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Paper 72
Entered: July 8, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PURDUE PHARMA L.P.,
Petitioner,

v.

DEPOMED, INC.,
Patent Owner.

Case IPR2014-00379
Patent 6,340,475 B2

Before ERICA A. FRANKLIN, GRACE KARAFFA OBERMANN, and TINA E. HULSE, *Administrative Patent Judges.*

HULSE, *Administrative Patent Judge.*

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

I. INTRODUCTION

Purdue Pharma L.P. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 43, 54, 55, 57, 58, and 66 of U.S. Patent No. 6,340,475 B2 (Ex. 1001, "the '475 patent"). Paper 1 ("Pet."). Depomed, Inc. ("Patent Owner") filed a Preliminary Response to the Petition. Paper 8 ("Prelim. Resp."). On July 10, 2014, we instituted an *inter partes* review of claims 43, 54, 55, 57, 58, and 66 on certain grounds of unpatentability alleged in the Petition. Paper 9 ("Dec. Inst."), 22. Patent Owner timely filed a Response (Paper 23, "PO Resp."), to which Petitioner timely filed a Reply (Paper 34, "Pet. Reply").

Both parties filed motions to exclude certain exhibits and testimony. Paper 40 (Petitioner); Paper 47 (Patent Owner). Both parties opposed the other's motion to exclude. Paper 55 (Patent Owner Opposition); Paper 50 (Petitioner Opposition). And both parties filed reply briefs in support of their motions to exclude. Paper 57 (Petitioner Reply); Paper 58 (Patent Owner Reply).

Patent Owner also filed a Motion for Observation (Paper 45) on certain cross-examination testimony of Petitioner's declarant Dr. Eric M. Gaier, and Petitioner filed a Response (Paper 51).

A consolidated oral hearing for this proceeding and Cases IPR2014-00377 and IPR2014-00378 was held on March 19, 2015, a transcript of which has been entered in the record.[1] Paper 71 ("Tr.")

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[1] Petitioner and Patent Owner filed Objections to Demonstrative Exhibits. Paper 66 (Patent Owner); Paper 67 (Petitioner). In this Final Written Decision, we rely directly on the arguments presented properly in the

We have jurisdiction 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 not shown by a preponderance of the evidence that claims 43, 54, 55, 57, 58, and 66 of the '475 patent are unpatentable.[2]

A. Related Proceedings

Petitioner and Patent Owner identify various district court actions involving the '475 patent, including an action involving the parties titled *Depomed, Inc. v. Purdue Pharma L.P.*, No. 3:13-00571 (D.N.J.). Pet. vii; Paper 5, 2–3.

Petitioner has also filed two related petitions for *inter partes* review. One petition involves U.S. Patent No. 6,635,280 B2, which is a continuation of the '475 patent. *See* IPR2014-00377. The other petition involves the '475 patent, as well, but challenges different claims. *See* IPR2014-00378. We issue Final Written Decisions in those two related proceedings concurrently herewith.

B. The '475 Patent (Ex. 1001)

The '475 patent relates to drugs formulated as unit oral dosage forms by incorporating them into polymeric matrices comprised of hydrophilic

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parties' briefs and the evidence of record. The demonstrative exhibits were only considered to the extent they are consistent with those arguments and evidence.

[2] On February 20, 2015, Patent Owner objected to Petitioner's use of a condensed font in Petitioner's Reply paper. Petitioner, however, appears to have used the same condensed font throughout this proceeding. *Compare* Pet. *with* Pet. Reply (using same font). In light of Patent Owner's late objection, we deem the objection to be waived.

polymers that swell upon imbibition of water to a size large enough to promote gastric retention of the drug during the fed mode. Ex. 1001, Abstract. Drugs administered by conventional tablets generally become available to body fluids at a high rate initially, followed by a rapid decline. *Id.* at 1:31–33. To address that issue, controlled drug delivery systems were introduced in the 1970's. *Id.* at 1:35–37. Many of the controlled delivery systems utilize hydrophilic, polymeric matrices that provide controlled release of sparingly soluble drugs. For soluble drugs, however, such matrices do not provide adequate control of drug release. *Id.* at 1:45–50.

The claimed invention allows drugs that are highly soluble in water to be administered orally in a way that will prolong their release rate throughout the duration of the fed mode. *Id.* at 5:32–36. This prolonged release rate reduces the problem of transient overdosing, and controls the dosage to safer and more effective levels over an extended period of time. *Id.* at 5:36–41. Moreover, particles exceeding about 1 cm in size are larger than the pylorus and are retained in the stomach for approximately 4 to 6 hours. *Id.* at 11:66–12:2. The Specification states that these benefits are due, in part, to using a polymeric matrix that is water-swellable rather than just hydrophilic, that has an erosion rate substantially slower than its swelling rate, and that releases the drug primarily by diffusion rather than erosion. *Id.* at 5:57–62. Preferred polymeric matrices include water-swellable polymers such as hydroxypropylmethylcellulose ("HPMC") and poly(ethylene) oxide ("PEO"). *Id.* at 7:54–8:51.

C. Illustrative Claim

Claim 43 is illustrative and is reproduced below:

> 43. A method of administering to a subject a drug that is therapeutic to said subject when absorbed in the stomach where said drug has at least one ionized group in the pH range 5 through 8, said method comprising orally administering to said subject a dosage form of said drug while said subject is in a fed mode, said dosage form comprising a solid polymeric matrix with said drug dispersed therein at a weight ratio of drug to polymer of from 0.01:99.99 to 80:20, said polymeric matrix being one that:
>
> (a) swells upon imbibition of gastric fluid is to a size large enough to promote retention in the stomach during said fed mode,
>
> (b) releases said drug into gastric fluid by the dissolving of said drug by said gastric fluid and either erosion of said matrix or diffusion of said dissolved drug out of said matrix,
>
> (c) retains at least about 40% of said drug one hour after such immersion in gastric fluid,
>
> (d) releases substantially all of said drug within about ten hours after such immersion, and
>
> (e) remains substantially intact until all of said drug is released,
>
> thereby extending the release rate of said drug with time during said fed mode while releasing substantially all of said drug within said stomach where said drug is maintained in an acidic environment.

