Trials@uspto.gov
571-272-7822

Paper 43
Entered: June 30, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BIODELIVERY SCIENCES INTERNATIONAL, INC.,
Petitioner,

v.

RB PHARMACEUTICALS LIMITED,
Patent Owner.

Case IPR2014-00325
Patent 8,475,832 B2

Before TONI R. SCHEINER, JACQUELINE WRIGHT BONILLA, and ZHENYU YANG, *Administrative Patent Judges*.

YANG, *Administrative Patent Judge*.

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

INTRODUCTION

BioDelivery Sciences International, Inc. ("Petitioner") filed a Petition for an *inter partes* review of claims 15–19 of U.S. Patent No. 8,475,832 B2 (Ex. 1001, "the '832 patent"). Paper 8 ("Pet."). On July 29, 2014, the Board instituted trial to review patentability of the challenged claims. Paper 17 ("Dec."). Thereafter, RB Pharmaceuticals Limited ("Patent Owner") filed a Corrected Response (Paper 25 ("PO Resp.")), and Petitioner filed a Reply (Paper 31). Petitioner also filed a Motion to Exclude Exhibit 2043. Paper 35. Patent Owner filed an Opposition to the Motion (Paper 37), and Petitioner filed a Reply in support of the Motion (Paper 38).

In support of their respective positions, Petitioner relies on the Declarations of Drs. Maureen Reitman (Ex. 1004), Philip T. Lavin (Ex. 1005), David W. Feigal (Ex. 1029), and Christine S. Meyer (Ex. 1031), and the deposition testimony of Dr. Thomas P. Johnston (Ex. 1028); Patent Owner relies on the Declaration of Dr. Johnston (Ex. 2003).

Oral hearing was held on March 20, 2015. *See* Paper 42 ("Tr.").

The Board has jurisdiction under 35 U.S.C. § 6(c) and issues this final written decision pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

Petitioner has established by a preponderance of the evidence that claims 15–19 of the '832 patent are unpatentable. In rendering this Decision, we do not rely on Exhibit 2043, the subject of Petitioner's Motion to Exclude. Thus, we dismiss the Motion as moot.

The '832 Patent

The '832 patent relates to compositions and methods for treating narcotic dependence using an orally dissolvable film comprising

buprenorphine and naloxone, wherein the film provides a bioequivalent effect to Suboxone®. Ex. 1001, 4:53–58. The '832 patent defines bioequivalent as "obtaining 80% to 125% of the Cmax and AUC values for a given active in a different product." *Id.* at 3:48–50. According to the '832 patent, "Cmax refers to the mean maximum plasma concentration after administration of the composition to a human subject," and "AUC refers to the mean area under the plasma concentration-time curve value after administration of the compositions." *Id.* at 3:9–14.

At the time of the '832 patent invention, Suboxone®, an orally dissolvable tablet of buprenorphine and naloxone, was on the market for treating opioid dependency. *Id.* at 4:51–55. Buprenorphine, an opioid agonist, provides an effect of satisfying the body's urge for the narcotics, but not the "high" associated with misuse. *Id.* at 1:36–40. Naloxone, an opioid antagonist, reduces the effect of buprenorphine, and, thus, decreases the likelihood of diversion and abuse of buprenorphine. *Id.* at 1:46–52.

The tablet form, however, still has the potential for abuse because it can be removed easily from the mouth for later extraction and injection of buprenorphine. *Id.* at 1:55–62. According to the '832 patent,

> There [was] a need for an orally dissolvable film dosage form that provides the desired absorption levels of the agonist and antagonist, while providing an adhesive effect in the mouth, rendering it difficult to remove once placed in the mouth, thereby making abuse of the agonist difficult.

Id. at 1:65–2:2.

The '832 patent relates to film dosage compositions comprising buprenorphine and naloxone. *Id.* at 2:6–3:2. Such compositions are particularly useful for treating narcotic dependence. *Id.* at 1:13–14.

Illustrative Claim

Among the challenged claims, claim 15 is the sole independent claim. It reads:

> 15. An orally dissolving film formulation comprising buprenorphine and naloxone, wherein said formulation provides an in vivo plasma profile having a Cmax of between about 0.624 ng/ml and about 5.638 ng/ml for buprenorphine and an in vivo plasma profile having a Cmax of between about 41.04 pg/ml to about 323.75 pg/ml for naloxone.

Reviewed Grounds of Unpatentability

The Board instituted trial on the following grounds of unpatentability:

Claims Challenged	Basis	Reference(s)
15–19	§ 102(b)	Labtec[1]
15–19	§ 103	Labtec, Birch,[2] and Yang[3]

ANALYSIS

Claim Construction

In an *inter partes* review, the Board interprets a claim term in an unexpired patent according to its broadest reasonable construction in light of the specification of the patent in which it appears. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 778 F.3d 1271, 1280–81 (Fed. Cir. 2015). Under that standard, absent any special definitions, we assign claim terms

[1] Leichs et al., Int'l Pub. No. WO 2008/040534 A2, published on April 10, 2008 (Ex. 1017, "Labtec").
[2] Birch et al., U.S. Patent Publication No. 2005/0085440 A1, published on April 21, 2005 (Ex. 1019, "Birch").
[3] Yang et al., U.S. Patent No. 7,357,891 B2, issued on April 15, 2008 (Ex. 1016, "Yang").

their ordinary and customary meaning, as understood by a person of ordinary skill in the art, in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

In the Decision to Institute, we concluded that "film formulation" encompasses film dosage, film composition, or film, but not a formulation that is not in the form of a film. Dec. 11. We also determined that the term "provides an in vivo plasma profile" needs no construction beyond its ordinary meaning. *Id.* at 12. During trial, the parties did not dispute these constructions. Having considered the complete record developed at trial, we see no reason to change our interpretation of those terms.

