

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. REDDY'S LABORATORIES, LTD. and
DR. REDDY'S LABORATORIES, INC.,
Petitioners,

v.

INDIVIOR UK LIMITED,
Patent Owner.

Case IPR2016-01113
Patent 8,475,832 B2

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

BONILLA, *Vice Chief Administrative Patent Judge*.

DECISION
Denying Petitioner's Request for Rehearing
37 C.F.R. § 42.71

I. INTRODUCTION

Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc. (collectively "Petitioner"), filed a Request for Rehearing under 37 C.F.R. § 42.71(d) of our Decision (Paper 16, "Decision" or "Dec.") denying *inter partes* review of claims 1–7 and 9–12 of U.S. Patent No. 8,475,832 B2 (Ex. 1001, "the '832 patent"). Paper 17 ("Req. Reh'g"). In our Decision, we denied institution as to all of the grounds set forth in the Petition (Paper 1, "Pet."). Dec. 2–4, 10–19. Petitioner's Request for Rehearing seeks reconsideration of our denial to institute each of the grounds. Req. Reh'g 1.

Under 37 C.F.R. § 42.71(c), "[w]hen rehearing a decision on petition, a panel will review the decision for an abuse of discretion." An abuse of discretion occurs when a "decision was based on an erroneous conclusion of law or clearly erroneous factual findings, or . . . a clear error of judgment." *PPG Indus., Inc. v. Celanese Polymer Specialties Co.*, 840 F.2d 1565, 1567 (Fed. Cir. 1988). The request for rehearing "must specifically identify all matters the party believes the Board misapprehended or overlooked, and the place where each matter was previously addressed in a motion, an opposition, or a reply." 37 C.F.R. § 42.71(d). A party who requests rehearing bears the burden of showing that a decision should be modified. *Id.*

II. ANALYSIS

Petitioner argues that we "erred in applying a legally improper, overly restrictive obviousness analysis and ignoring the ample evidence provided by Petitioner and its expert." Req. Reh'g 3. Specifically, Petitioner takes issue with our statement in the Decision that Petitioner did "not point to

where the SBOA,¹ the Suboxone® 2002 Label,² and/or LabTec³ suggest that anyone actually measured a local pH for the Suboxone tablets in an oral cavity, much less determined that local pH should be from about 3 to about 3.5.” *Id.* at 4, 10 (quoting Dec. 13). Petitioner states that we “applied an overly restrictive standard in requiring the SBOA, the Suboxone® 2002 Label, and/or LabTec to ‘actually measure a local pH for the Suboxone tablets in an oral cavity’ or to ‘[determine] that a local pH should be from about 3 to about 3.5,’” and that we “ignored the teachings in these references of the importance of pH, including specifically teaching that a pH range exists, for dissolution and transmucosal absorption.” *Id.* at 10 (alteration in original) (quoting Dec. 13).

Petitioner alleges that our Decision took a teaching from LabTec out of context, namely that “[f]or a basic active ingredient,” one would lower the pH for the purpose of “retarding absorption of the active ingredient through the oral mucosa.” *Id.* at 9 (alteration in original) (emphasis omitted) (quoting Dec. 17). Petitioner also repeats its argument that given the teachings of the applied references, including “knowledge of the pH dependence of the transmucosal absorption of buprenorphine and naloxone,” it only would have required routine experimentation to obtain an optimal pH range, and to arrive at the claimed pH range of about 3 to about 3.5. *Id.* at 13.

Petitioner further argues that it did not rely solely on the SBOA,

¹ Suboxone® Tablet Summary Basis of Approval (“SBOA”) (Ex. 1009).

² Suboxone® 2002 Label (Ex. 1008).

³ WO 2008/040534 A2, published Apr. 10, 2008 (“LabTec”) (Ex. 1007).

Suboxone[®] 2000 Label, and LabTec. *Id.* at 4. Specifically, the Request for Rehearing summarizes the Petition's description of LabTec, Oksche,⁴ Yang,⁵ the Suboxone[®] 2002 Label, the SBOA, Dr. Çelik's testimony (Ex. 1003), Birch,⁶ and the '055 publication,⁷ and argues that as supported by Dr. Çelik's testimony, LabTec and Oksche provided a motivation to develop the film version of Suboxone[®] tablets, and Yang established a reasonable likelihood of success in manufacturing a film product bioequivalent to Suboxone[®] tablets. Req. Reh'g 4–8.

The Request for Rehearing also asserts that Birch taught administration of buprenorphine-containing formulations to the nasal mucosa at a pH of about 3.5, which successfully resulted in transmucosal absorption of buprenorphine and the desired bioequivalence, such that as a result, there was a motivation to use a pH of 3.4 for a film dosage form of buprenorphine and naloxone with a reasonable likelihood of success of achieving bioequivalence to the tablet form. *Id.* at 6, 11–12. Petitioner relies on Dr. Çelik's testimony in support of this assertion. *Id.* at 11–12. Furthermore, Petitioner alleges that we erred in discounting Dr. Çelik's testimony regarding similar anatomy of the oral and nasal mucosa as conclusory. *Id.*

We disagree with Petitioner that we applied an overly restrictive

⁴ WO 2008/025791 A1, published Mar. 6, 2008 (“Oksche”) (Ex. 1005).