D. Grounds of Unpatentability Instituted for Trial

We instituted trial based on the following grounds of unpatentability:

Claims	**Basis**	**References**
43, 54, 55, 57, 58, and 66	§ 102	the ’803 patent[3]

[3] Wong et al., US 6,120,803, issued Sept. 19, 2000 (Ex. 1005)

Claims	Basis	References
43, 57, 58, and 66	§ 103	the '837 patent,[4] Baveja,[5] and Colombo,[6]
54 and 55	§ 103	the '837 patent, Baveja, Colombo, and the '125 patent[7]

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 778 F.3d 1271, 1279–81 (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). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

[4] John W. Shell, US 5,582,837, issued Dec. 10, 1996 (Ex. 1006).
[5] Baveja et al., *Zero-Order Release Hydrophilic Matrix Tablets of β-adrenergic Blockers*, 39 INT'L J. OF PHARM. 39-45 (1987) (Ex. 1013).
[6] Colombo et al., *Drug Release Modulation by Physical Restrictions of Matrix Swelling*, 63 INT'L J. OF PHARM. 43-48 (1990) (Ex. 1014).
[7] Cherng-ju Kim, US 5,945,125, issued Aug. 31, 1999 (Ex. 1015).

1. Prior Construed Claim Terms

We construed the following claim terms in the Decision to Institute.

Claim Term	Claim	Construction
"gastric fluid"	43	"[b]oth 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" (Dec. Inst. 6)
"releases substantially all of said drug within about ten hours after such immersion"	43	"[a]t least 80% of the drug has been released after ten hours of immersion in gastric fluid" (Dec. Inst. 6)
"substantially intact"	43	"a polymeric matrix in which the polymer portion substantially retains its size and shape without deterioration due to becoming solubilized in the gastric fluid or due to breakage into fragments or small particles" (Dec. Inst. 7)

Because nothing in the full record developed during trial persuades us to deviate from our prior constructions, we adopt those constructions for purposes of this Decision.

Patent Owner requests construction of two additional terms, which we address below.

2. "until all of said drug is released"

Claim 43 recites the phrase "remains substantially intact until all of said drug is released." We have construed the term "substantially intact," but Patent Owner also requests construction of the phrase "until all of said drug is released." Patent Owner asserts that the phrase should be construed

to mean "until the plateau of the dissolution profile characterizing drug release from the swollen dosage form is reached." PO Resp. 14. Petitioner does not challenge Patent Owner's construction in its Reply.

Patent Owner argues that the '475 Specification discloses drug release profiles that "show a release plateau for metformin from the dosage forms of the invention that typically does not reach 100%." *Id.* at 14–15(citing Ex. 1001, Fig. 1). Patent Owner also relies on the FDA guidance documents that state a dissolution assay should be run until "either 80% of the drug from the drug product is released or an asymptote is reached." *Id.* at 15 (quoting Ex. 2009, 6) (emphasis omitted). Finally, Patent Owner asserts that its declarant, Dr. Harold B. Hopfenberg agrees with its construction. *Id.* (citing Ex. 2010 ¶ 60).

We are not persuaded by Patent Owner's arguments. The plain meaning of "until *all* of said drug is released" is evident. If we were to adopt Patent Owner's argument that "all" can mean "less than all," we would be ignoring the plain meaning of the term. Moreover, although Patent Owner is correct that certain other embodiments in the Specification plateau at less than 100% of drug release, we note that certain embodiments do plateau at 100%. *See* Ex. 1001, Fig. 1 (curve marked by filled diamonds); *see also August Tech. Corp. v. Camtek, Ltd.*, 655 F.3d 1278, 1285 (Fed. Cir. 2011) ("The mere fact that there is an alternative embodiment disclosed in the [asserted patent] that is not encompassed by [our] claim construction does not outweigh the language of the claim, especially when [our] construction is supported by the intrinsic evidence.") (citation omitted).

Furthermore, as noted above, we have determined that, as properly construed, the phrase "releases substantially all" in claim 43 means "at least

80% of the drug has been released." If we were to interpret "all" to mean the point at which the drug release profile plateaus—even if less than 80%—then it would be possible for a dosage form to release "all" of a drug, but not "substantially all" of the drug. Such an inconsistency within the claim would not be a reasonable construction of the term "all." Accordingly, we decline to construe "until all of said drug is released" as broadly as Patent Owner requests and, instead, construe it according to its plain, ordinary meaning.

3. "substantially all"

Patent Owner asserts that the term "substantially all," as it appears in the phrase "releasing substantially all of said drug within said stomach where said drug is maintained in an acidic environment" of claim 43 should be construed as "at least 80%." PO Resp. 16. Patent Owner notes that this construction would be consistent with our prior constructions of "releases substantially all of said drug after such immersion." Dec. Inst. 6. Petitioner does not object to Patent Owner's proposed construction in its Reply.

Based on the information presented and for the same reasons stated in our Decision to Institute (*id.*), we determine that the broadest reasonable interpretation of "substantially all" as used in the claims is "at least 80%."

B. Principles of Law

To prevail in its challenges to the patentability of the claims, Petitioner must prove unpatentability by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d).

To establish anticipation, each limitation in a claim must be found in a single prior art reference, arranged as recited in the claim. *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008). While the

limitations must be arranged or combined in the same way as in the claim, identity of terminology is not required. *In re Gleave*, 560 F.3d 1331, 1334 (Fed. Cir. 2009); *In re Bond*, 910 F.2d 831, 832 (Fed. Cir. 1990). Moreover, a reference anticipates a claim "if it discloses the claimed invention such that a skilled artisan could take its teachings in combination with his own knowledge of the particular art and be in possession of the invention." *In re Graves*, 69 F.3d 1147, 1152 (Fed. Cir. 1995). Thus, "it is proper to take into account not only specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom." *In re Preda*, 401 F.2d 825, 826 (CCPA 1968).

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter 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. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

"[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. "[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine elements in the way the claimed new invention does." *Id.* Moreover, a person of ordinary skill in the art must have had a

reasonable expectation of success of doing so. *PAR Pharm., Inc. v. TWi Pharms., Inc.*, 773 F.3d 1186, 1193 (Fed. Cir. 2014).