In its Response, however, Patent Owner presents arguments with respect to two additional terms. PO Resp. 18–26. First, Patent Owner challenges Petitioner's position that the wherein clause of claim 15 is not entitled to patentable weight. *Id.* at 18–20. Second, Patent Owner contends that "the challenged claims should be construed as requiring a film formulation that provides, and as reciting pharmacokinetic ranges resulting from, oral transmucosal absorption." *Id.* at 20–26. We address each issue in turn.

The "Wherein" Clause

Claim 15 recites an orally dissolving film formation, "wherein said formulation provides" specific pharmacokinetic profiles. Ex. 1001, 24:56–61. Petitioner argues that the wherein clause merely recites a desired result, and is not entitled to patentable weight. Pet. 23–26. Patent Owner counters that the pharmacokinetic ranges recited in the wherein clause "give crucial meaning to, and provide defining characteristics provided by the film formulation at issue." PO Resp. 19–20. We agree with Patent Owner.

A wherein clause is not given patentable weight if it merely expresses the intended result of a process. *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329 (Fed. Cir. 2005). But, when the wherein clause states a condition that is material to patentability, it cannot be ignored. *Id.*

Here, a film formulation that meets the requirements of claim 15 must be capable of producing the pharmacokinetic profile recited in the wherein clause of the claim. Petitioner does not contend that all orally dissolving films comprising buprenorphine and naloxone would provide the in vivo plasma profile recited in the wherein clause. As a necessary property of the claimed formulation, the pharmacokinetic profile gives meaning and purpose to the claim. *See Griffin v. Bertina*, 285 F.3d 1029, 1033–34 (Fed. Cir. 2002).

After reviewing the entirety of the patent, we conclude that the wherein clause of claim 15 (as well as claims 16 and 17) is a meaningful limitation and, thus, is entitled to patentable weight.

Oral Transmucosal Absorption

Patent Owner asserts that "the challenged claims should be construed as requiring a film formulation that provides, and as reciting pharmacokinetic ranges resulting from, oral transmucosal absorption." PO Resp. 20. We disagree.

First, it is a bedrock principle of patent law that the words of the claims themselves define the scope of the patented invention. *In re Baxter Int'l, Inc.*, 678 F.3d 1357, 1362 (Fed. Cir. 2012). None of the challenged claims includes any language to the effect of requiring oral transmucosal absorption. Instead, the claims recite an "orally dissolving film

formulation." Dissolution and absorption are two distinct properties. Thus, "orally dissolving" does not translate into oral transmucosal absorption.

Second, the specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *In re Abbott Diabetes Care Inc.*, 696 F.3d 1142, 1149 (Fed. Cir. 2012). Here, contrary to Patent Owner's assertion, the Specification does not "make[] clear that . . . the claimed film delivers buprenorphine through the oral mucosa." *See* PO Resp. 21. The '832 patent describes its invention as an "orally dissolvable film" that is "preferably administered to a patient through the oral cavity of the patient, but may be administered in any desired means." Ex. 1001, 15:12–15; *see also id.* at 15:1–3 (stating administering the film "most desirably into the oral cavity"). These disclosures suggest that the film of the '832 patent can be administered through routes other than the oral cavity, albeit not preferred or most desired.

Patent Owner relies on various portions of the Specification. PO Resp. 21–23. None of the cited language, however, supports Patent Owner's position. For example, Patent Owner points out that the title of the '832 patent reads "Sublingual and Buccal Film Composition." *Id.* at 21. But, "if we do not read limitations into the claims from the specification that are not found in the claims themselves, then we certainly will not read limitations into the claims from the patent title." *Pitney Bowes, Inc. v. Hewlett–Packard Co.*, 182 F.3d 1298, 1312 (Fed. Cir. 1999).

Patent Owner refers to the Specification for disclosing "a method of treating narcotic dependence by providing an orally dissolvable film dosage, which provides a bioequivalent effect to Suboxone®." PO Resp. 22

(quoting Ex. 1001, 4:51–58). According to Patent Owner, a skilled artisan would have understood that Suboxone® delivers buprenorphine through the oral mucosa and that the claimed film formulation is "intended to work the same way." *Id.* As support, Patent Owner cites the Specification for disclosing: "In a dosage form that is to be placed in the oral cavity, it is desired to ***absorb the agonist [buprenorphine] bu[c]cally*** so as to provide rapid integration of the agonist into the body of the user." *Id.* (quoting Ex. 1001, 11:10–13). This sentence, however, states that the buccal absorption (i.e., oral transmucosal absorption) is merely "desired," and not required.

