Patent Owner's Motion to Exclude (Paper 54, "Pet. Exclude Opp."), and Patent Owner filed a Reply (Paper 59, "PO Exclude Reply"). Patent Owner also filed observations on the cross-examination of Petitioner's declarant (Paper 52), to which Petitioner filed a response (Paper 55).

An oral argument was held on June 15, 2015. A transcript ("Tr.") of the oral argument is included in the record.[5] Paper 67.

B. Related Proceedings

Petitioner informs us that the '340 patent is involved in the following co-pending federal district court cases: *Depomed, Inc. v. Actavis Elizabeth LLC*, 3:12-cv-01358-JAP-TJB (D.N.J.); *Depomed, Inc. v. Endo Pharms.*

[4] Patent Owner filed a confidential Patent Owner Response (Paper 24) and a public Patent Owner Response (Paper 25) to which Petitioner filed a confidential Reply (Paper 40) and a public Reply (Paper 41). All citations in this Final Written Decision are to the public Patent Owner Response (Paper 25) and public Petitioner Reply (Paper 41).

[5] The parties filed joint Objections to Demonstrative Exhibits. Paper 64. In this Final Written Decision, we rely directly on the arguments presented properly in the parties' briefs and the evidence of record. The demonstrative exhibits were only considered to the extent they are consistent with those arguments and evidence, therefore, the objections are overruled.

Inc., 3:13-cv-02467-JAP-TJB (D.N.J.)*; Depomed, Inc. v. Purdue Pharma L.P.*, 3:13-00571 JAP-TJB (D.N.J.)*; Depomed, Inc. v. Zydus Pharm. (USA), Inc*., 3:12-cv-02813-JAP-TJB (D.N.J.)*; Depomed, Inc. v. Sun Pharma Global FZE*, 3:11-CV-03553 (D.N.J.)*; Depomed, Inc. v. Impax Labs., Inc.*, 3:12-CV-02154 (D.N.J.)*; Depomed, Inc. v. Lupin Pharms., Inc.*, 4:09-CV-05587. Pet. 1. In addition, Petitioner filed several petitions requesting *inter partes* review of related patents. *Id*. at 2. Those cases are: IPR2014-00651 (involving the '340 patent); IPR2014-00653 and IPR2014-00654 (involving U.S. Patent No. 6,340,475 B2); and IPR2014-00655 and IPR2014-00656 (involving U.S. Patent No. 6,635,340 B2). *Id.* We consolidated the oral hearings for the three instituted proceedings: IPR2014-00652, IPR2014-00654, and IPR2014-00656. *See* Paper 57.

C. The '340 Patent

The '340 patent relates to drugs formulated as unit oral dosage forms by incorporating them into matrices formed of a combination of poly(ethylene oxide) ("PEO") and hydroxypropyl methylcellulose ("HPMC"). Ex. 1001, Abstract. The matrices swell upon exposure to gastric fluid to a size large enough to promote retention (*id*. at Abstract, 11:66–67) and release the drugs into the stomach or upper gastrointestinal ("GI") tract, rather than the lower portions of the GI tract (*id*. at 1:10–13). The '340 patent discloses that when nutritive materials enter the stomach, the stomach is in "fed mode" and the pyloric sphincter is open partially. *Id*. at 1:62–2:9. During the "fed mode," particles exceeding about 1 cm in size are retained in the stomach, because they are too large to pass through a partially open pyloric sphincter. *Id*. at 2:5–11.

PEO and HPMC are both water-swellable polymers. *Id*. at 3:11–15, 3:23–25, 10:38–46, Fig. 5. According to the '340 patent, the swelling and controlled release properties of PEO are balanced with the predictable erosion behavior of HPMC, which modulates the extent and progress of the overall swelling of a combined polymeric matrix. *Id*. at 3:40–43. The '340 patent discloses that the competing, yet complementary, actions of swelling and erosion allow for slower and more even disintegration compared to tablets made solely or primarily with PEO. *Id*. at 3:50–54.

Certain embodiments in the specification of the '340 patent teach that for highly soluble drugs, the PEO component of the matrix limits the initial release of the drug while imparting gastric retention through swelling. *Id*. at 4:5–7. In other embodiments, the specification teaches that for sparingly soluble drugs, the HPMC component of the matrices prevents premature release of the drugs by retarding the erosion rate of the PEO, while the PEO provides gastric retention. *Id*. at 4:10–14.

The specification further teaches that prolonged release rates reduce the problem of transient overdosing, and control the dosage to safer and more effective levels over an extended period of time. *Id*. at 7:44–49.

D. Illustrative Claim

As noted above, an *inter partes* review was instituted as to claims 1, 3–5, and 10–13 of the '340 patent, of which claim 1 is the only independent claim. Claim 1 is illustrative of the challenged claims and is reproduced below (with paragraphing):

> 1. A controlled-release tablet for releasing a drug into at least a portion of a region defined by the stomach and the upper gastrointestinal tract, said tablet comprising a solid monolithic matrix with said drug dispersed therein,

> said matrix comprising a combination of poly(ethylene oxide) and hydroxypropyl methylcellulose at a weight ratio that causes said matrix to swell upon contact with gastric fluid to a size large enough to provide gastric retention,
> wherein said drug has a solubility in water that exceeds one part of said drug per ten parts of water, by weight, and
> wherein said poly(ethylene oxide) has a viscosity average molecular weight of from about 2,000,000 to about 10,000,000 daltons, and
> wherein said hydroxypropyl methylcellulose has a viscosity of from about 4,000 centipoise to about 200,000 centipoise, measured as a 2% solution in water.

Id. at 11:60–12:9.

II. DISCUSSION

A. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *see also In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1278–79 (Fed. Cir. 2015) ("Congress implicitly approved the broadest reasonable interpretation standard in enacting the AIA," and "the standard was properly adopted by PTO regulation."), *reh'g en banc denied*, 793 F.3d 1297 (Fed. Cir. 2015). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

In the Decision to Institute, we construed the terms "monolithic matrix," "to swell upon contact with gastric fluid to a size large enough to provide gastric retention," and "gastric fluid" in independent claim 1. *See* Dec. to Inst. 6–10. During the course of the trial, neither party challenged

our constructions of these claim terms. PO Resp. 11–12. Thus, we see no reason to alter the constructions of these claim terms as set forth in the Decision to Institute, and we incorporate our previous analysis for purposes of this decision. Therefore, for the reasons set forth in the Decision to Institute, we interpret various claim terms of the '340 patent as follows:

Term(s)	Interpretation
"monolithic matrix"	"a matrix constructed as a single piece"
"to swell upon contact with gastric fluid to a size large enough to provide gastric retention"	"to increase in size upon contact with gastric fluid such that the tablet remains in the stomach"
"gastric fluid"	"both the fluid in the stomach and simulated or artificial fluids recognized by those skilled in the art as a suitable model for the fluid of the human stomach"

See Dec. to Inst. 6–10.

All other claim terms will be given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention.

B. Principles of Law

To prevail in its challenges to the patentability of the claims, a petitioner must establish facts supporting its challenges by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406 (2007). The question of obviousness is resolved on the basis of underlying factual determinations, including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness, i.e., secondary considerations. *See Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

We analyze the instituted grounds of unpatentability in accordance with the above-stated principles.

C. Level of Ordinary Skill in the Art

In determining whether an invention would have been obvious at the time it was made, we consider the level of ordinary skill in the pertinent art at the time of the invention. *Graham*, 383 U.S. at 17. "The importance of resolving the level of ordinary skill in the art lies in the necessity of maintaining objectivity in the obviousness inquiry." *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991).