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

C. The Level of Ordinary Skill in the Art

In large part, the parties agree as to the level of ordinary skill in the art. Pet. 10; PO Resp. 10. Both agree that a person of ordinary skill in the art would be a person with a Ph.D. degree in at least pharmaceutical science, chemistry, or chemical engineering along with at least two years of industry experience in the development of controlled-release oral dosage forms. Pet. 10; PO Resp. 10. Both also agree that a person of ordinary skill in the art may have an equivalent level of skill through similar education, training, and industry experience. Pet. 10; PO Resp. 10. In light of the parties' agreement, we adopt that description of the level of ordinary skill in the art for purposes of this proceeding.

D. Anticipation by the '803 Patent

Petitioner asserts that claims 43, 54, 55, 57, 58, and 66 of the '475 patent are anticipated by the '803 patent. Pet. 19–25; Pet. Reply 2–4. Petitioner relies on the Declaration of Dr. Roland Bodmeier. Ex. 1012 ¶¶ 80–94. Patent Owner disagrees with Petitioner's assertions (PO Resp. 27–30), relying on the Declaration of Dr. Hopfenberg (Ex. 2010 ¶¶ 94–101, 156–60).

1. The '803 Patent (Ex. 1005)

The '803 patent relates to a drug dosage form adapted for retention in the stomach to deliver a drug over a sustained period of time. Ex. 1005, 1:10-14. The dosage form includes a drug and a polymer matrix formed of a

swellable, water-soluble polymer that expands when contacted with fluids in the stomach, and a rigid or semi-rigid band of insoluble material in which swelling of the water-soluble polymer is constrained. *Id.* at 5:12-18. The insoluble band "facilitates the dosage form remaining in the stomach of a subject over a prolonged period of time." *Id.* at 5:18-21. The insoluble band also prolongs the period of time that the polymer matrix "retains its integrity in an expanded state." *Id.* at 5:28-30. It is thought that the band "reduces the rate of erosion of the polymer matrix, thus maintaining a larger effective size of the dosage form and reducing the chance for its expulsion from the stomach, for a longer period of time than would otherwise occur if the band was not present." *Id.* at 14:33-40. As the dosage form erodes in the stomach or as the active agent diffuses from the matrix, active agent will be released and absorbed in either the stomach or small intestine. *Id.* at 5:38-42.

2. Analysis

As an initial matter, Patent Owner argues that the '803 patent is not prior art under 35 U.S.C. § 102(e) because the '475 patent claims priority to U.S. Patent Application No. 08/870,509 ("the '509 application"), which was filed on June 6, 1997. PO Resp. 19–20. Petitioner disagrees, stating the method claims of the '475 patent were added in a later continuation-in-part application filed March 29, 1999, and are therefore not entitled to the benefit of the June 6, 1997, filing date of the '509 application. Pet. Reply 1–2. At oral argument, Patent Owner conceded this point. Tr. 75:15–21 (stating "I believe we agree [the method claims are] entitled to a 1999 date"). Accordingly, we determine that the '803 patent is prior art to the method claims at issue in this proceeding.

Petitioner contends that independent claim 43 and its dependent claims 54, 55, 57, 58, and 66 are anticipated by the '803 patent. Pet. 19–25. Petitioner asserts, for example, that the '803 patent teaches the limitation of "remains substantially intact until all of said drug is released" in teaching that the addition of an "insoluble material or band (or bands if more than one band is utilized) prolongs the period of time in which the polymer matrix retains its integrity in an expanded state and increases the residence time of the dosage form in the stomach." *Id.* at 22. Petitioner also argues that the '803 patent teaches the use of poly(ethylene) oxide ("PEO") and various other types of highly viscous polymers that "will create formulations that will remain intact." *Id.* at 22–23 (citing Ex. 1012 ¶ 88).

Patent Owner argues that the '803 patent does not disclose the "substantially intact" limitation because it expressly states that the polymer matrix erodes significantly. PO Resp. 27. For example, the '803 patent states that "[e]rosion of the matrix will continue to deliver active agent to the stomach until the matrix has *substantially eroded* so that no significant amount of active agent remains." *Id.* at 27–28 (quoting Ex. 1005, 16:14–19).

We are not persuaded that Petitioner has established by a preponderance of the evidence that the '803 patent teaches the "substantially intact" limitation of claim 43. We construed "substantially intact" to mean "a polymeric matrix in which the polymer portion substantially retains its size and shape without deterioration due to becoming solubilized in the gastric fluid or due to breakage into fragments or small particles."

Petitioner argues that the '803 patent teaches that its formulations substantially maintain their size and shape until all the drug is released,

stating "the active agent dosage form comprises . . . solid active agent in a gel-forming, erodible polymer matrix having a first portion that swells in the stomach while maintaining its physical integrity for a prolonged period of time." Pet. Reply 2 (quoting Ex. 1005, 7:16–20). Petitioner reasons that even though erosion occurs over time, "the polymer matrix maintains its physical integrity for a prolonged period." *Id.*

Patent Owner argues that the '803 patent does not anticipate the "substantially intact" limitation of claim 43 because it discloses several embodiments that "*erode significantly* such that nearly all of the polymeric matrix has eroded by the final stage of drug release." PO Resp. 27–28 (citing Ex. 1005, 14:19–22, 14:36–40, 16:14–19, Figs. 2–4). While we agree with Patent Owner's characterization of those specific embodiments, that does not preclude Petitioner from showing that the '803 patent teaches the limitation expressly or inherently. We find, however, that Petitioner has not made this showing.

Under claim 43, a dosage form must remain substantially intact "until all of said drug is released." Even if "maintain[ing] its physical integrity" did disclose a dosage form that remains "substantially intact," Petitioner has not shown that maintaining the physical integrity of the dosage form for a "prolonged period of time" expressly or inherently discloses doing so "until all of said drug is released." In other words, a "prolonged period of time" is not necessarily the same as the time period within which "all of said drug is

released."[8] Thus, we are not persuaded that Petitioner has established that the '803 patent discloses the "substantially intact" limitation of claim 43.

Accordingly, after considering the parties' arguments and evidence, we determine that Petitioner has not shown by a preponderance of the evidence that the '803 patent anticipates claims 43, 54, 55, 57, 58, and 66 of the '475 patent.