Patent Owner also contends "the specification notes that a key criterion in polymer selection is 'the time period for which it is desired to maintain the film in contact with the mucosal tissue,'" because different actives may require different lengths of time "for ***delivery through the mucosal tissue***." PO Resp. 23 (quoting Ex. 1001, 6:42–47). According to Patent Owner, this "[f]urther confirm[s] the oral transmucosal nature of the claimed film." *Id.* Patent Owner, however, neglects to note the sentence immediately preceding the ones quoted, which reads: "Although a variety of different polymers may be used, it is *desired* to select polymers that provide mucoadhesive properties to the film, as well as a desired dissolution and/or disintegration rate." Ex. 1001, 6:39–42 (emphasis added). This disclosure provides the context for the language Patent Owner emphasizes. Because mucoadhesiveness is only a desired property, we again, decline to read it, or oral transmucosal absorption, into the challenged claims.

Patent Owner further asserts that the Specification "repeatedly emphasizes the important role" of "local pH." PO Resp. 23. According to Patent Owner,

> The skilled person would appreciate that *the specification's strong emphasis on the use of a buffer to provide a local pH (in the presence of saliva as the matrix dissolves adjacent to the oral mucosa) is solely applicable to oral transmucosal absorption*.

Id. at 24. The challenged claims, however, do not recite a local pH. This is in sharp contrast to the unchallenged claims, all of which, either directly or through their dependency, require a local pH of about 3 to about 3.5. As a result, Patent Owner's reliance on the importance of a local pH does not support its argument on oral transmucosal absorption in relation to the challenged claims.

In addition, Patent Owner argues that a person of ordinary skill "would understand that *all* of the pharmacokinetic data provided about the test film formulations was intended to and did result from oral transmucosal absorption." *Id.* at 25. This, according to Patent Owner, is because "*all* of the pharmacokinetic data and ranges in the specification relating to Suboxone® sublingual tablets . . . result or would be expected to result from oral transmucosal absorption, the known route employed by that commercial product." *Id.* We are not persuaded.

First, the '832 patent does not mention that the pharmacokinetic data for Suboxone® tablets result from oral transmucosal absorption. In fact, when characterizing Suboxone®, the Specification only describes it as "an orally ingestible" (Ex. 1001, 1:54) or "an orally dissolvable" tablet (*id.* at 4:53). Neither can be reasonably equated with oral transmucosal absorption.

Second, during his deposition, Dr. Johnston explained:

> [I]f you give an orally dissolving film, and if the drug is not absorbed across the oral mucosa, sublingual, buccal, whatever, then it has to be swallowed, because the patient -- where else would it go? The patient doesn't expectorate that saliva drug solution. So to answer your question, it has to be swallowed.

Ex. 1028, 237:9–17, *see also id.* at 125:8–12 (testifying that Suboxone® tablets "dissolve[] in saliva, the majority of which is absorbed sublingually, then that saliva of buprenorphine solution is swallowed"). As a result, we find the evidence of record does not support Patent Owner's position that "*all* of the pharmacokinetic data" of Suboxone® tablets result from oral transmucosal absorption.

Third, Dr. Johnston opines that "[o]ne of ordinary skill in the art would understand that Suboxone® sublingual tablets deliver buprenorphine through the oral mucosa." Ex. 2003 ¶ 66. Patent Owner argues the same. PO Resp. 22–23. As support, they both rely on the March 2006 version of the Data Sheet for Suboxone® tablets, which states:

> When taken orally, buprenorphine undergoes first-pass metabolism with N-dealkylation and glucuroconjugation in the small intestine and the liver. The use of SUBOXONE by the oral route is therefore inappropriate. SUBOXONE tablets are for sublingual administration.

PO Resp. 16 (quoting Ex. 2007, 2); Ex. 2003 ¶ 43 (quoting Ex. 2007, 2). Petitioner, however, pointing to the same document—indeed, the same page of the same Data Sheet—argues that the bioavailability of orally administered buprenorphine overlaps with that of sublingually administered Suboxone® tablets. Reply 9–10 (citing Ex. 2007, 2). We find that the evidence of record supports Petitioner's position.

During his deposition, Dr. Johnston testified that the mean absolute bioavailability of buprenorphine from oral administration is "anywhere from 5 percent to 14 percent." Ex. 1028, 76:8–14. The Data Sheet for Suboxone® tablets states that the mean absolute bioavailability of buprenorphine from sublingual administration is 13.6% (range 5.1–24.9%). Ex. 2007, 2. When questioned about this statement during a deposition, Dr. Johnston stated that he disagreed with the data. Ex. 1028, 77:4–23, 80:14–19. At the hearing, counsel for Patent Owner downplayed the data as "numbers in that one study that's in the label." Tr. 23:23–24, *see also id.* at 24:19–21 (stating that "yes . . . the 13.6 is in the Suboxone tablet label, but that was one study"). According to Dr. Johnston, "the upper range thereof, essentially 25 percent, the upper range falls more in line with reported values." Ex. 1028, 78:19–23. Specifically, Patent Owner directs our attention to some "lengthy" and "extensive" review articles, including page 663 of Exhibit 2016[4] and page 302 of Exhibit 2029,[5] as "deal[ing] specifically with this issue about absorption." Tr. 24:7–11.