Petitioner contends that a person of ordinary skill in the art at the time of the '340 patent would have "at least a bachelor's degree in chemistry, chemical engineering, pharmaceutical science and/or material science, as well as substantial experience (for example, at least several years of industrial or academic work) in the design and/or development of controlled release oral drug dosage forms." Pet. 10 (citing Ex. 1008). Petitioner further contends that a person of ordinary skill in the art "would also need to possess, or have access to, the skill of a pharmacologist familiar with how such medicines work in the body." *Id.* According to Petitioner's declarant, Dr. Clive Wilson, a person of ordinary skill in the art "would have experience, or access to other persons with experience, in the field of

pharmacology, with particular emphasis on the pharmacokinetics and pharmacodynamics of oral drugs absorbed in the GI tract." Ex. 1008 ¶ 26.

Patent Owner does not disagree with Petitioner's assertion regarding the level of skill in the art, nor does Patent Owner offer its own explanation regarding who would qualify as a person of ordinary skill in the art relevant to the '340 patent offer. PO Resp. 11.

Based on our review of the '340 patent and the types of problems and solutions described in the '340 patent and cited prior art, we conclude a person of ordinary skill in the art at the time of the '340 patent would have a Bachelor's degree in chemistry or a similar discipline, and at least several years of work experience in the design and/or development of controlled release oral drug dosage forms. We further note that the applied prior art reflects the appropriate level of skill at the time of the claimed invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

D. Alleged Obviousness of Claims 1, 3–5, and 10–13 in View of the Shell 1998 Publication

Petitioner alleges that claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103 in view of the Shell 1998 publication. Pet. 25–28. Patent Owner disputes Petitioner's position, arguing that although the Shell 1998 Publication discloses the use of both PEO and HPMC alone, it does not disclose, teach, or suggest the combination of PEO and HPMC as required by the challenged claims. PO Resp. 13. We have reviewed the Petition, the Patent Owner Response, and Petitioner's Reply, as well as the relevant evidence discussed in those papers. For reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that claims 1, 3–5, and 11–13 of the '340 patent are unpatentable in view of the Shell 1998 publication. We also determine Petitioner has not

shown by a preponderance of the evidence that claim 10 would have been obvious in view of the Shell 1998 publication.

1. Overview of the Shell 1998 Publication

The Shell 1998 Publication discloses drugs formulated as unit oral dosage forms by incorporating them into polymeric matrices that can be compressed into tablets. Ex. 1003, Abstract. The dosage forms are solid prior to administration to a patient, water-swellable, and gastric retentive in a fed mode (a state triggered by food ingestion that lasts for a period of time). *Id*. at 2:23–32, 3:2–5. The Shell 1998 Publication specifically discloses polymeric matrices made from (i) cellulose polymers and their derivatives, (ii) polysaccharides and their derivatives, (iii) polyaklylene oxides, and (iv) crosslinked polyacrylic acids and their derivatives. *Id*. at 5:4–6. Particularly preferred alkyl-substituted celluloses are hydroxyethylcellulose and HPMC. Ex. 1003, 5:17–18. A particularly preferred polyalkylene oxide is PEO. *Id*. at 5:22–23.

The Shell 1998 Publication further discloses that in terms of their viscosities, one class of preferred alkyl-substituted celluloses includes those whose viscosity is within the range of about 100 to about 110,000 centipoise as a 2% aqueous solution at 20°C, while another class includes those whose viscosity is within the range of about 1,000 to about 4,000 centipoise as a 1% aqueous solution at 20°C. *Id*. at 5:13–16. For PEO, the Shell 1998 Publication teaches that a preferred viscosity range is about 50 to about 2,000,000 centipoise for a 2% aqueous solution at 20°C. *Id*. at 5:26–28.

The Shell 1998 Publication teaches that the water-swellable polymers it discloses can be used individually or in combination with each other. *Id*. at 6:32. According to the Shell 1998 Publication, "[c]ertain combinations

will often provide a more controlled release of the drug than their components when used individually." *Id*. at 6:32–34. The Shell 1998 Publication gives examples of such combinations, including combining cellulose-based polymers with gums, such as hydroxyethyl cellulose or hydroxypropyl cellulose combined with xanthan gum, or combining PEO with xanthan gum. *Id*. at 6:34–36.

The polymer mixture can then be impregnated or combined with a drug and formed into particles, tablets, or retained in capsules. *Id*. at 7:3–4, 7:24–26. According to the Shell 1998 Publication, the disclosed invention applies to drugs that are "freely soluble" in water, meaning that one part of the drug dissolves in less than about ten parts water. *Id*. at 4:7–9. "The matrix itself is solid prior to administration and, once administered, remains undissolved in (*i.e*., uneroded by) the gastric fluid for a period of time sufficient to permit a majority of the drug to be released . . . ." *Id*. at 3:3–4.

2. Analysis

a. The Shell 1998 Publication Teaches or Suggests All the Recited Limitations of Independent Claim 1

Independent claim 1 requires a solid monolithic matrix made of PEO and HPMC with a drug dispersed in the matrix. Ex. 1001, 11:60–12:9. The claim characterizes PEO and HPMC by a specified viscosity and states that the drug must be water soluble. *Id.* The claim further recites that the weight ratio of the polymers in the matrix must cause the matrix to swell when the tablet gets to the stomach, so the tablet is retained in the stomach. *Id.*

According to Petitioner, the Shell 1998 Publication identifies a small number of preferred polymers, including "particularly preferred" polymers PEO and HPMC, used to create a solid polymeric matrix in which a drug is

dispersed. Pet. 25. Petitioner explains that the Shell 1998 Publication teaches the use of the polymers individually or in combination. *Id.*; *see* Ex. 1008 ¶ 83. For example, the Shell 1998 Publication discloses polymeric matrices made from combinations of PEO and hydroxyethyl cellulose. Pet. 25 (citing Ex. 1003, 12:13–16, 13:27–30). The Shell 1998 Publication also lists hydroxyethyl cellulose and HPMC as two "[p]articularly preferred alkyl-substituted celluloses" that can be used in the polymeric matrices. Ex. 1003, 5:17–18. Petitioner supports its position with the declaration of Dr. Clive Wilson, who testifies that based on the disclosure of the Shell 1998 Publication, it would have been obvious for a skilled artisan to use combinations of HPMC and PEO polymers to achieve a gastric retentive controlled-release dosage form as recited in challenged claim 1. Ex. 1008 ¶ 88. Petitioner, thus, concludes that the Shell 1998 Publication teaches or at least suggests the combination of PEO and HPMC for polymeric matrices and renders the challenged claims obvious. Pet. 28.

Patent Owner contests Petitioner's conclusion that the Shell 1998 Publication teaches or suggests a matrix made from a combination of PEO and HPMC as required by independent claim 1. PO Resp. 13. To the contrary, Patent Owner contends the Shell 1998 Publication does not disclose or contemplate a matrix comprising the combination of PEO and HPMC. *Id*. at 14. Patent Owner specifically argues that (1) the overwhelming majority of polymeric matrices taught by the Shell 1998 Publication are made of just one polymer, and (2) the combinations taught by the Shell 1998 Publication all use xantham gum or hydroxyethyl cellulose because these polymer combinations "provide a more controlled release of the drug than their components when used individually." PO Resp. 14

(citing Ex. 1003, 6:32–36, 12:13–16, 13:22–14:5). Patent Owner also contends that the Shell 1998 Publication does not include PEO and HPMC on a "short list" of polymers that could be combined to form a polymeric matrix. *Id.* at 18. Rather, Patent Owner argues that PEO and HPMC are on a "short list" to be used either independently or in combination with other polymers (such as xantham gum or hydroxyethyl cellulose) that did not meet certain performance criteria for controlled drug release. *Id.* According to Patent Owner, HPMC is not interchangeable with xantham gum or hydroxyethyl cellulose for the purposes of creating gastric retentive, controlled release tablets, because, as shown in Figure 6 of the Shell 1998 Publication, PEO and xantham gun were beneficial in a mixture with hydroxyethyl cellulose, whereas HPMC was not. *Id.* at 18–19 (citing Ex. 1003, Fig. 6); Ex. 2009 ¶ 70.