⁵ Yang et al., U.S. Patent No. 7,357,891 B2, issued Apr. 15, 2008 (“Yang”) (Ex. 1006).

⁶ Birch et al., U.S. Patent Application Publication No. 2005/0085440 A1, published Apr. 21, 2005 (“Birch”) (Ex. 1004).

⁷ Yang et al., U.S. Patent Application Publication No. 2005/0037055 A1, published Feb. 17, 2005 (“the '055 publication”) (Ex. 1010).

obviousness analysis. In stating that Petitioner did “not point to where the SBOA, the Suboxone® 2002 Label, and/or LabTec suggest that anyone actually measured a local pH for the Suboxone tablets in an oral cavity, much less determined that local pH should be from about 3 to about 3.5, as recited in the challenged claims,” we addressed Petitioner’s reliance on those three references as collectively teaching or suggesting the claim limitations “[a] buffer in an amount to provide a local pH” of “about 3 to about 3.5.” Dec. 13 (citing Pet. 27–32). We concluded that those three references did not provide sufficient evidence to establish those claim limitations as known prior art elements. *See id.* at 13–14.

Petitioner is incorrect that we ignored teachings in those three references concerning pH. Rather, we considered the Suboxone® Label’s disclosure of a buffering system consisting of citric acid and sodium citrate and Petitioner’s contention, relying on Dr. Çelik’s testimony, that a citric acid and sodium citrate buffer operates within the range of 3.0 to 6.2. *Id.* at 12–13 (citing Pet. 31–32). We also considered the SBOA’s disclosure of *in vitro* dissolution studies identifying redacted pH values, and Petitioner’s conclusion based on the SBOA, “that in order for buprenorphine to dissolve, the local pH of the saliva had to be below a certain value, and for naloxone to dissolve, the pH had to be above a certain value because the solubility profiles of these drugs are dependent on pH.” *Id.* at 11 (quoting Pet. 29); *id.* at 13 (citing Pet. 29–32). And we further considered LabTec’s disclosure of the relationship between pH and absorption. *Id.* at 11 (citing Pet. 27–28); *id.* at 17. We found, however, insufficient evidence to support a conclusion that a local pH value for Suboxone® in the oral cavity or a local pH range of about 3 to about 3.5 were known or obvious. *Id.* at 11–14.

We considered Petitioner’s argument that “‘it would have been nothing more than routine experimentation’ to identify ‘the claimed pH range of 3 to 3.5 as optimal.’” *Id.* at 16 (quoting Pet. 33). As we discussed in our Decision, however, the relationship between pH and absorption that LabTec discloses is that “[f]or a basic active ingredient, one would adjust the pH of the solution to below the pKa of the conjugate acid” as a “means for retarding absorption of the active ingredient through the oral mucosa.” *Id.* at 17 (alteration in original) (emphasis omitted) (quoting Ex. 1007, at 15). In other words, for a basic active ingredient like buprenorphine, this teaching suggests to lower the pH where the goal is to *retard oral absorption*. See *id.*; see also Ex. 1009, at 28 (describing buprenorphine as a “weak base” and stating that “[a]bsorption of lipophilic weak bases should increase with salivary pH increases”). As such, as noted in our Decision, LabTec does not suggest preparing a film that lowers a local pH to 3–3.5 in the saliva for the purpose of increasing absorption of an active ingredient such as buprenorphine. Dec. 17. In contrast, the claims of the ’832 patent require adjusting the local pH to “optimize absorption of said buprenorphine,” and the specification further explains that “[i]n a dosage form that is to be placed in the oral cavity, it is desired to absorb the agonist [buprenorphine] buccally, so as to provide rapid integration of the agonist into the body of the user.” Ex. 1001, 11:10–13, 23:65–67, 24:33–35.

We disagree with Petitioner that our Decision takes LabTec’s teaching out of context. According to Petitioner,

Naloxone, which is disclosed in LabTec at page 27, is precisely the active ingredient a POSA desires to be retarded from transmucosal absorption in the presence of buprenorphine. Moreover, while the pH of a basic active ingredient can be

adjusted below the pKa of the conjugate acid, common sense dictates that the converse is equally true. That is, for a basic active ingredient, one would adjust the pH of the solution to above the pKa of the conjugate acid to enhance transmucosal absorption. This very application was discussed in Dr. Çelik's testimony. Success by a POSA would be reasonably expected since enhanced buprenorphine transmucosal absorption was achieved along with retarded naloxone transmucosal absorption by the Suboxone® tablets.