According to Exhibit 2016, "[s]tudies utilizing specific assays have reported buprenorphine sublingual solution's mean bioavailability of 28–51%. The plasma bioavailability of the sublingual tablet has been estimated as 49–63% that of the sublingual solution." Ex. 2016, 663 (internal citations omitted). Thus, the bioavailability of buprenorphine sublingual tablet could

---

[4] Elkader and Sproule, *Buprenorphine Clinical Pharmacokinetics in the Treatment of Opioid Dependence*, 44 CLIN. PHARMACOKINET. 661–80 (2005).

[5] Johnson et al., *Buprenorphine: Considerations for Pain Management*, 3 J. PAIN AND SYMPTOM MANAGEMENT 297–326 (2005).

be 13.72% (28% x 49%), in line with the 13.6% average reported in the Data Sheet for Suboxone® tablets.

Exhibit 2029 notes, for buprenorphine sublingual tablets, an average systemic bioavailability of 55%. Ex. 2029, 302. This number, however, is not without qualification. Indeed, it is reported "with large intersubject variability." *Id.* Moreover, it appears to be based on the administration of 0.4 or 0.8 mg doses for postoperative pain management (*id.*),[6] significantly lower than the 2, 4, 8, or 16 mg doses of Suboxone® tablets for treating narcotic dependency (Ex. 1001, 16:40–17:13).

Considering the data in Exhibit 2007 relied on by Petitioner against the data in Exhibits 2016 and 2029 relied on by Patent Owner, we assign the former more weight. We do so because a party may not selectively point to one portion of an exhibit to buttress its argument, and, meanwhile, ask us to disregard another part of the same document that undermines its contention. Here, Patent Owner relies on Exhibit 2007 to support its position. *See* Prelim. Resp. 16 (quoting Ex. 2007, 2); Ex. 2003 ¶ 43 (quoting Ex. 2007, 2). We accord Exhibit 2007 more weight also because it is the Data Sheet for Suboxone® tablets, an official document from Patent Owner itself, informing both regulatory agencies and the public of its own Suboxone® tablet data. As a result, we decline to discount the 13.6% bioavailability of

[6] Exhibit 2029 cites two references (endnotes 76 and 77) in support of this portion of the discussion. Ex. 2029, 302. They are entitled "*Sublingual buprenorphine used postoperatively: Clinical observations and preliminary pharmacokinetic analysis*," and "*Sublingual buprenorphine used postoperatively: Ten-hour plasma drug concentration analysis*," respectively. *Id.* at 319–20.

sublingual Suboxone® tablets, shown on the same page of the same document, as a single-study abnormality.

Given that the undisputed bioavailability of buprenorphine from oral administration is "anywhere from 5 percent to 14 percent," we find that the evidence of record supports Petitioner's position that the bioavailability of orally administered buprenorphine overlaps with that of sublingually administered Suboxone® tablets.

In sum, we decline to construe the challenged claims as requiring oral transmucosal absorption, because the challenged claims do not explicitly recite such a limitation, and because neither the '832 patent nor any other evidence Patent Owner relies on sufficiently demonstrates otherwise.

Patentability Analysis

Prior Art Disclosures[7]

Labtec describes "non-mucoadhesive orally disintegrating film dosage forms that mimic the pharmacokinetic profile of orally administered drug products such as tablets." Ex. 1017, 2. It lists Suboxone® as such a tablet. *Id.* at 22.

Specifically, Table A of Labtec lists "[e]xamples of doses for specific pharmaceutically active agents that can be delivered per one strip of rapidly dissolving oral film . . . along with preferred dosing schedules and

[7] Petitioner relies on Birch for its discussion of a pH range. Pet. 43. As explained in our Decision to Institute, because the challenged claims do not recite any pH levels, "we do not rely on Birch in our obviousness determination." Dec. 17–18. We, therefore, do not discuss the teachings of Birch.

pharmacokinetic parameters." *Id.* at 20. One such example is a film that mimics the pharmacokinetic profile of Suboxone®. *Id.* at 22. The example discloses the combination of buprenorphine HCl/naloxone HCl dehydrate as the pharmaceutically active agents. *Id.* It also describes the Cmax for buprenorphine and naloxone and AUC for buprenorphine. *Id*.

Yang "relates to rapidly dissolving films and methods of their preparation." Ex. 1016, 1:27–28. It teaches a process for making a film from a polymer component, polar solvent, and an active component. *Id.* at 4:23–35. Yang is one of the two U.S. patents incorporated by reference into the '832 patent for disclosing suitable processes to form the claimed film. Ex. 1001, 15:29–31.

Anticipation by Labtec

Petitioner asserts that Labtec anticipates claims 15–19. Pet. 38–41. After reviewing the entire record, we conclude Petitioner has shown by a preponderance of the evidence that Labtec discloses each and every limitation of the challenged claims.