Patent Owner further contends that not only does the Shell 1998 Publication fail to disclose, suggest, or teach the exact combination of PEO and HPMC, but based on the Shell 1998 Publication, a person of ordinary skill in the art specifically would not have contemplated combining PEO and HPMC. PO Resp. 16; Ex. 2009 ¶ 58. Patent Owner contends that PEO and HPMC performed adequately on their own to control drug release, and there was no indication that combining PEO and HPMC would improve on their independent performance, or would have been "promising to try." *Id.* Patent Owner specifically argues that without first identifying a deficiency in the performance of individual polymers (*e.g.*, PEO and HPMC alone), a person of ordinary skill in the art would not have combined them, and even if a person of ordinary skill in the art would have combined the polymers, the behavior of the resultant mixture would not have been predictable. *Id.*

(citing Ex. 2009 ¶¶ 59–63). Patent Owner relies on the declaration of Dr. Hopfenberg to support its position. Dr. Hopfenberg testifies that:

> [C]ombining polymers introduces uncertainty related to the structure and properties of the combination of individual polymers comprising the combination. These structural variations can significantly affect the properties that are critical for a gastric-retentive controlled release form, including swelling, drug release, mechanical integrity, and the tendency to undergo long term degradation of the matrix of the dosage form subsequent to the designed release.

Ex. 2009 ¶ 59.

> The results set forth in Figure 6 of the Shell 1998 [publication] reveal that, with respect to drug retention in the dosage form after immersion for one hour, the behavior of the mixtures was unpredictable based on the behavior of the corresponding homopolymers . . . [t]he HEC/PEO and HEC/XG mixtures [used in the immersion experiment] showed significant improvement over HEC alone, yet the HEC/HPMC mixture, similar to HEC alone, failed to retain at least 40% of the drug after one hour. The dramatically different effect on drug retention following immersion resulting from forming an HEC combination with HPMC, as opposed to forming an HEC combination with PEO or XG, could not have been predicted.

Id. ¶ 63.

Thus, Patent Owner concludes that given the unpredictability of mixing two different polymers, a person of ordinary skill in the art would not set out to do so, absent a compelling motivation, and the Shell 1998 Publication provides no such motivation. PO Resp. 17–18 (citing Ex. 2009 ¶ 64).

We do not agree with Patent Owner, because an obviousness analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and

creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418; *see In re Translogic Tech., Inc.*, 504 F.3d. at 1259. A combination would have been obvious under § 103 if "there are a finite number of identified, predictable solutions" to a known problem and when a path has been identified that "leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." *KSR*, 550 U.S. at 418. The Court of Appeals for the Federal Circuit has elaborated that the identified path must "present a finite (and small in the context of the art) number of options easily traversed to show obviousness." *Ortho–McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed.Cir. 2008).

Although the Shell 1998 Publication does not disclose a polymeric matrix made from a combination of PEO and HPMC, it does disclose a short list of polymers to be used individually in producing a solid matrix for controlled drug release, of which HPMC (Ex. 1003, 5:17–18) and PEO (*id.* at 5:22–23) are particularly preferred polymers. The Shell 1998 Publication also teaches that polymers can be combined to form a polymeric matrix. *Id.* at 6:32–34. The Shell 1998 Publication does not limit which polymers could be combined or suggest that certain polymers would not function properly in a combination matrix. *Id.*; *see In re Susi*, 440 F.2d 442, 445 (CCPA 1971) (affirming obviousness rejection where the disclosure of the prior art was "huge, but it undeniably include[d] at least some of the compounds recited in appellant's generic claims and it is of a class of chemicals to be used for the same purpose as appellant's additives"). Furthermore, we credit the testimony of Dr. Wilson, who stated that "as of October 2001, PEO and HPMC were widely known polymers in the art for use in controlled release

drug delivery systems" and "the Shell 1998 Publication identifies only a limited number of particularly preferred polymers, including PEO and HPMC." Ex. 1044 ¶ 28. Those facts support a conclusion that one would have understood that the Shell 1998 Publication "teaches that these polymers can be used in combination." *Id.* Thus, given the teachings in the Shell 1998 Publication, we determine that there were a finite number of identified, predictable polymers that could be used individually or in combination to create a solid matrix for controlled drug release and we further determine that the combination of PEO and HPMC, identified by the Shell 1998 Publication as particularly preferred polymers, would have been obvious to one of ordinary skill in the art at the time of the '340 patent. *KSR*, 550 U.S. at 421 (describing that a person of ordinary skill possesses "ordinary creativity, [and is] not an automaton").

Patent Owner, however, argues that even if a person of skill in the art would have contemplated a combination of PEO and HPMC in light of the Shell 1998 publication, there would not have been a reasonable expectation of success because it could not be predicted whether the disclosed polymer mixtures would have worked. PO Resp. 21 (citing Ex. 2009 ¶ 63). Yet, obviousness does not require absolute predictability. *Allergan, Inc. v. Apotex, Inc.*, 754 F.3d 952, 965 (Fed. Cir. 2014); *In re O'Farrell*, 853 F.2d 894, 903 (Fed.Cir.1988). What does matter is whether the prior art gives direction as to what parameters are critical and which of many possible choices may be successful. *Allergan*, 754 F.3d at 965. While success in employing the disclosed polymers to form a solid matrix for controlled drug release may not have been guaranteed, we are satisfied that explicitly identifying PEO and HPMC as particularly preferred polymers sufficiently

provided guidance as to what parameters and polymers would lead to a reasonable expectation of success.

Therefore, we determine that the Shell 1998 Publication at least suggests a polymeric matrix made from a combination of PEO and HPMC and, given the Shell 1998 Publication's teachings, we find that a person of ordinary skill in the art would have been able to make and use the claimed invention without anything more than routine experimentation. Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

b. The Shell 1998 Publication Teaches or Suggests the Recited Limitations of Dependent Claims 3–5 and 11–13

Petitioner contends dependent claims 3–5 and 10–13 are unpatentable under 35 U.S.C. § 103(a) for obviousness over the Shell 1998 Publication. Pet. 27–28. Patent Owner contests Petitioner's position, arguing that the challenged dependent claims share the same material requirement of a PEO/HPMC combination as independent claim 1, and therefore, for the same reasons that claim 1 is not obvious over the Shell 1998 Publication, the dependent claims also are not obvious over the Shell 1998 Publication. PO Resp. 24. We agree with Petitioner's position, as supported by the testimony of Dr. Wilson, that the Shell 1998 Publication teaches the HPMC and PEO molecular weight and viscosities required by dependent claims 3 and 4 (Ex. 1003, 4:33–5:1, 5:13–15, 5:28–30), as well as the drug water solubility required by dependent claim 5 (*id.* at 4:9–12) and the proportions of the dosage form made up by the combination of PEO and HPMC required by dependent claims 11–13 (*id.* at Example 1, 8). *See* Ex. 1008 ¶¶ 82, 91, 125,

130, 131, 135, 141, 144, 147. Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that dependent claims 3–5 and 11–13 are unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

c. The Shell 1998 Publication Fails to Teach or Suggest the Recited Limitations of Dependent Claim 10

Petitioner contends dependent claim 10 is unpatentable under 35 U.S.C. § 103(a) for obviousness over the Shell 1998 Publication. Pet. 27–28. Patent Owner contests Petitioner's position, arguing that the challenged dependent claim 10 shares the same material requirement of a PEO/HPMC combination as independent claim 1, and therefore, for the same reasons that claim 1 is not obvious over the Shell 1998 Publication, claim 10 also is not obvious over the Shell 1998 publication. PO Resp. 24.