Req. Reh'g 9–10 (citations omitted). The problem with Petitioner's conclusion, however, is that the evidence of record shows that both naloxone and buprenorphine are weak bases with similar pKas. See Prelim Resp. 3, 14–17; Ex. 1001, 11:46–48; Ex. 1003 ¶¶ 46, 55 (stating that “[t]he pKa of naloxone is 7.94 and “[t]he pKa of buprenorphine is 8.42,” and quoting a statement made by the applicants in the prosecution history that both buprenorphine and naloxone “are conjugate acids with pKa's at approximately 8”); Ex. 1009, at 28. Petitioner provides no explanation for why, when decreasing the pH to retard transmucosal absorption of the naloxone component as desired, one of ordinary skill in the art would have expected the opposite result (enhanced transmucosal absorption) to occur for the buprenorphine component, when both naloxone and buprenorphine are basic active ingredients having similar pKas.

In addition, our Decision also was not limited to an analysis of the LabTec, Suboxone® 2002 Label, and SBOA references alone. We considered Petitioner's arguments concerning Birch, including the argument that Birch taught that transmucosal absorption of buprenorphine was optimal within the pH range of about 3 to about 3.5, specifically, 3.4. Dec. 14 (citing Pet. 32–33). We were unpersuaded by Petitioner's arguments, however, finding that Birch, which taught buprenorphine formulations (lacking

naloxone), exclusively applied to intranasal administration. *Id.* at 14–15. We found insufficient evidence to suggest that the pH values disclosed in Birch would have been applicable to optimal buprenorphine absorption in the context of oral administration. *Id.* Rather, we found that Birch indicated that buprenorphine pharmacokinetics (e.g., $C_{\max}$ and bioavailability) differed when administered to oral versus nasal mucosa. *Id.* at 15 (citing Prelim. Resp. 27; Ex. 1004, at 16 tbl.11).

We disagree with Petitioner that we erred in finding Dr. Çelik’s statement that the “anatomy of the oral and nasal mucosa is quite similar, thus, one of ordinary skill would expect that the same principle of drug delivery will apply to both tissues” (Ex. 1003 ¶ 105) is merely conclusory. In the Request for Rehearing, Petitioner argues that Dr. Çelik’s testimony in the same paragraph as this statement provides support. Req. Reh’g 12 (citing Ex. 1003 ¶ 105). We have reviewed this paragraph of Dr. Çelik’s declaration, however, and we find that with the exception of the paragraph’s final sentence (which is the statement at issue), the entirety of the paragraph is a summary of Birch’s disclosures and concerns delivery to the nasal mucosa. *See* Ex. 1003 ¶ 105. Before the final sentence of the paragraph, the testimony in this paragraph fails to mention oral mucosa, let alone provide reasoning or support for why Dr. Çelik concludes that “[t]he anatomy of the oral and nasal mucosa is quite similar” or why it would have been expected “that the same principle of drug delivery will apply to both tissues.” *See id.*

Finally, the Request for Rehearing reiterates the Petition’s discussion of various teachings of individual references, including LabTec, Oksche, Yang, the Suboxone® 2002 Label, the SBOA, and Birch. *See* Req. Reh’g 4–6. In our Decision, however, we considered and addressed Petitioner’s

arguments regarding each of those references. *See* Dec. 10 (citing Pet. 24–27) (LabTec and Yang); *id.* at 11–13 (SBOA and Suboxone[®] 2002 Label); *id.* at 14–15 (Birch); *id.* at 18 (citing Pet. 40–50) (Oksche). Petitioner further asserts that the Petition discussed how it would have been obvious from LabTec and Oksche to develop a film version of Suboxone[®] and how Yang would have provided a reasonable expectation of success in manufacturing an oral film bioequivalent to Soboxone[®] tablets. Req. Reh’g 6–8. The Petition, however, did not provide evidence accounting for the claim limitations pertaining to the local pH range discussed above. Likewise, the Request for Rehearing refers to Dr. Çelik’s testimony regarding the known absorption and nonabsorption characteristics of the buprenorphine and naloxone components, respectively, of the Suboxone[®] tablet (*id.* at 5–6 (citing Pet. 17; Ex. 1003 ¶¶ 75, 83)), and further refers to the Petition’s discussion of the ’055 publication (*id.* at 6). But again, neither the ’055 publication (which Petitioner only relied on in relation to dependent claims 3, 11, and 12 (*see* Pet. 11–12)), nor this testimony from Dr. Çelik, provides adequate evidence of the claimed local pH range.

III. CONCLUSION

The Request for Rehearing does not identify any matters that we misapprehended or overlooked, nor does it show that our Decision denying institution was based on an erroneous conclusion of law, clearly erroneous factual findings, or a clear error of judgment.

IV. ORDER

Accordingly, it is

ORDERED that Petitioner’s Request for Rehearing is denied.

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