According to Petitioner, Labtec discloses a film comprising pharmaceutical active agents, a film-forming agent, and other ingredients. *Id.* at 39 (citing Ex. 1017, 13–14). Specifically, Labtec discloses an orally disintegrating film comprising buprenorphine and naloxone, as recited in claim 15. *Id.* at 38 (citing Ex. 1017, 20, 22). In addition, Labtec discloses formulating a film to ensure bioequivalence between the film and an existing product, such as the Suboxone® tablets. *Id.* at 40 (citing Ex. 1017, 2, 22). It discloses formulating the film to mimic the known pharmacokinetics of Suboxone®, including Cmax and mean AUC of buprenorphine and

naloxone, as recited in claims 15–17. *Id.* (citing Ex. 1017, 2, 12, 22). Labtec further discloses preferred doses for buprenorphine and naloxone, as recited in claims 18 and 19. *Id.* at 41 (citing Ex. 1017, 22).

Patent Owner contends that Labtec does not anticipate the challenged claims because it only discloses films designed to provide absorption through the gastrointestinal ("GI") tract, while the claimed film requires oral transmucosal absorption. PO Resp. 27–30. Patent Owner also argues that Labtec merely discloses a wish or a goal, and not the claimed film itself. *Id.* at 30–32. Further, Patent Owner asserts that, because Labtec fails the enablement requirement, it is not an anticipatory reference. *Id.* at 32–38. We address each argument in turn.

First, as explained above in the Claim Construction section, we reject Patent Owner's proposal to read oral transmucosal absorption into the challenged claims. As a result, Patent Owner's attempt to distinguish the claimed invention over Labtec based on the route of absorption is unpersuasive.

Second, Patent Owner is correct that Labtec does not disclose any specific embodiment of a buprenorphine-containing film. PO Resp. 30–31. As we explained in our Decision to Institute, however, "anticipation does not require actual performance of suggestions in a disclosure." Dec. 16 (quoting *Novo Nordisk Pharm., Inc. v. Bio-Tech. Gen. Corp.*, 424 F.3d 1347, 1355 (Fed. Cir. 2005)). In other words, a reference may anticipate a claim "even if the author or inventor did not actually make or reduce to practice that subject matter." *Id.* (quoting *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1380 (Fed. Cir. 2003)). We stated our position in the context of enablement. *See id.* Patent Owner, however, appears to argue Labtec's

lack of an example of a buprenorphine-containing film in its disclosure in the context of insufficient written description. PO Resp. 31.

Nevertheless, the written description requirement does not demand examples or an actual reduction to practice either. *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2010) (en banc). Instead, "a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Id.* In this case, Labtec lists Suboxone® in Table A as a drug of interest, and describes an oral film that mimics the pharmacokinetics of Suboxone®. Ex. 1017, 22. Labtec describes that the film formulation comprises buprenorphine and naloxone, as recited in claim 15. *Id.* It states that buprenorphine is to be dosed at 4–16 mg/day. *Id.* Cmax is 1.84 and 3.0 ng/ml and AUC_{0-48} is 12.52 and 20.22 hr.ng/ml, for 4 mg and 8 mg buprenorphine, respectively. *Id.* Labtec further states that "[m]ean peak naloxone levels range from 0.11 to 0.28 ng/ml in dose range of 1–4 mg." *Id.* This description amounts to a constructive reduction to practice that describes an oral film with the specified composition and pharmacokinetic profile. Nothing more is needed. Thus, Labtec does not fail as anticipatory prior art merely because it does not disclose any specific embodiment of the recited film.

Third, Patent Owner asserts that Labtec fails to enable a skilled artisan to practice the claimed invention. PO Resp. 32. According to Patent Owner, a skilled artisan would have recognized that, as Labtec is devoted to films

with peroral delivery[8] of the active ingredients, listing Suboxone®, a sublingual tablet absorbed through oral mucosa, "must simply be a mistake." *Id.* at 32–33. In addition, regardless of whether the challenged claims are limited to oral transmucosal films, Patent Owner contends, Labtec is inoperable if applied to Suboxone® (*id.* at 33–35), and a buprenorphine film formulated for GI-tract absorption would not be therapeutically acceptable (*id.* at 35–36). We are not persuaded.

Patent Owner's arguments center on the alleged "large differences in bioavailability" of buprenorphine and naloxone when absorbed through oral mucosal membrane compared to when absorbed through the GI tract. *Id.* at 34. But, as explained above, the evidence of record supports Petitioner's position that the bioavailability of orally administered buprenorphine overlaps with that of sublingually administered Suboxone® tablets. *See supra* at 11–13. Thus, regardless of whether Labtec is limited to providing GI-tract absorption only, we are not persuaded that Labtec is not enabled with respect to buprenorphine.

We similarly are not persuaded that Labtec is not enabled with respect to naloxone. We conclude so although we disagree with Petitioner's argument that orally and sublingually administered naloxone have "similar bioavailability" (Reply 10), and Petitioner's characterization of Dr. Johnston's deposition testimony as "reluctantly admitt[ing] that the mean absolute bioavailability of oral naloxone is 'one-third' that of a Suboxone tablet" (*id.* at 12 (citing Ex. 1028, 45:7–20)). We conclude so

[8] According to Dr. Johnston, peroral delivery "means a dosage form is swallowed for subsequent absorption in the gastrointestinal tract." Ex. 1028, 3:23–25.

also despite our recognition of Patent Owner's evidence showing that oral administration of naloxone, even at 4 mg or 5 mg, cannot achieve the Cmax range recited in claim 15. *See* PO Resp. 37–38 (citing Ex. 2003 ¶¶ 90–92).