While we agree with Petitioner that the Shell 1998 Publication teaches or suggests the limitations of claims 1, 3–5, and 11–13, we are not satisfied that Petitioner has shown by a preponderance of the evidence that the Shell 1998 Publication teaches or suggests the PEO:HPMC weight ratio set forth in dependent claim 10. The testimony of Petitioner's declarant, Dr. Wilson, merely provides that the Shell 1998 Publication "disclose[s] a controlled-release dosage form dispersed in a water-swellable polymeric matrix, and that the polymers of the matrix, including PEO and HPMC, can be used individually or in combination." *See* Ex. 1008 ¶¶ 138, 140. Neither Petitioner nor Dr. Wilson provide an explanation of how the Shell 1998 Publication renders the specific PEO:HPMC weight ratios set forth in dependent claim 10 obvious. A determination of obviousness cannot be sustained by mere conclusory statements; instead, there must be some

articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *KSR*, 550 U.S. at 418; *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006).

Furthermore, we must be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the reference would produce the claimed invention. *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1368 (Fed. Cir. 2012) (quoting *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008)); *see also KSR*, 550 U.S. at 421 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.").

Accordingly, we hold that Petitioner has not shown by a preponderance of the evidence that dependent claim 10 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

E. Alleged Obviousness of Claims 1, 3–5, and 10–13 in View of the Shell 1998 Publication and Papadimitriou

Petitioner contends claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103 in view of the Shell 1998 Publication and Papadimitriou. Pet. 29–32. Patent Owner disputes Petitioner's position, arguing that that one of skill in the art would not have combined the Shell 1998 Publication and Papadimitriou. PO Resp. 24–34. We have reviewed the Petition, the Patent Owner Response, and Petitioner's Reply, as well as the relevant evidence discussed in those papers. For reasons that follow, we determine that Petitioner has shown by a preponderance of the evidence that

the challenged claims would have been obvious in view of the Shell 1998 Publication and Papadimitriou.

1. Overview of Papadimitriou

Papadimitriou discloses a sustained drug delivery system achieved "by the use of hydrophilic polymer excipients, which swell in the presence of water." Ex. 1007, 232. Papadimitriou examines the percolation threshold for polymeric matrices and the impact of varying the concentration of hydrophilic polymer excipients in the matrices on drug release rates from lattice-type matrices. *Id*. at 232–33. Papadimitriou teaches the use of HPMC and PEO as hydrophilic water-swellable polymers, alone or in combination. *Id*. at 233, Fig. 1. The polymers are compressed into tablets that have a diameter of 9 mm and a height of 8mm. *Id*. As shown in Figure 1 of Papadimitriou, reproduced below, a polymer matrix containing PEO and HPMC swelled by at least 40% of its original size within 30 minutes.

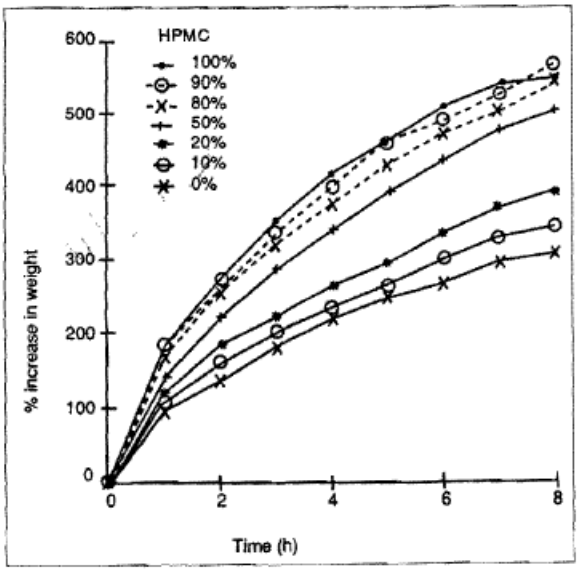

Figure 1 of Papadimitriou illustrates increases in weight (%) as a function of time for matrices composed of HPMC and/or PEO.

Based on the results indicated in Figure 1, Papadimitriou states "all the tablets were observed to swell significantly, as indicated by the large weight increase." Ex. 1007, 233.

Papadimitriou discloses PEO with a viscosity average molecular weight of from about 2,000,000 to 10,000,000 daltons. *Id*. at 233. Papadimitriou also discloses HPMC (i.e., Methocel K100M) with a viscosity in a range of approximately 4,000–200,000 centipoise, measured as a 2% solution in water. *Id*. at 233. Papadimitriou further discloses combinations of HPMC and PEO with ratios ranging from 100% HPMC:0% PEO to 0%HPMC:100%PEO. *Id*. at 233.

2. Overview of the Shell 1998 Publication

The disclosure of the Shell 1998 Publication is discussed in detail above in Section II.D.1.

3. Analysis

a. The Shell 1998 Publication and Papadimitriou Teach or Suggest All the Recited Limitations of Independent Claim 1

As discussed previously, independent claim 1 requires a solid monolithic matrix made of PEO and HPMC with a drug dispersed in the matrix. Ex. 1001, 11:60–12:9. Petitioner contends the Shell 1998 Publication in combination with Papadimitriou, as summarized above, teaches each limitation of claim 1. Pet. 28–31. Specifically, Petitioner argues that (1) the Shell 1998 Publication identifies a small number of preferred polymers, including "particularly preferred" polymers PEO and HPMC, that can be used individually or in combination to create a solid polymeric matrix in which a drug is dispersed, and (2) Papadimitriou likewise discloses a sustained drug delivery system achieved "by the use of

hydrophilic polymer excipients, which swell in the presence of water" and expressly teaches the use of HPMC and PEO as hydrophilic, water-swellable matrix polymers, alone or in combination. *Id.*; *see* Ex. 1008 ¶ 92 (citing Ex. 1003, 6:32; Ex. 1007, 232), ¶ 93 (citing Ex. 1007, 232, Fig. 1). Petitioner further notes that Papadimitriou specifically discloses Methocel K100M, a commercially available HPMC having a viscosity of 100,000 centipoise. Pet. 29; Ex. 1008 ¶¶ 93, 101.

According to Petitioner, a person of ordinary skill in the art would have been led to combine the teachings of the Shell 1998 Publication with Papadimitriou, because the disclosures share the common goal of releasing a drug in a controlled or sustained manner by using a swellable polymeric matrix. Pet. 30–31; *see* Ex. 1008 ¶ 94. Petitioner supports its position with the declaration of Dr. Wilson, who testifies that a skilled artisan "reading the Shell 1998 Publication would look to Papadimitriou for further examples of polymer matrices that would be compatible with the teachings of the Shell 1998 Publication." Ex. 1008 ¶ 94. Petitioner then concludes that the polymer matrix of Papadimitriou comprising a combination of HPMC and PEO can be used in the drug dosage form of the Shell 1998 Publication. Pet. 31; *see* Ex. 1008 ¶ 94.

Patent Owner disagrees with Petitioner's contention that one of ordinary skill in the art would look to combine the teachings of the Shell 1998 Publication and Papadimitriou. PO Resp. 24. First, Patent Owner argues that Papadimitriou does not disclose, teach, or suggest **any benefit** of the PEO/HPMC combination to any dosage form, let alone a gastric retentive one, but instead focuses on the unpredictable polymer-to-polymer interactions in such mixtures in order to underscore the **complexities and**

pitfalls of such polymer mixtures. *Id*. at 26; Ex. 2009 ¶ 74. Patent Owner then argues "[Petitioner] concedes that Papadimitriou does not teach or suggest gastric retentive drug dosage forms at all" because Petitioner's claim charts do not cite to Papadimitriou in relation to gastric retention. PO Resp. 28 (citing Pet. 20–21).