E. Obviousness over the '837 Patent, Baveja, and Colombo

Petitioner asserts that claims 43, 57, 58, and 66 of the '475 patent are unpatentable as obvious over the '837 patent, Baveja, and Colombo. Pet. 25–41, 43; Pet. Reply 2–4. Petitioner relies on the Declaration of Dr. Bodmeier. Ex. 1012 ¶¶ 95–103, 110. Patent Owner disagrees with Petitioner's assertions (PO Resp. 30–38), relying on the Declaration of Dr. Hopfenberg (Ex. 2010 ¶¶ 162–75).

1. The '837 Patent (Ex. 1006)

The '837 patent relates to the field of alkyl-substituted cellulose-based sustained-release drug dosage forms. Ex. 1006, 1:17–19. Specifically, the dosage form disclosed in the '837 patent comprises a plurality of solid particles of a drug dispersed within a non-crosslinked alkyl-substituted cellulose that "swells unrestricted dimensionally via imbibition of water from gastric fluid to increase the size of the particles to promote gastric retention of the pellets in fed-mode induced patients." *Id.* at 1:58–65. The '837 patent teaches that the particles will normally swell to a size of about 6 to 18 mm. *Id.* at 5:8–12. According to the '837 patent specification, the

[8] This is true under Petitioner's proposed construction of "until all of said drug is released" and under our final construction of the phrase.

dosage form is particularly useful for delivering drugs in a sustained manner within the stomach. *Id.* at 2:39–43.

The '837 patent also discloses drug release experiments using drug dosage forms comprised of hydroxypropylcellulose ("HPC") and aspirin ("ASA"). *Id.* at 7:25–57. The results of the drug release experiments, which were performed in simulated gastric fluid, are shown in Figure 1, which is reproduced below.

Fig. 1

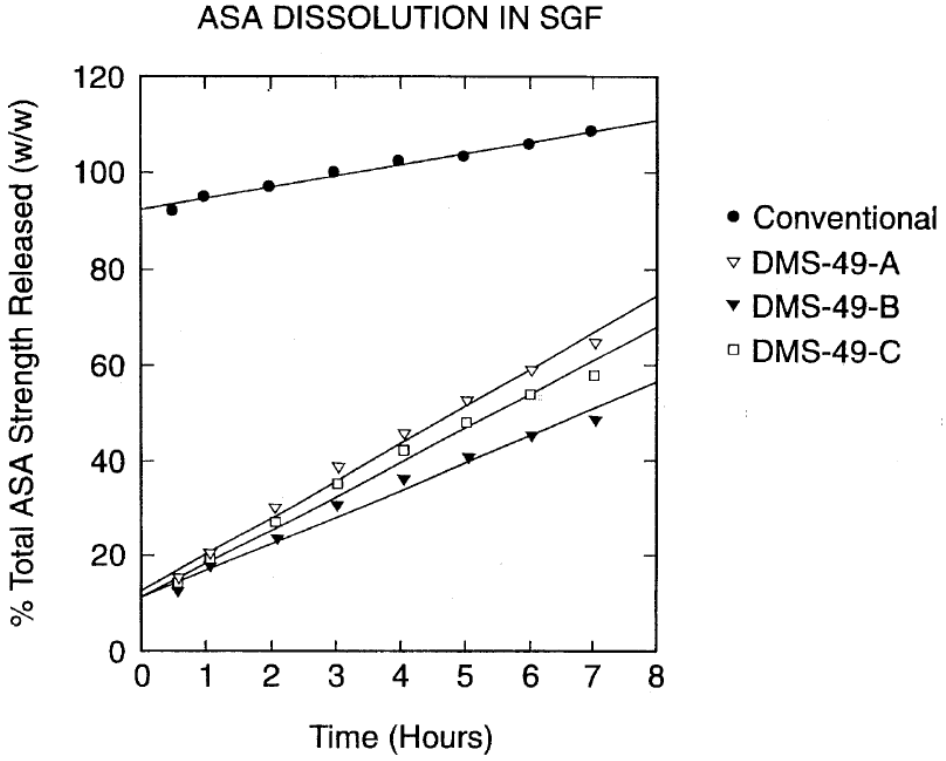

Figure 1 depicts the percentage of aspirin released over time for the various drug formulations tested, including conventional aspirin without HPC. *Id.* at 7:47–52. The release of aspirin was measured at various intervals up to seven hours. *Id.*

2. Baveja (Ex. 1013)

Baveja discloses a dosage form comprised of a swellable hydrophilic matrix that exhibits zero-order (i.e., constant) release of a drug. Ex. 1013, Summary. Baveja uses β-adrenergic blockers propranolol hydrochloride, alprenolol hydrochloride, and metoprolol tartrate as model drugs. *Id.* at 40. Baveja describes tablets with different ratios of HPMC, sodium carboxymethylcellulose ("Na CMC"), and drug, which are then subjected to an in vitro dissolution study. The in vitro dissolution study involves placing the tablets into a dissolution rate test apparatus with diluted HCl (pH 3.0) for three hours and then in 0.2 M phosphate buffer (pH 7.4) for another 9 hours. *Id.*

The results of the dissolution studies for tablets formed from just HPMC and drug are shown in Figures 1–3. For example, Figure 2 is reproduced below:

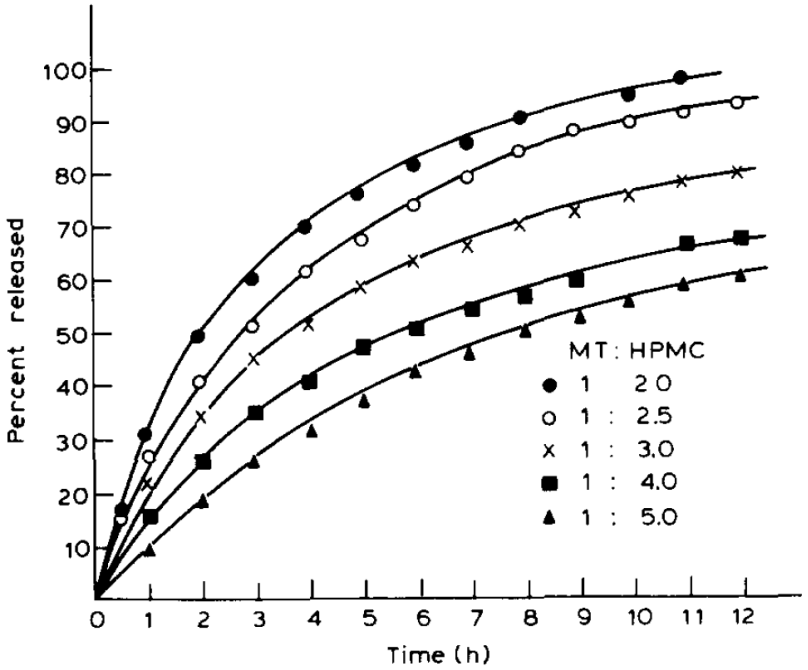

Fig. 2. Release of metoprolol tartrate (cumulative percent) as a function of time from tablets containing drug: HPMC in the ratios given.