We conclude so because we agree with Petitioner that "Labtec is not limited to 'peroral GI-absorbed dosages.'" *See* Reply 5. We note Patent Owner's argument that Labtec summarizes its invention as providing "film dosage forms that are formulated or administered for gastrointestinal absorption of the active pharmaceutical agent, and that are bioequivalent to and interchangeable with existing orally administered drug products." PO Resp. 32 (citing Ex. 1017, 2). We further note Patent Owner's argument that Labtec describes its film as "non-mucoadhesive," and defines the term to mean that "the dosage form is not designed for administration of the active pharmaceutical agent through the oral mucosa." *Id.* at 27 (citing Ex. 1017, 8).

Petitioner, on the other hand, points to Labtec for disclosing an invention that "provides an orally disintegrating film comprising: (a) an active pharmaceutical agent that is absorbable through the oral mucosa when dissolved; and (b) means for retarding absorption of said active pharmaceutical ingredient through the oral mucosa." Reply 5 (citing Ex. 1017, 14). Labtec also discloses various means, for example, using pH adjusting agents, for retarding absorption of the active ingredient through the oral mucosa. *Id.* (citing Ex. 1017, 14–15).

The evidence of record supports a finding that the active ingredients in Labtec's films are absorbed through not only the GI tract, but also the oral mucosa. Despite its stated object to formulate the film to promote GI-tract absorption, Labtec explains in its Summary of the Invention that the active

ingredients from its non-mucoadhesive film dosages are absorbed "predominantly" through the GI tract. Ex. 1017, 3; *see also id.* at 14 ("The active ingredient from the dosage form is preferably absorbed predominantly through the gastrointestinal tract."). The question, then, is whether the rest of the active ingredient is absorbed through the oral mucosa, or not absorbed at all. Evidence supports a finding that the answer is the former.

According to Petitioner, "Labtec discloses that, in some embodiments, as little as about 60% of the active ingredient is delivered to the GI tract." Reply 6 (citing Ex. 1017, 14). In those cases, Petitioner argues, "as much as about 40%" is absorbed through the oral mucosa. *Id.* Patent Owner disputes this conclusion, arguing that "the point [is] not just delivery. It's absorption, gastrointestinal absorption." Tr. 34:11–12. Patent Owner correctly notes that delivery is not the same as absorption. In fact, Labtec makes clear this distinction:

> [O]f the active ingredient absorbed, the predominant amount (greater than 60, 70, 80, 90, 95 and up to 100 wt.%) is preferably *absorbed* through the GI tract. Therefore, the means should be able to *deliver* greater than 60, 70, 80, 90 or 95 and up to 100 wt.% of the active ingredient to the gastrointestinal tract.

Ex. 1017, 14 (emphases added). For this analysis, we focus our attention on the delivery of the drug.

During his deposition, Dr. Johnston testified:

> [I]f you give an orally dissolving film, and if the drug is not absorbed across the oral mucosa, sublingual, buccal, whatever, then it has to be swallowed, because the patient -- where else would it go? The patient doesn't expectorate that saliva drug solution. So to answer your question, it has to be swallowed. If it isn't absorbed, it has to go somewhere.

Ex. 1028, 237:9–17. In other words, after an orally dissolving film is administered through the oral cavity, because a patient does not spit out the drug, the amount of the drug that is swallowed and, thus, delivered to the GI tract, is the amount not absorbed in the mouth. Thus, we are persuaded that, when only 60% of the active ingredient reaches the GI tract, the rest (40%) must have been absorbed through the oral mucosa. *See* Tr. 21:3–7.

Labtec discloses a film with 2.0 mg naloxone (Ex. 1017, 22), within the "about 0.5 to about 4 mg of naloxone" range recited in claim 19. For a film that delivers 60% of naloxone to the GI tract, 0.8 mg (2.0 mg x 40%) naloxone is absorbed through the oral mucosa. Because plasma level increases as the dose of naloxone increases (Ex. 2007, 2; Ex. 1028, 51:20–52:4), the Cmax and AUC for 0.8 mg naloxone would necessarily fall within the ranges recited in claims 15 and 17.[9] *See* Ex. 1001, 17:20–48 (disclosing the Cmax and mean AUC ranges for naloxone as between 80% of the Cmax and AUC for 0.5 mg naloxone and 125% of those for 4 mg naloxone).

Patent Owner contends that "[d]ue to its much lower bioavailability, peroral delivery of a given amount of buprenorphine or naloxone cannot possibly give close to the same or substantially bioequivalent Cmax and AUC values (80–125%) compared to oral-transmucosal delivery of the same amounts of those active ingredients." PO Resp. 34. As explained above, the challenged claims are not limited to oral transmucosal absorption, and Labtec is not limited to GI-tract absorption. Thus, the comparison argued by Patent Owner is not meaningful in our analysis. Furthermore, the challenged

[9] To illustrate our point in this analysis, we compare the pharmacokinetic profile as if the claims were, as Patent Owner urges, limited to oral transmucosal absorption.

claims do not recite any dosage amount of either buprenorphine or naloxone. Nor does the Specification include any dosage requirement when defining what is considered bioequivalent. Ex. 1001, 17:42–48. During the oral argument, the panel inquired whether orally administering 16 mg buprenorphine to achieve a Cmax of 0.624 ng/ml would be considered bioequivalent. Tr. 25:16–19, 27:12–19. Counsel for Patent Owner responded affirmatively (*id.* at 25:20–22, 27:20–21), even though 16 mg is the upper limit of the buprenorphine dosing range, whereas 0.624 ng/ml is the lower limit of the Cmax range, calculated based on 80% of the Cmax of sublingually administered buprenorphine (2 mg) Suboxone® tablets. *See* Ex. 1001, 17:30–40. In other words, according to the '832 patent, to be considered the same or substantially bioequivalent does not require peroral delivery of the *same amount* of buprenorphine or naloxone as in oral-transmucosal delivery.