Second, Patent Owner argues that a person of ordinary skill in the art would not have combined Papadimitriou with the Shell 1998 Publication, because Papadimitriou is not related to gastric retention, which was an essential component of the problem solved by the '340 patent. *Id*. at 28. Patent Owner supports its argument that Papadimitriou is not directed to a gastric retentive dosage form with the fact that the swelling experiments in Papadimitriou were conducted at a neutral pH of 7.4, instead of an acidic pH similar to that of gastric fluid. *Id*. at 28–29 (citing Ex. 1007, 233); Ex. 2009 ¶ 79. Patent Owner then argues that Papadimitriou's experiments are deficient because Papadimitriou did not present any drug release profiles, and in fact, did not even include drug in any experiment. *Id.* at 30 (citing Ex. 1007, 233 ("In this work, the degree of swelling of combinations of the two excipients alone (i.e. **without drug** or other excipients) is considered.")) (emphasis added); Ex. 2009 ¶ 80. According to Patent Owner, the presence of drug would further impact how the polymers swelled. PO Resp. 30. Patent Owner further argues that the assays reported in Papadimitriou were carried out in phosphate buffer, which was known to be problematic for PEO because it leads to phase separation. *Id.* (citing Ex. 2009 ¶ 81; Ex. 2015 ¶ 29). Patent Owner relies on the testimony of Dr. Hopfenberg, whose testimony reiterates Patent Owner's contentions regarding the teachings in Papadimitriou. Ex. 2009 ¶¶ 74–87. Based on the postulated problems with

the experimental designs disclosed in Papadimitriou, Patent Owner asserts that a skill artisan would not rely on Papadimitriou in the creation of a controlled release dosage form, let alone a gastric retentive one. *Id*. at 30.

Lastly, Patent Owner argues that the combination of the Shell 1998 Publication and Papadimitriou would not have provided a person of ordinary skill in the art with a reasonable expectation of success in practicing the '340 patent claims. *Id*. at 31. According to Patent Owner, (i) a person of ordinary skill in the art would not have found the teachings of the Shell 1998 Publication and Papadimitriou compatible or directed to similar issues (*id*. at 31), and (ii) the unpredictable interactions of polymers as disclosed by Papadimitriou indicates that a person of ordinary skill "could not predict whether the disclosed xantham-based and HEC-based polymer combinations would work, as reflected by 'failed' combinations such as HEC/HPMC" (*id*. at 32–33 (citing Ex. 2009 ¶ 63)). Thus, Patent Owner concludes that a combination of the Shell 1998 Publication and Papadimitriou is based on impermissible hindsight because a skilled artisan would not have combined the teachings of the two references. *Id*. at 33.

Despite Patent Owner's arguments, we agree with Petitioner that challenged claims 1, 3–5, and 10–13 would have been obvious over the Shell 1998 Publication and Papadimitriou. Specifically, we find that a skilled artisan would look to the teachings of Papadimitriou in combination with the Shell 1998 Publication's disclosure in attempts to solve the problem of releasing a drug in a controlled or sustained manner by using a combination of PEO and HPMC, both of which are swellable hydrophilic polymers. This finding is based on the fact that Papadimitriou's disclosure is directed specifically to "sustained drug delivery . . . by the use of

hydrophilic polymeric excipients" (Ex. 1007, 232), while the Shell 1998 Publication is directed to sustained release unit dosage forms incorporated into polymeric matrices made of hydrophilic polymers (Ex. 1003, Abstract). *See id.* at 2:30–32, 3:8–11, 6:32–34; Ex. 1007, Abstract, 233; *see also* Ex. 1008 ¶ 92 ("[T]he Shell 1998 patent publication discloses that the water-swellable polymer matrix in which the drug is dispersed may be formed of an individual polymer or a combination of polymers (Exh. 1003, 6:32) . . . Papadimitriou expressly teaches the use of HPMC and PEO as hydrophilic, water-swellable matrix polymers, alone or in combination. (Exh. 1007, p. 233, Fig. 1).") Therefore, contrary to Patent Owner's statements, the references are directed to similar issues and disclose PEO and HPMC as swellable hydrophilic polymers. Accordingly, we hold that a skilled artisan at the time of the invention would have considered the teachings of Papadimitriou compatible with the teachings of the Shell 1998 Publication, and would apply the disclosures in combination.

We also are not persuaded by Patent Owner's arguments, as they narrowly focus on small differences between Papadimitriou and the Shell 1998 Publication and fail to consider the collective teachings of Papadimitriou and the Shell 1998 Publication from the perspective of one of ordinary skill in the art. *See KSR*, 550 U.S. at 420 ("[F]amiliar items may have obvious uses beyond their primary purpose, 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.") The fact that Papadimitriou uses PEO and HPMC, which are called out specifically in the Shell 1998 Publication as particularly preferred polymers to use, weighs in favor of finding that a person of ordinary skill in the art would "fit the teachings" of Papadimitriou and the

Shell 1998 Publication together to render the challenged claims obvious. Additionally, the arguments presented by Patent Owner appear to attack Papadimitriou individually, rather than in combination with the Shell 1998 Publication. *See* PO Resp. 26–30. Nonobviousness cannot be established by attacking the references individually when a challenge is predicated upon a combination of prior art disclosures. *See In re Merck & Co., Inc.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). In attacking Papadimitriou individually, Patent Owner fails to address Petitioner's actual challenges or, therefore, establish an insufficiency in the combined teachings of the references.

Furthermore, we are not persuaded by Patent Owner's arguments that the combination of the Shell 1998 Publication and Papadimitriou would not have provided a person of ordinary skill in the art with a reasonable expectation of success in practicing the '340 patent claims because the nature of polymer mixtures is unpredictable. The case law is clear that obviousness cannot be avoided simply by showing some degree of unpredictability in the art, as long as there was a reasonable probability of success. *See Pfizer, Inc. v. Apotex*, 480 F.3d 1348, 1369 (Fed. Cir. 2007); (holding that "a skilled artisan would have had a reasonable expectation of success with the besylate salt form of amlodipine at the time the invention was made"); *In re Corkill*, 771 F.2d 1496, 1500 (Fed. Cir. 1985) ("Although [the inventor] declared that it cannot be predicted how any candidate will work in a detergent composition, but that it must be tested, this does not overcome [the prior art's] teaching that hydrated zeolites will work.").

This is not a case where the prior art merely teaches to pursue a "general approach that seemed to be a promising field of experimentation" or "gave only general guidance as to the particular form of the claimed

invention or how to achieve it." *O'Farrell*, 853 F.2d at 903 ("Obviousness does not require absolute predictability of success . . . [A]ll that is required is a reasonable expectation of success."); *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed.Cir.2006) ("While the definition of 'reasonable expectation' is somewhat vague, our case law makes clear that it does not require a *certainty* of success.") (internal citations omitted). Although success in employing the disclosed polymers to form a solid matrix for controlled drug release may not have been guaranteed, we are satisfied that the Shell 1998 Publication in view of Papadimitriou sufficiently provided guidance as to what parameters and polymers would lead to a reasonable expectation of success by explicitly identifying PEO and HPMC as particularly preferred polymers.

Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication and Papadimitriou.

b. The Shell 1998 Publication and Papadimitriou Teach or Suggest the Recited Limitations of Dependent Claims 3–5 and 10–13

Petitioner contends dependent claims 3–5 and 10–13are unpatentable under 35 U.S.C. § 103(a) for obviousness over the Shell 1998 Publication and Papadimitriou. Pet. 31–32. Patent Owner contests Petitioner's position, arguing that the challenged dependent claims share the same material requirement of PEO/HPMC combinations as independent claim 1, and therefore, for the same reasons that claim 1 is not obvious over the Shell 1998 Publication and Papadimitriou, the dependent claims also are not

obvious over the Shell 1998 Publication and Papadimitriou. PO Resp. 34. For reasons stated above, we find that position unpersuasive.

We agree with Petitioner's further position, as supported by the testimony of Dr. Wilson, that the Shell 1998 Publication and Papadimitriou teach (a) the HPMC and PEO molecular weight and viscosities required by dependent claims 3 and 4 (Ex. 1003, 4:33–5:1, 5:13–15, 5:28–30), (b) the drug water solubility required by dependent claim 5 (*id.* at 4:9–12), (c) the weight ratio of PEO to HPMC as required by dependent claim 10 (Ex. 1007, 233), and (d) the proportions of the dosage form made up by the combination of PEO and HPMC required by dependent claims 11–13 (Ex. 1003, Example 1, 8). *See* Ex. 1008 ¶¶ 91, 92, 127, 128, 133–137, 139, 141–149. Accordingly, we hold that Petitioner has shown by a preponderance of the evidence that dependent claims 3–5 and 10–13 are unpatentable under 35 U.S.C. § 103(a) for obviousness in view of the Shell 1998 Publication.

F. Alleged Obviousness of Claims 1, 3–5, and 10–13 in View of Edgren and Papadimitriou

Petitioner contends claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103 in view of Edgren and Papadimitriou. Pet. 39–42. Patent Owner disputes Petitioner's position, arguing that one of skill in the art would not have had reason to combine Edgren and Papadimitriou. PO Resp. 34–42. We have reviewed the Petition, the Patent Owner Response, and Petitioner's Reply, as well as the relevant evidence discussed in those papers. For reasons that follow, we determine that Petitioner has not shown by a preponderance of the evidence that the challenged claims are unpatentable as obvious over Edgren and Papadimitriou.

1. Overview of Edgren

Edgren describes a controlled-release dosage form for delivering a drug in the gastrointestinal tract comprising a beneficial drug and at least two different cellulose ethers (*i.e.*, a polymer matrix) that swell when hydrated. Ex. 1006, 1:12–13, 2:37–52; 3:17, 11:23–28. Edgren further discloses that its polymeric matrices are composed of a low number average molecular weight HPMC and a high number average molecular weight HPMC. *Id*. at Abstract, 5:10–26, 11:23–28. The drugs disclosed in Edgren include those that are very soluble, such as captopril and ranitidine. *Id*. at 2:53–56, 2:61–68, 5:27–67, 8:47; 9:1–2. Edgren describes a drug dosage form comprising at least thirty weight percent of HPMC polymers and up to seventy weight percent of a soluble drug. *Id*. at 1:17–19, 1:30–32, 3:8–10. According to Edgren, the drug/HPMC mixture can be fed into a hopper of a compression machine, where about two tons of pressure is applied to compress the composition together into a dosage form. *Id*. at 7:27–31.

Edgren teaches that the disclosed HPMC polymers make "available a drug delivery matrix suitable for retention in the stomach for gastric retention over the drug releasing life time of the dosage system." *Id*. at 10:65–68. Edgren further teaches that the HPMC polymers swell extensively when hydrated and reduce irritation of mucosal tissue by the drug because there is less direct drug contact with the tissue. *Id*. at 11:23–28.

2. Overview of Papadimitriou

The disclosure of Papadimitriou is discussed in detail above in Section II.E.2.

3. Analysis

Petitioner contends Edgren, as summarized above, in combination with Papadimitriou teaches or suggests each limitation of claims 1–5 and 10–13 of the '340 patent. Pet. 39–42. Petitioner specifically contends that Edgren teaches the use of polymeric ethers in combination and does not teach away from using PEO with HPMC. Reply 8. Petitioner supports its position with a declaration of Dr. Wilson, who testifies that the "Background of the Invention" section of Edgren describes disadvantages of prior art formulations that used HPMC with other cellulosic ethers, however, none of the prior art cited in Edgren used PEO. Ex. 1044 ¶ 63. Dr. Wilson, therefore, opines that Edgren cannot be considered as teaching away from using polymers, such as PEO and HPMC, in combination. *Id.* ¶ 64.

Petitioner also contends that a person of ordinary skill in the art would have been led to combine the teachings of Edgren with Papadimitriou, because the disclosures share the common goal of releasing a drug in a controlled or sustained manner by using a swellable polymeric matrix. *Id.* at 40–41; *see* Ex. 1008 ¶¶ 115–116. According to Petitioner, a skilled artisan reading Edgren would look to Papadimitriou for further examples of polymer matrices that would be compatible with the teachings of Edgren. Petitioner then contends that one of the goals of Edgren was to provide greater mechanical integrity than the dosage forms of the prior art, and PEO, as disclosed in Papadimitriou, was a readily available polymer with high swelling potential that was known to increase mechanical integrity. Reply 9 (citing Ex. 1043 ¶ 65; Ex. 1006, 1:27–44, 3:1–7, 11:3–7; Ex. 2023, 145:4–149:2). Petitioner concludes that because it was known that polymers could be combined to provide better controlled release (*see, e.g.*, Ex. 1003), it

would have been obvious to a skilled artisan that the polymer matrix of Papadimitriou, comprising a combination of HPMC and PEO, could have been used in the drug dosage form of Edgren. Pet. 41; Reply 9 (citing Ex. 1043 ¶ 65).

Patent Owner disagrees with Petitioner's contention, arguing the claim would not have been obvious in view of the combination of Edgren and Papadimitriou, for several reasons. PO Resp. 34–41. First, Patent Owner argues that a skilled artisan would not have combined Edgren with Papadimitriou because Edgren teaches away from the claimed PEO/HPMC combination. *Id.* at 35. According to Patent Owner, Edgren specifically discourages combining HPMC with polymeric ethers (of which PEO is a member). *Id.* Second, Patent Owner argues there is no reason why a skilled artisan would have thought to combine the elements of Edgren and Papadimitriou, because (i) Edgren is directed to combining two forms of HPMC, (ii) Edgren does not disclose PEO, (iii) PEO and HPMCs are not interchangeable, (iv) Papadimitriou – and its disclosure of a PEO/HPMC combination – does not apply to gastric retentive dosage form, and (v) reading Edgren and Papadimitriou together would not provide a skilled artisan with a reasonable expectation that the unique PEO/HPMC combination of the'340 patent would work for the intended purpose of providing gastric retention and controlled drug release. *Id.* at 37–39; *see* Ex. 2009 ¶¶ 92–93.

On the record developed at trial, we are not persuaded that Petitioner has shown by a preponderance of the evidence that a person of ordinary skill in the art would have had a reason to combine the references with a reasonable expectation of success. Although the references may have

interrelated teachings because they both are directed to polymers, Petitioner has not explained persuasively *how or why* a person of ordinary skill in the art would have exchanged one of the HPMCs in the Edgren formulation with PEO in the formulation of Papadimitriou.

Edgren specifically discloses using "at least two cellulose ethers that function together for enhancing the pharmaco-release kinetics of the dosage form" and using a "cellulose ether formulation [of high molecular weight HPMC and low molecular weight HPMC that] operate[s] as a unit in a moving fluid for controlling the rate of release of a beneficial drug from the dosage form." Ex. 1006, 2:33–45. Despite this disclosure, Petitioner argues that a skilled artisan would have used PEO in the Edgren formulation simply because "PEO was a readily available polymer with high swelling potential that was known to increase mechanical integrity." *See* Reply 9; Ex. 1043 ¶ 65. Petitioner provides insufficient evidence that a person of skill in the art would have found PEO (a non-cellulose ether) to be interchangeable with low molecular weight HPMC (a cellulose ether) or that PEO would have been able to act as a unit with high molecular weight HPMC as described in Edgren. In fact, at deposition, Petitioner's declarant, Dr. Wilson, testified that PEOs and low molecular weight HPMCs are not interchangeable.