Figure 2 illustrates the cumulative percent of metoprolol tartrate released as a function of time from tablets containing metoprolol tartrate and HPMC in the ratios shown. *Id.* at 41.

As explained by Baveja, the rate of release of the tablets made of drug and HPMC decreases with time, which may be due to "an increase in diffusional path length for the drug[,] which in turn may be due to slower erosion rate of the rubbery layer and faster advancement of swelling front into the glassy polymer." *Id.*

Baveja also describes tablets formed from HPMC, Na CMC, and drug in varying amounts that exhibit a nearly zero-order rate of release. *Id.*, Abstract.

3. Colombo (Ex. 1014)

Colombo relates to swellable matrix systems in the form of a tablet comprising a mixture of the drug diltiazem, HPMC, ethylcellulose, and mannitol. Ex. 1014, 44. Colombo discloses three different matrices: Case 0, the plain matrix; Case 1, the matrix coated with cellulose acetate propionate ("CAP") on one face; and Case 2, the matrix coated with CAP on both faces. *Id*. Colombo describes "[s]welling and release experiments" in which the matrices were swollen in deionized water for 120 minutes, and the drug release measurements were obtained concomitantly with the matrix swelling observations. *Id.*

Colombo describes and depicts the morphological changes in the matrices over time, observing that, in the uncoated system (Case 0), "[v]ery quickly (after 15 min) the swelling of the matrix moves both in axial and radial directions." *Id.* Colombo also discloses the drug release profiles of the systems. *Id.* at 45. Figure 5 of Colombo is reproduced below:

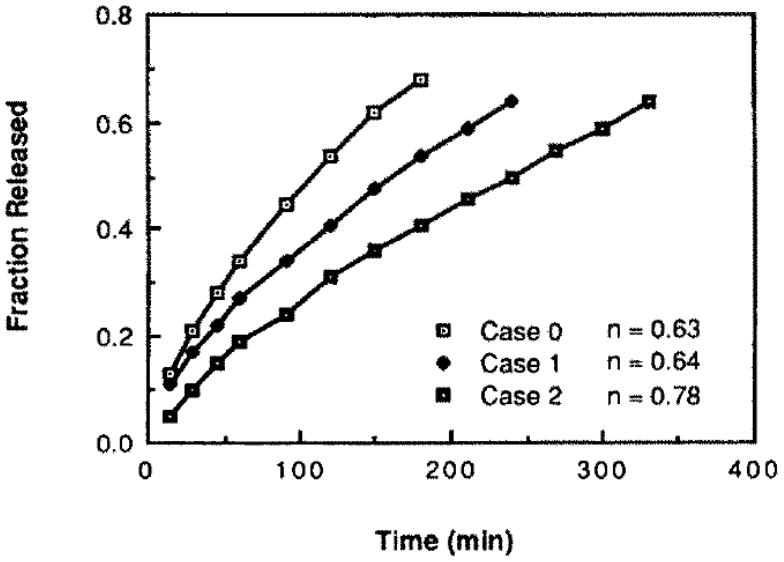

Fig. 5. Drug release profiles of the systems. Calculated values of exponent *n* of Eqn 2 are also shown.

Figure 5 depicts the fraction of diltiazem released over time for the Case 0, Case 1, and Case 2 matrices.

4. Analysis

Petitioner asserts that claims 43, 57, 58, and 66 of the '475 patent are unpatentable as obvious over the '837 patent, Baveja, and Colombo. Petitioner argues that Colombo and Baveja each "disclose every limitation set forth in claim 43 except for the method of administration, which is expressly disclosed by the '837 patent." Pet. 41. Petitioner further contends that a person of ordinary skill in the art would have been motivated to combine the teachings of the '837 patent with Baveja and Colombo given the nature of the problem to be solved and the interrelated teachings of the art. *Id.* at 40.

Looking first at the limitations that Petitioner contends are expressly disclosed, Patent Owner disagrees with Petitioner's contentions, arguing that Baveja does not disclose, either expressly or inherently, drug release by "dissolution and diffusion." PO Resp. 30. Indeed, Patent Owner contends that Baveja actually teaches away from drug release by dissolution and diffusion because it describes the dosage form relied upon by Petitioner as having a "major disadvantage" because it does not exhibit zero-order release. *Id.* at 23. We find, however, that Baveja teaches "dissolution and diffusion" expressly when it states that "Figs. 1–3 reveal that the rate of release decreased with time and this may be due to an increase in diffusional path length for the drug which in turn may be due to slower erosion rate of the rubbery layer and faster advancement of swelling front into the glassy polymer." Ex. 1013, 41. Moreover, the fact that Baveja may prefer dosage forms that exhibit zero-order release, over those that do not, does not teach

away from the claimed invention. *See In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012) ("This court has further explained that just because better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes.").

For the remaining limitations of claim 43 that Petitioner contends are expressly disclosed, based on the evidence presented, we are persuaded that Petitioner has established that Baveja teaches those limitations expressly. Pet. 29–33; Ex. 1012 ¶¶ 98–103. We further agree with Petitioner that Baveja does not expressly disclose a matrix that "swells upon the imbibition of gastric fluid to a size large enough to promote retention in the stomach during said fed mode" (i.e. the "swelling" limitation) and that "remains substantially intact until all of said drug is released" (i.e., the "substantially intact" limitation). *See* Pet. 30–33.

Petitioner, however, asserts that Baveja inherently teaches the "swelling" limitation and the "substantially intact" limitation. Pet. 30–32 . To prove inherency, Petitioner must establish that "the missing descriptive matter is necessarily present in the thing described in the reference." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). We are not persuaded that Petitioner has met this test for either limitation.