Patent Owner recognizes so, but qualifies its admission "with the caveat that if [the active ingredient is administered] perorally, it would be understood to be therapeutically unacceptable because of the variability involved with the peroral dosing." Tr. 27:20–24. We are not persuaded. As Petitioner points out, the Data Sheet for Suboxone® tablets (again, an official drug label from Patent Owner itself) acknowledges "a wide inter-patient variability" in the absorption of buprenorphine and naloxone even from sublingually administered Suboxone® tablets. Reply 10 (citing Ex. 2007, 2). Further, naloxone has no detectable pharmacological activity whether administered orally or sublingually. Ex. 2007, 1. We, therefore, are not persuaded that Labtec is not enabled with respect to naloxone.

For the foregoing reasons, Labtec, disclosing an oral film comprising buprenorphine and naloxone with the pharmacokinetic profiles recited in the challenged claims, anticipates claims 15–19.

Obviousness over Labtec, Birch, and Yang

Petitioner argues that the challenged claims would have been obvious over the combination of Labtec, Birch,[10] and Yang. Pet. 44–45. After reviewing the complete record, we conclude Petitioner has shown by a preponderance of the evidence that one of ordinary skill in the art would have had reason to combine the teachings of Labtec and Yang to make an orally dissolving film as recited in the challenged claims, and would have had a reasonable expectation of success in doing so.

According to Petitioner, because "[t]he law provides three year market exclusivity for new dosages of existing drug products" (*id.* at 45 (citing Ex. 1024[11,12])), a skilled artisan would have been motivated to create a film formulation of Suboxone® to enjoy the market exclusivity. *Id.* Petitioner argues that Labtec already discloses components suitable for making films. *Id.* But, to the extent Labtec's teaching on how to make a film is insufficient, Yang teaches such methods. *Id.*

Patent Owner does not dispute that Yang teaches processes for making a film but contends that the teaching of Yang "does not address the

---

[10] *See supra* at 14 n.7.
[11] M.A. VOET, THE GENERIC CHALLENGE: UNDERSTANDING PATENTS, FDA & PHARMACEUTICAL LIFE-CYCLE MANAGEMENT 110 (Brown Walker Press 2d ed. 2008).
[12] Petitioner mistakenly cites "Ex. 1025" but correctly describes Exhibit 1024. Pet. 45.

deficiencies of Labtec." PO Resp. 45. According to Patent Owner, one of ordinary skill in the art would not look to Labtec to develop a buprenorphine film, and would not have had a reasonable expectation of success in combining the teachings of Labtec and Yang. *Id.* at 40–47. Patent Owner rests these arguments on the premise that Labtec is limited to peroral delivery of films formulated for GI-tract absorption only. *See id.* at 39–41, 45–47. As explained above, however, Labtec is not so limited. *See supra* at 18–20. Thus, we reject Patent Owner's contentions on this basis.

In addition, even if we were to find that films according to Labtec's invention deliver active ingredients solely for absorption through the GI tract, we still would be unpersuaded by Patent Owner's arguments. Patent Owner asserts that Labtec merely makes "an obviously mistaken and unintentional suggestion to pursue" a buprenorphine film "that was understood to be therapeutically ineffective and unacceptable." PO Resp. 41. In addition, Patent Owner contends that a skilled artisan would not have a reasonable expectation of success because combining the prior art to arrive at the claimed invention would "transmogrify Labtec beyond recognition." *Id.* at 47. We are not persuaded.

"Under an obviousness analysis, a reference need not work to qualify as prior art; it qualifies as prior art, regardless, for whatever is disclosed therein." *Geo. M. Martin Co. v. Alliance Mach. Sys. Int'l LLC*, 618 F.3d 1294, 1302 (Fed. Cir. 2010) (citations and internal quotation marks omitted). As Patent Owner points out, Labtec recognizes that several manufacturers proposed film formulations for the delivery of prescription drugs. PO Resp. 27 (citing Ex. 1017, 2). According to Labtec, "[t]he vast majority of these formulations are 'mucoadhesive' formulations designed for adhesion of the

dosage form to the mucosal tissue in the mouth, and transmission of the drug from the dosage form through the mucosal tissue into the systemic circulation." Ex. 1017, 1. Labtec acknowledges that the "advantage of these mucoadhesive films resides in their ability to bypass the gastrointestinal tract, and barriers in the gastrointestinal tract to drug absorption such as first pass metabolism and decomposition of the active ingredient in the stomach." *Id.* at 2.