> Q. Is it your position that all of the Polyoxes that make up the class of Polyoxes and all of the low molecular weight HPMCs that make up that class are interchangeable in terms of their ability to absorb water?
>
> A. No.
>
> Q. They are not interchangeable?
>
> A. They are not interchangeable.
> You would get a different characteristic
> but then you would blend backwards and

> forwards to get the required uptake of water you are seeking.
>
> Q. So there are differences amongst the various Polyox and low molecular weight HPMCs in terms of their ability to absorb water, correct?
>
> A. Yes, there is, yes.
>
> Q. And there are, likewise, differences in terms of their ability to swell?
>
> A. Yes.
>
> Q. And in terms of their ability to erode, correct?
>
> A. That's true.

Ex. 2023, 279:21–280:21.

Given this testimony, we find that Petitioner's argument is fraught with hindsight bias. *See KSR*, 550 U.S. at 418 ("A patent composed of several elements is not proved obvious by merely demonstrating that each of its elements was, independently, known in the prior art."); *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1368–69 (Fed. Cir. 2012) ("[Smith & Nephew] never offered evidence articulating why a person having ordinary skill in the art would combine the primary references to obtain the disclosed inventions."); *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1373–74 (Fed. Cir. 2008) ("We must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention."). In the absence of PEO and low molecular weight HPMC being readily interchangeable, Petitioner needed to explain what would have led a person of ordinary skill in the art at the time of the invention to replace low molecular weight HPMC in the Edgren formulation with PEO. Petitioner failed to provide such an explanation.

Petitioner must demonstrate obviousness by a preponderance of the evidence. *See Yamaha Int'l Corp. v. Hoshino Gakki Co.*, 840 F.2d 1572, 1580 n.11 (Fed. Cir. 1988) (stating that the ultimate burden of persuasion [to establish a fact by a preponderance of the evidence] is only critical in the situation where the evidence is so evenly balanced that no preponderance emerges. In that event, the party having the burden of persuasion necessarily loses.). After considering the parties' arguments and evidence, however, we are not persuaded that Petitioner has made a sufficient showing that a person of ordinary skill would have combined the teachings in the manner contended by Petitioner. Accordingly, we hold that Petitioner has not shown by a preponderance of the evidence that independent claim 1 is unpatentable under 35 U.S.C. § 103(a) for obviousness in view of Edgren and Papadimitriou. For the same reasons, we are hold Petitioner has failed to establish the unpatentability of dependent claims 3–5 and 10–13 by a preponderance of the evidence.

G. Secondary Considerations of Non-Obviousness

Factual inquiries for an obviousness determination include secondary considerations based on evaluation and crediting of objective evidence of nonobviousness. *See Graham*, 383 U.S. at 17. Notwithstanding what the teachings of the prior art would have suggested to one of ordinary skill in the art at the time of the invention, the totality of the evidence submitted, including objective evidence of nonobviousness, may lead to a conclusion that the challenged claims would not have been obvious to one of ordinary skill in the art. *In re Piasecki*, 745 F.2d 1468, 1471–72 (Fed. Cir. 1984). Secondary considerations may include any of the following: long-felt but unsolved needs, failure of others, unexpected results, commercial success,

copying, licensing, and praise. *See Graham*, 383 U.S. at 17; *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007).

To be relevant, evidence of nonobviousness must be commensurate in scope with the claimed invention. *In re Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) (citing *In re Tiffin*, 448 F.2d 791, 792 (CCPA 1971)); *In re Hiniker Co.*, 150 F.3d 1362, 1369 (Fed. Cir. 1998). In that regard, in order to be accorded substantial weight, there must be a nexus between the merits of the claimed invention and the evidence of secondary considerations. *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995). "Nexus" is a legally and factually sufficient connection between the objective evidence and the claimed invention, such that the objective evidence should be considered in determining nonobviousness. *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988). The burden of showing that there is a nexus lies with the patent owner. *Id.*; *see Paulsen*, 30 F.3d at 1482. Here, Patent Owner argues that commercial success, licensing, long-felt but unresolved need, unexpected results, and the length of time it took to invent the challenged claims indicates that the claims would not have been obvious to a person of ordinary skill in the art. PO Resp. 43–55.

1. Commercial Success

Patent Owner argues that it has successfully commercialized the patented inventions in multiple drugs on the market. PO Resp. 49. As its example, Patent Owner cites the drug Gralise® and its sales and market share data. *Id.* at 50–51. As explained above, evidence of commercial success is "only significant if there is a nexus between the claimed invention and the commercial success." *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1311–12 (Fed. Cir. 2006). To establish a nexus between a claimed

invention and the commercial success of a product, there must be "proof that the sales [of the allegedly successful product] 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." *See In re GPAC, Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) ("For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention."); *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988), *cert. denied* (1988) ("A prima facie case of nexus is generally made out when the patentee shows both that there is commercial success, and that the thing (product or method) that is commercially successful is the invention disclosed and claimed in the patent."); *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1539 (Fed. Cir. 1983) (holding that patent owner failed to show nexus between the merits of the invention and the commercial success of a tubing product). On the record before us, we are not persuaded that the evidence shows sufficiently a nexus between any success of Patent Owner's products and the invention claimed in the '340 patent.

Specifically, Patent Owner has not shown sufficiently in its Patent Owner Response that Gralise® embodies the claims of the '340 patent. Instead, Patent Owner cites its declarant, Dr. Hopfenberg, and claim charts, stating only that Dr. Hopfenberg "opines that there is a direct nexus between the '340 patented technology and the Gralise® product." PO Resp. 49 (citing Ex. 2009 ¶¶ 96–97). Patent Owner then states that "[b]y claim charts, he finds that the Gralise® product embodies each and every limitation of the claims of the '340 Patent." *Id.* at 49–50 (citing Ex. 2009 ¶ 97 (citing Ex.

2011, a 9-page claim chart)). We determine that merely citing to a claim chart as support—without any explanation in the Patent Owner Response—is insufficient to demonstrate a nexus and violates our rule against incorporation by reference.[6] *See* 37 C.F.R. § 42.6(a)(3) ("Arguments must not be incorporated by reference from one document into another document.").

Accordingly, absent an adequate demonstration of nexus in the Petition, we give little weight to Patent Owner's argument that the alleged commercial success of Gralise® is evidence that the claims are not obvious.

2. Licensing

Patent Owner also argues that its licensing program establishes that the claims are not obvious. PO Resp. 51. Patent Owner asserts that it has "entered into 10 different license agreements (two of them with one licensee) since 2002 for the '340 patented technology (known as the Acuform® technology)." *Id.* at 51–52. Patent Owner further asserts that its licenses have "generated substantial upfront, milestone, and royalty payments for [Patent Owner]." *Id.* at 52. Patent Owner concludes that "[t]he fact that so many different third parties have acknowledged [Patent Owner's] patented technology and voluntarily made substantial payments for licenses to the '340 patented technology is strong evidence that the patented inventions were [not] obvious at their time." *Id.* at 52–53.

[6] We recognize the challenge of fully addressing the nexus issue within our default page limits. We note, however, that Patent Owner did not request additional pages for its Response or even attempt to address at least a single claim in the Response.