Regarding the "swelling" limitation, Petitioner asserts that Baveja discloses a tablet that is 11 mm in diameter prior to imbibition of water and uses HPMC that is a water soluble, swellable polymer. Pet. 30 (citing Ex. 1012 ¶ 102); *see* Ex. 1013, Abstract, 40. Petitioner also relies on the test results from Dr. Kinam Park, which allegedly "confirm that Baveja's formulations swell to a size of about 13.5–14.5 mm after immersion in [simulated gastric fluid]." Pet. 30 (citing Ex. 1016, Ex. 1012 ¶ 102).

Petitioner asserts that Baveja inherently discloses the "swelling" limitation because "[s]welling of a tablet of the size described in Baveja . . . will promote retention in the stomach during the fed mode." *Id.* Petitioner bases its argument in part on the '475 patent Specification's disclosure regarding tablet size. *Id.* at 31 (citing Ex. 1012 ¶ 53). Although Baveja does disclose a "swelling front" (Ex. 1013, 41), we are not persuaded that Petitioner has shown sufficiently that Baveja inherently teaches the entirety of the "swelling" limitation. Specifically, we are not persuaded that Petitioner has shown that Baveja necessarily teaches swelling that "will promote retention in the stomach during the fed mode." For example, it is not clear whether having a tablet that is 11 mm in size in diameter (without knowing any other dimension of the tablet) will necessarily remain in the stomach.

As for the "substantially intact" limitation, Petitioner argues that Baveja's formulation inherently would remain substantially intact. Pet. 32. As support, Petitioner relies on both the testimony of Dr. Bodmeier and the test results of Dr. Kinam Park. *Id.* According to Petitioner, Dr. Park re-created two formulations in Baveja to determine the release kinetics and swelling properties of the dosage forms. Pet. 33–39. Because Dr. Park did not provide evidence of a positive control, however, we cannot conclude with sufficient certainty that Dr. Park's dosage forms were, in fact, the same dosage forms disclosed by Baveja. During oral argument, Petitioner accepted our finding. Tr. 29:21–22 ("We accept the Board's conclusion regarding the prior test results . . . ."). We also do not give persuasive weight to Dr. Bodmeier's unsupported opinion that the Baveja tablets will remain substantially intact. *See* 37 C.F.R. § 42.65(a) (opinion testimony that does not disclose underlying facts or data "is entitled to little or no weight");

Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 294 (Fed. Cir. 1985) (a lack of objective support for expert opinion "may render the testimony of little probative value in a validity determination"). Accordingly, we are not persuaded that Baveja inherently teaches the "substantially intact" limitation.

Similarly, we are not persuaded that Colombo teaches the "swelling" or "substantially intact" limitations, either expressly or inherently. Petitioner asserts that Colombo teaches the "swelling" limitation because it discloses the use of a 7 mm x 2.65 mm tablet prior to imbibition of deionized *water*. Pet. 30 (citing Ex. 1014, 44). The "swelling" limitation of the claims, however, requires "imbibition of *gastric fluid*." Petitioner directs us to no persuasive evidence that Columbo swells by imbibition of gastric fluid, as required by the claims. That is, Petitioner has not established that deionized water is an "artificial fluid[] recognized by those skilled in the art as a suitable model for the fluid of the human stomach," as required by our construction of "gastric fluid." Thus, we are not persuaded that Colombo teaches the "swelling" limitation, either expressly or inherently.

As for the "substantially intact" limitation, Petitioner asserts that Colombo's swelling studies, conducted in water, teach this limitation. Pet. 32. Specifically, Petitioner asserts that the results indicate that the Case 0 formulations "swell significantly and remain substantially intact over the course of at least six hours." *Id.* (citing Ex. 1014, Figs. 1–4; Ex. 1012 ¶ 99). The "substantially intact" limitation, however, requires that the matrix remain substantially intact "until all of said drug is released." We are

not persuaded that Petitioner has shown that Colombo teaches this limitation expressly or inherently.[9]

Petitioner provides, however, an alternative source for teaching these two limitations missing from Baveja and Colombo. Petitioner asserts that the '837 patent discloses expressly the "swelling" and "substantially intact" limitations. Pet. 16–18. We agree. The '837 patent discloses that "swollen particles will be of a size that promotes their retention in the stomach . . . particularly when the patient is in the fed mode." Ex. 1006, 5:9–11. The '837 patent also discloses that because alkyl-substituted celluloses "dissolve very slowly in gastric fluid, the particles maintain their integrity over at least a substantial portion (i.e., at least about 90% and preferably over 100% of the intended dosing period)." *Id.* at 4:42–46.

We are persuaded, therefore, that Petitioner has established that each limitation of claim 43 was known in the art, as evidenced by the teachings of Baveja, Colombo, and the '837 patent. A patent, however, "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. Petitioner must also show that there was a reason to combine those elements to achieve the claimed invention with a reasonable expectation of success. *See PAR Pharm.*, 773 F.3d at 1193. To make that determination, we can look to "interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background

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[9] Of note, we are also not persuaded that Colombo teaches releasing "substantially all of said drug within about ten hours after such immersion." Figure 5 of Colombo, cited by Petitioner, does not show any formulation that ever releases at least 80% of the drug. Ex. 1014, Fig. 5.

knowledge possessed by a person having ordinary skill in the art." *Id.* We can also look to the nature of the problem to be solved. *In re Gartside*, 203 F.3d 1305, 1319 (Fed. Cir. 2000) (holding that suggestion to combine "may come from, *inter alia*, the teachings of the references themselves and, in some cases, from the nature of the problem to be solved"). After considering the parties' arguments and evidence, however, we are not persuaded that Petitioner has established that a person of ordinary skill would have combined the teachings in the manner contended by Petitioner.

Petitioner argues that a person of ordinary skill in the art would have been led to combine the teachings of Baveja, Colombo, and the '837 patent for several reasons. Pet. 38. First, Petitioner argues that a person of ordinary skill in the art would have had a reason to combine Baveja, Colombo, and the '837 patent given the nature of the problem to be solved: "to formulate a swellable, controlled release oral dosage form for releasing a drug with particular release kinetics and that will remain substantially intact and be retained in the stomach during the fed mode." *Id.* at 40.