Patent Owner emphasizes that these teachings appear in the background section of Labtec. A person of ordinary skill, however, would read a reference for all that it teaches, including uses beyond its primary purpose. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 418–21 (2007); *see also Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551 (Fed. Cir. 1989) (stating that a prior art reference is relevant "for all that it teaches" to those of ordinary skill in the art). Here, regardless of which section the teaching of "mucoadhesive film" appears in, Labtec suggests a film formulated for oral mucosal absorption. Thus, a person of ordinary skill in the art would have considered Labtec, and combining Labtec and Yang would not be, as Patent Owner contends, "completely antithetical" to Labtec's teaching and a skilled artisan's expectation. *See* PO Resp. 26.

Patent Owner further argues that even if the prior art references are combined, it would require undue experimentation to arrive at the claimed invention. *Id.* at 48–53. Undue experimentation is part of the enablement inquiry. *See Impax Labs., Inc. v. Aventis Pharms. Inc.*, 545 F.3d 1312, 1314 (Fed. Cir. 2008) ("[A] prior art reference must enable one of ordinary skill in the art to make the invention without undue experimentation."). A reference, however, qualifies as prior art in determining obviousness,

independent of enablement. *In re Antor Media Corp.*, 689 F.3d 1282, 1292 (Fed. Cir. 2012); *see also In re Morsa*, 713 F.3d 104, 111–12 (Fed. Cir. 2013) (remanding for proper enablement analysis in anticipation rejection, but affirming obviousness rejection based on the same prior art). Thus, we do not engage in enablement analyses in our obviousness determination.[13]

Instead, we interpret Patent Owner's undue-experimentation argument as an assertion of no reasonable expectation of success. Here, Patent Owner presents contentions based on the alleged different delivery and absorption routes (*see* PO Resp. 50–53), which we have addressed above. We also note Patent Owner's emphasis on how recent and complex pharmaceutical film technology is, and how extensive research and development was required to develop Suboxone® film. PO Resp. 48–50. Obviousness, however, does not require absolute predictability of success. *In re O'Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988). Instead, all that is required is a reasonable expectation of success. *Id.* Based on evidence before us, we are persuaded that the teachings of Labtec, as explained above, combined with the information in Yang, which the '832 patent itself relies on as teaching suitable processes to make the claimed film (Ex. 1001, 15:29–32), provides such a reasonable expectation of success.

Patent Owner asserts that objective indicia support a finding of nonobviousness. PO Resp. 53–57. Specifically, Patent Owner argues that "Suboxone® sublingual films, which are covered by the challenged claims of the '832 patent, have achieved significant commercial success and have

[13] As explained above in the discussion of the anticipation ground, we are not persuaded by Patent Owner's enablement challenge of Labtec. *See supra* at 17–22.

received praise from others in the field, which provides objective indicia that claims 15–19 are nonobvious." *Id.* at 53. The evidence of record, however, does not persuade us that the asserted commercial success and praise overcome Petitioner's showing of obviousness here.

For objective evidence of secondary considerations to be accorded substantial weight, Patent Owner must establish a nexus between the evidence and the merits of the claimed invention. *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1246 (Fed. Cir. 2010). In this case, Suboxone® tablets, with the combination of buprenorphine and naloxone as the pharmaceutical ingredients, were already on the market when the application for the '832 patent was filed. Ex. 1013. Thus, the alleged inventive aspect of the challenged claims resides only in the film dosage form. According to Patent Owner, evidence shows that in 2013, "sales of Suboxone sublingual film increased to more than $1.3 billion in the U.S. while the total market grew to more than $1.7 billion." PO Resp. 55 (citing Ex. 2046, 2). But, Patent Owner fails to account for the market share of, and revenue generated by, Suboxone® tablets before the film dosage form was introduced. Here, the lack of such information is critical for analyzing secondary considerations, especially in view of the fact that on March 18, 2013, Patent Owner voluntarily withdrew Suboxone® tablets from the US market. Pet. 3; Ex. 1003, 3. With the tablets no longer on the market, it is unclear whether the sales increase or the alleged patient preference was due to the film dosage form, or because film was the only available form. As a result, we find the evidence of secondary considerations in this case cannot overcome the evidence of obviousness.

Motion to Exclude

Petitioner filed a Motion to Exclude Exhibit 2043. Paper 35. According to Petitioner, Exhibit 2043 is a paper filed by a subsidiary of Petitioner in an unrelated IPR proceeding. *Id.* at 1. Patent Owner opposed the Motion. Paper 37. Because we do not rely on Exhibit 2043 in rendering our Decision, we dismiss the Motion as moot.

CONCLUSION

Petitioner has shown, by a preponderance of the evidence, that Labtec anticipates claims 15–19, and that the combination of Labtec, Birch, and Yang would have rendered claims 15–19 obvious.

ORDER

Accordingly, it is

ORDERED that claims 15–19 of the ’832 patent are determined to be unpatentable;

FURTHER ORDERED that Petitioner’s Motion to Exclude is *dismissed as moot*.

For PETITIONER:

Danielle L. Herritt
dherritt@mccarter.com

Kia L. Freeman
kfreeman@mccarter.com

For PATENT OWNER:

James M. Bollinger
james.bollinger@troutmansanders.com

Daniel A. Ladow
daniel.ladow@troutmansanders.com