We are not persuaded. As with evidence of commercial success, "only little weight can be attributed to such evidence if the patentee does not demonstrate a nexus between the merits of the invention and the licenses of record." *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995) (citation omitted). Moreover, our reviewing court has held that "without a showing of a nexus, 'the mere existence of . . . licenses is insufficient to overcome the conclusion of obviousness.'" *In re Antor Media Corp.*, 689 F.3d 1282, 1293 (Fed. Cir. 2012) (quoting *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1324 (Fed. Cir. 2004)).

Like the applicant in *Antor Media*, Patent Owner has done little more than list the licenses and their respective sales revenue. *See id.* at 1293–94. The cited testimony of Dr. Nicholson only details the revenues for each license and does not establish whether the licensing program was successful because of the merits of the claimed invention or for other economic reasons, such as to avoid litigation or because of prior business relationships. *See* Ex. 2014 ¶¶ 46, 77; *see also Antor Media*, 689 F.3d at 1294 (affirming Board's finding that evidence of existence of licenses was insufficient to overcome prima facie case of obviousness).

Accordingly, we give little weight to Patent Owner's argument that its licensing program is evidence that the claims are not obvious.

3. Long-Felt but Unsolved Need

Patent Owner argues that Dr. Berner (inventor of the '340 patent) "provides credible information that there was a long-felt need for a once daily, gastric-retentive, controlled-release dosage form to deliver highly soluble drugs slowly, evenly, and reproducibly." PO Resp. 53 (citing Ex. 2009 ¶¶ 98–99). Patent Owner also describes the use of the drugs

Metformin and gabapentin to reduce side-effects and increase patient-compliance of prior art drugs. *Id.* at 53–54.

We are not persuaded. Patent Owner must show that any evidence of long-felt need "demonstrates both that a demand existed for the patented invention, and that others tried but failed to satisfy that demand." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1082 (Fed. Cir. 2012). Patent Owner's argument is lacking as to the latter element. That is, Patent Owner offers no evidence that others tried and failed.

Accordingly, we give little weight to Patent Owner's argument that there was a long-felt but unmet need that overcomes Petitioner's showing of obviousness in this case.

4. Undue Experimentation and Unexpected Results

Patent Owner argues that the '340 patent claims would not have been obvious because it took the inventors one and a half years of extensive experimentation to first recognize the "unexpectedly beneficial performance" of PEO and HPMC for gastric retention and controlled drug release. PO Resp. 44 (citing Ex. 2014 ¶ 24). According to Patent Owner, "anything-but-'routine experimentation' was necessary" to conceive of the claimed inventions in the '340 Patent. *Id.* (citing Ex. 2014 ¶ 27). We find this argument unpersuasive in light of Exhibits 2018 and 2019. As Petitioner notes, PEO was used by scientists (working on a project for Patent Owner) on the first day of the project, January 21, 1999 (Ex. 2018, 138), and HPMC was suggested for use in the formulation on February 17, 1999 (*id.* at. 180). We cannot pinpoint the exact date of invention for the '340 patent claims, because we are limited to the evidence of record. Given the record

that is available to us, we are not persuaded the inventors of the ’340 patent took “approximately one and a half years of extensive experimentation” to conceive the ’340 patent. The lengthy experiments performed in Exhibits 2018 and 2019 do not show lack of invention, because it appears Patent Owner undertook that work to satisfy particular commercial requirements. *See CFMT, Inc. v. Yieldup Int’l Corp.*, 349 F.3d 1333, 1340 (Fed. Cir. 2003) (“In general, few patented inventions are an immediate commercial success. Rather, most inventions require further development to achieve commercial success.”).

Accordingly, we give little weight to Patent Owner’s argument that the evidence of alleged unexpected results overcomes Petitioner’s showing of obviousness in this case.

III. MOTIONS TO EXCLUDE EVIDENCE AND MOTION FOR OBSERVATIONS REGARDING DEPOSITION TESTIMONY

Both parties filed motions to exclude evidence offered by the other side. The party moving to exclude evidence bears the burden of proving that it is entitled to the relief requested—namely, that the material sought to be excluded is inadmissible under the Federal Rules of Evidence. *See* 37 C.F.R. §§ 42.20(c), 42.62(a). We address each party’s motion in turn.

A. Petitioner’s Motion to Exclude Evidence

Petitioner filed a Motion to Exclude Evidence seeking to exclude Exhibits 2163 and 2164, which were introduced during the deposition of Petitioner’s Declarant, Dr. Wilson. Paper 51 (“Mot.”). Even without excluding this evidence, we have determined that Petitioner has established, based on a preponderance of the evidence, the unpatentability of claims 1, 3–5, and 10–13 of the ’340 patent. Furthermore, Petitioner’s arguments on

these items go to the weight to be accorded to the evidence. The Board is capable of determining and assigning the appropriate weight to the evidence.

For these reasons, we *deny* Petitioner's motion.

B. Patent Owner's Motion to Exclude

Patent Owner filed a Motion to Exclude Evidence seeking to exclude Exhibits 1030 and 1031 as constituting inadmissible new prior art. PO Mot. Exclude. Patent Owner further seeks to exclude Exhibit 1021 as irrelevant and prejudicial. *Id.* at 1. Petitioner opposes Patent Owner's Motion, arguing that (1) Exhibits 1030 and 1031 were submitted with Petitioner's Reply as proper rebuttal evidence to arguments made Patent Owner's Response, and (2) the Office Patent Trial Practice Guide (77 Fed. Reg. 48,756, 48,764 (Aug. 14, 2012)) allows a Petitioner to attach claim charts from another proceeding to its Petition (such as Exhibit 1021). Pet. Exclude Opp., 1.

Patent Owner's arguments on these items go to the weight to be accorded to the evidence. It is within our discretion to assign the appropriate weight to be accorded to evidence. *See, e.g.*, *Yorkey v. Diab*, 601 F.3d 1279, 1284 (Fed. Cir. 2010) (holding the Board has discretion to give more weight to one item of evidence over another "unless no reasonable trier of fact could have done so"); *In re Am. Acad. of Sci. Tech Ctr.*, 367 F.3d 1359, 1368 (Fed. Cir. 2004) ("[T]he Board is entitled to weigh the declarations and conclude that the lack of factual corroboration warrants discounting the opinions expressed in the declarations."); *Velander v. Garner*, 348 F.3d 1359, 1371 (Fed. Cir. 2003) ("In giving more weight to prior publications than to subsequent conclusory statements by experts, the Board acted well within [its] discretion."). The Board is capable of determining and assigning the appropriate weight to the evidence.

For this reason, we *deny* Patent Owner's Motion to Exclude Exhibits 1030 and 1031.

Additionally, on this record, we need not decide Patent Owner's Motion regarding Ex. 1021, because our analysis does not rely upon the information in that particular exhibit. Consequently, Patent Owner's Motion to Exclude Exhibit 1021 is dismissed as moot.

IV. CONCLUSION

We conclude Petitioner has shown by a preponderance of the evidence that claims 1, 3–5, and 10–13 of the '340 patent are unpatentable under 35 U.S.C. § 103(a) for obviousness over (1) the Shell 1998 publication, and (2) the Shell 1998 Publication in view of Papadimitriou.

Petitioner's Motion to Exclude Exhibits 2163 and 2164 is denied. Patent Owner's Motion to Exclude Exhibit 1021 is dismissed, and Patent Owner's Motion to Exclude Exhibits 1030 and 1031 is denied.

V. ORDER

For the reasons given, it is

ORDERED that, by a preponderance of the evidence, claims 1, 3–5, and 10–13 of the '340 patent are unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude Exhibits 2163 and 2164 is denied;

FURTHER ORDERED that Patent Owner's Motion to Exclude Exhibit 1021 is dismissed;

FURTHER ORDERED that Patent Owner's Motion to Exclude Exhibits 1030 and 1031 is denied;

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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