Second, Petitioner argues that the references have interrelated teachings. According to Petitioner, each of the references is directed to controlled-release dosage forms that contain HPMC with similar drug-to-polymer weight ratios. *Id.*; Ex. 1012 ¶¶ 101–02. For example, Baveja's matrix contains a drug-to-polymer ratio that falls within the weight ratio range disclosed by the '837 patent. Pet. 40 (citing Ex. 1013, Figs. 1 and 2 and Ex. 1014, 44); Ex. 1012 ¶ 121. Moreover, Petitioner argues that "Baveja and Colombo (1990) both teach oral dosage forms formulated with drugs that have at least one ionized group within the pH range 5–8, including alprenolol HCl (Ex. 1013) and diltiazem HCl (Ex. 1014)." Pet. 40.

Petitioner then concludes that "it would be natural for a [person of ordinary skill in the art] to combine the teachings of these references." *Id.* at 40–41.

In response, Patent Owner argues that Petitioner has failed to demonstrate a motivation to combine the cited references with a reasonable expectation of success. Patent Owner challenges Dr. Bodmeier's statement that it would be "natural" to combine Baveja, Colombo, and the '837 patent. PO Resp. 36–37. According to Patent Owner, Dr. Bodmeier fails to provide any substantive evidence to support his testimony that it would take him "a week" to come up with the claimed invention. *Id.* at 37 (quoting Ex. 2018, 80:19–81:8). In contrast to Dr. Bodmeier's testimony, Patent Owner notes that Jenny-Louie Helm, an inventor of the '475 patent ("Inventor Helm"), testified that it "took years of research and testing in the laboratory to manipulate different variables, such as type of polymer, molecular weight, particle size, dosage size, matrix chemical structure, and manufacturing processes, to come up with the claimed inventions." *Id.* at 38; Ex. 2016 ¶ 21 (Helm Decl.) ("It took me three years testing various polymers with guidance of Dr. Shell to achieve the Captopril formulation that contained the aspects of the claims of the '475 and '280 Patents."). Consistent with Inventor Helm's testimony, Patent Owner asserts that its declarant, Dr. Hopfenberg, testified that a person of ordinary skill in the art would not have reasonably expected to successfully achieve the claimed invention given that a "vast array of structural considerations affect polymer and matrix properties." PO Resp. 38 (citing Ex. 2010 ¶ 65).

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, as Petitioner asserts, Petitioner has not explained persuasively *how or why* a person of ordinary skill in the art would have combined the "swelling" and "substantially intact" features of the '837 patent with the dosage formulation of Baveja and Colombo.

In its Reply, Petitioner asserts that "the advantages and techniques of formulating controlled release dosage forms that are retained in the stomach were well-known at the time of the alleged invention." Pet. Reply 11. Petitioner also asserts another reason to combine the cited references:

> A [person of ordinary skill in the art] would look to (1) Baveja to learn how to adjust the rate of drug release by varying the drug-to-polymer (HPMC) weight ratio and (2) either Colombo or the '837 patent for confirmation that the same type of polymer used in Baveja will (a) swell to a size that will promote gastric retention in the fed mode, and (b) remain substantially intact until all of the drug is released.

Pet. Reply 11 (citing Ex. 1012 ¶¶ 101–103). But here, again, Petitioner speaks in generalizations and does not explain persuasively *why* a person of ordinary skill in the art, learning from Baveja how to adjust the rate of drug release by varying the drug-to-polymer weight ratio, would need or want to look to Colombo or the '837 patent "for confirmation" of the "swelling" and "substantially intact" properties. *See InTouch Techs., Inc. v. VGO Commc'ns, Inc.*, 751 F.3d 1327, 1351 (Fed. Cir. 2014) (reversing district court's judgment of invalidity where expert's testimony "was vague and did not articulate reasons why a person of ordinary skill in the art at the time of the invention would combine these references").

To the extent Petitioner relies on the nature of the problem to be solved to supply the reason for the combination, we remain unpersuaded.

Petitioner's recitation of the nature of the problem to be solved is essentially a recitation of claim 43 itself: "to formulate a swellable, controlled release oral dosage form for releasing a drug with particular release kinetics and that will remain substantially intact and be retained in the stomach during the fed mode." Pet. 40. As our reviewing court has recently reminded us, however, "[d]efining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness." *Insite Vision, Inc. v. Sandoz, Inc.*, 783 F.3d 853, 859 (Fed. Cir. 2015) (quoting *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 881 (Fed. Cir. 1998)). As such, the Federal Circuit stated that when considering the reason to combine, "the problem examined is not the specific problem solved by the invention." *Id.* (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). Here, the claim represents the specific problem solved by the invention, rather than the general problem facing the inventors. Thus, we find that by defining the nature of the problem to be solved as the specific problem solved by the invention, Petitioner has relied on impermissible hindsight to supply the reason to combine the references. *See id.* (affirming the district court's recognition that "an overly narrow 'statement of the problem [can] represent[] a form of prohibited reliance on hindsight, [because] [o]ften the inventive contribution lies in defining the problem in a new revelatory way'") (quoting *Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1372, 1377 (Fed. Cir. 2012) (alterations in original)).

Even if we were to find that Petitioner has established that a person of ordinary skill in the art would have had a reason to combine the teachings of Baveja, Colombo, and the '837 patent, we are still not persuaded that

Petitioner has established that a person of ordinary skill in the art would have had a reasonable expectation of success in doing so.

Petitioner argues that a person of ordinary skill in the art "following logical design preferences and readily available and known options would have necessarily developed a method and controlled-release dosage form that included all recited claim limitations." Pet. 26. For example, Petitioner and its declarant argue that it was known to a person of ordinary skill in the art "how to formulate a dosage form with a swellable, hydrophilic, polymeric matrix that would remain substantially intact until substantially all of the drug is released, like those described and claimed in the '475 patent." *Id.* at 28 (citing Ex. 1012 ¶¶ 54–59).

We are not persuaded that a person of ordinary skill in the art would have had a reasonable expectation of success, in part, because both parties' declarants testified about the number of formulation considerations at play when preparing a drug formulation. For example, Petitioner's declarant testified that there were formulation considerations such as "molecular weight, chemical substitution, particle size, hydration rate effect, polymer content, dosage form, dosage size and manufacturing processes." Ex. 1004 ¶ 37. Similarly, Patent Owner's declarant stated that "[a] person of ordinary skill in the art understands that formulation of a polymer matrix involves a vast array of interacting 'formulation considerations' affecting polymer and matrix properties." Ex. 2010 ¶ 65. Despite this testimony from its own declarant (as confirmed by Patent Owner's declarant), we find that Petitioner does not address sufficiently why a person of ordinary skill in the art would believe it could modify the formulation of Baveja to incorporate the "swelling" and "substantially intact" features of the '837 patent without, for

example, affecting the other properties of the original Baveja formulation (e.g., the drug release profile). Nor has Petitioner identified any combinations of Baveja, Colombo, and the '837 patent that would be most promising to try. As such, we reach the same conclusion as the Federal Circuit in *Leo Pharmaceutical Products, Ltd. v. Rea*, 726 F.3d 1346, 1357 (Fed. Cir. 2013). That is, we find that "[w]ithout a reasonable expectation of success or clues pointing to the most promising combinations, an artisan could have spent years experimenting without success." *Id.*

After considering the parties' arguments and the supporting evidence, we determine that Petitioner has not shown by a preponderance of the evidence that claims 43, 57, 58, and 66 are unpatentable as obvious over the '837 patent, Baveja, and Colombo.

F. Obviousness of Claims 54 and 55 over the '837 Patent, Baveja, Colombo, and the '125 Patent

Petitioner asserts that claims 54 and 55 of the '475 patent—which depend from claim 43—are unpatentable as obvious over the '837 patent, Baveja, Colombo, and the '125 patent. Pet. 41–43; Pet. Reply 12–13. Patent Owner disagrees with Petitioner's assertions. PO Resp. 38–39.

1. The '125 Patent (Ex. 1015)

The '125 patent relates to controlled release tablets comprising a pharmaceutical agent and an excipient, which includes a water-swellable polymer and a lubricant. Ex. 1015, Abstract. The '125 patent teaches that the polymers of choice include uncrosslinked PEO and HPMC, either alone or mixed together. *Id.* at 4:18-30.

The release of drugs from the tablet is dependent upon the relative magnitude of the rate of polymer swelling and the rate of polymer erosion.

Id. at 4:30-34. The '125 patent states that "[i]t is most preferable to attain the synchronization of the velocities of the swelling front and the erosion front in order to achieve zero-order [i.e., constant] release kinetics from hydrophilic polymer matrices." *Id.* at 4:37-41.

2. Analysis

Claims 54 and 55 depend from claim 43 and recite the method of claim 43 where the polymeric matrix comprises PEO at a molecular weight in the range of at least about 4,000,000 (claim 54) or a range of from about 4,500,000 to about 10,000,000 (claim 55). Ex. 1001, 26:52-58. The '125 patent teaches a drug dosage form comprising a drug and PEO having a molecular weight of 5,000,000. Ex. 1015, 12:3-5.

Because claims 54 and 55 depend from claim 43, and Petitioner relies on the same rationale for combining the teachings of the references, we determine for the same reasons stated above that Petitioner has failed to establish that a person of ordinary skill in the art would have had a reason to combine the teachings of the '837 patent, Baveja, Colombo, and the '125 patent to achieve the claimed invention with a reasonable expectation of success.

After considering the parties' arguments and the supporting evidence, we determine that Petitioner has not shown by a preponderance of the evidence that claims 54 and 55 are unpatentable as obvious over the '837 patent, Baveja, Colombo, and the '125 patent.

G. Secondary Considerations of Nonobviousness

In light of our determination that Petitioner has not shown by a preponderance of the evidence that any of the challenged claims are

unpatentable as obvious, we need not reach the merits of Patent Owner's evidence of secondary considerations of nonobviousness.

III. MOTIONS TO EXCLUDE EVIDENCE

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 ("FRE"). *See* 37 C.F.R. §§ 42.20(c), 42.62(a). We address each party's motion in turn.

1. Petitioner's Motion to Exclude Evidence

Petitioner moves to exclude portions of Dr. Hopfenberg's declaration and a claim chart for Gralise® (Ex. 2013) as improperly incorporated by reference and as irrelevant because they are improperly incorporated. Paper 40, 3–5. We decline to do so. As explained in our prior Order (Paper 29), to the extent any such violations have occurred, we have not considered such evidence in reaching our decision. Therefore, we dismiss Petitioner's motion as moot.

Petitioner also moves to exclude certain testimony of Inventor Helm. Paper 40, 10–13. We decline to do so. To the extent we have relied on the testimony of Inventor Helm, that testimony was based on her own work. *See* Ex. 2016 ¶ 21 (testifying how long it took her to develop an embodiment of the claims). Such testimony based on her own personal knowledge is relevant and proper lay witness testimony under FRE 701, 602, and 401/402/403. Accordingly, we deny Petitioner's motion as to this evidence.

Petitioner also moves to exclude certain evidence relating to Patent Owner's assertions of commercial success, licensing, long-felt but unmet need, and unexpected results. Paper 40, 5–15. Given our determination that

we need not reach Patent Owner's evidence of secondary considerations, we need not reach the merits of Petitioner's Motion to Exclude.

2. Patent Owner's Motion to Exclude Evidence

Patent Owner also moves to exclude (1) Exhibits 1055, 1056, and 1065 (Paper 47, 1–8); (2) Exhibit 1071 and the related testimony of Dr. Bodmeier (*id.* at 8–10); and (3) portions of the cross-examination testimony of Dr. Eric Gaier (*id.* at 11–13). Because we did not rely on any of these exhibits or testimony in reaching our Decision here, we dismiss Patent Owner's motion to exclude this evidence as moot.

IV. CONCLUSION

We conclude that Petitioner has not shown by a preponderance of the evidence that claims 43, 54, 55, 57, 58, and 66 of the '475 patent are unpatentable under 35 US.C. §§ 102 or 103.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that claims 43, 54, 55, 57, 58, and 66 of the '475 patent are not held unpatentable;

FURTHER ORDERED that Petitioner's Motion to Exclude Evidence is *denied in part and otherwise dismissed*;

FURTHER ORDERED that Patent Owner's Motion to Exclude Evidence is *denied in part and otherwise dismissed*; and

FURTHER ORDERED that, because this is a Final Written Decision, the 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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