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Paper No. 48
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ALTAIRE PHARMACEUTICALS, INC.,
Petitioner,

v.

PARAGON BIOTECK, INC.,
Patent Owner.

Case PGR2015-00011
Patent 8,859,623 B1

Before SHERIDAN K. SNEDDEN, ZHENYU YANG, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

YANG, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 328(a) and *37 C.F.R. § 42.73*

INTRODUCTION

Altaire Pharmaceuticals, Inc. ("Petitioner") filed a Petition for a post-grant review of claims 1–13 of U.S. Patent No. 8,859,623 B1 ("the '623 patent," Ex. 1001). Paper 1 ("Pet."). On November 16, 2015, the Board instituted trial to review patentability of the challenged claims. Paper 14 ("Dec."). Thereafter, Paragon Bioteck, Inc. ("Patent Owner") filed a Response (Paper 20 ("PO Resp.")), and Petitioner filed a Reply (Paper 35). Oral hearing was held on July 12, 2016. *See* Paper 47 ("Tr.").

The Board has jurisdiction under 35 U.S.C. § 6 and issues this final written decision pursuant to 35 U.S.C. § 328(a) and 37 C.F.R. § 42.73.

For the reasons provided below, we determine that Petitioner has not met its burden of proving the unpatentability of claims 1–13 of the '623 patent by a preponderance of the evidence. *See* 35 U.S.C. § 326(e).

The '623 Patent

The '623 patent "is directed to methods and compositions of stabilizing phenylephrine formations." Ex. 1001, Abstract. "Phenylephrine is a selective α1-adrenergic receptor agonist used primarily as a decongestant, as an agent to dilate the pupil, and to increase blood pressure." *Id.* at 1:6–8. At the time of the '623 patent invention, it was known that R-phenylephrine, but not S-phenylephrine, was useful to dilate the pupil. *Id.* at 6:21–30. According to the '623 patent, "it is important that an eye drop containing Phenylephrine Hydrochloride used for dilation of the pupil contains predominantly the R-isomer in order to maintain maximum efficacy of the ophthalmic solution." *Id.* at 6:30–33.

In addition, according to the '623 patent, generally, commercially available phenylephrine hydrochloride ophthalmic solutions were stored at 20 to 25 degree Celsius, with the container tightly closed. *Id.* at 2:60–65. A solution under such condition, however, often turns brown over time and cannot be used. *Id.* at 2:66–3:3. The '623 patent states that it "provides the improvement to overcome such instability problem." *Id.* at 3:4–5.

Specifically, the '623 patent provides "a composition comprising at least 95% R-phenylephrine hydrochloride and an aqueous buffer, wherein the composition substantially maintains an initial chiral purity of R-phenylephrine hydrochloride for at least 6 months stored between –10 to 10 degree Celsius." *Id.* at 1:16–21. It also discloses "methods of dilating the pupil comprising administering a composition comprising R-phenylephrine hydrochloride topically to a mammal, wherein the composition substantially maintains the initial chiral purity of R-phenylephrine hydrochloride for at least 6 months." *Id.* at 1:38–42.

Illustrative Claim

Claims 1 is the sole independent claim. It reads:

> 1. A method of using an ophthalmic composition for pupil dilation, the composition comprising R-phenylephrine hydrochloride having an initial chiral purity of at least 95% and an aqueous buffer, wherein the chiral purity of R-phenylephrine hydrochloride is at least 95% of the initial chiral purity after 6 months, the method comprising:
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> administering the composition into an eye of an individual in need thereof, wherein the composition is stored between –10 to 10 degree Celsius prior to administration, and wherein the

composition comprises R-phenylephrine hydrochloride having a chiral purity of at least 95% when administered after storage.

Reviewed Ground of Unpatentability

The Board instituted trial to review whether claims 1–13 of the '623 patent are unpatentable as obvious over Altaire's Product, i.e., the phenylephrine hydrochloride ophthalmic solution Lot # 11578 and Lot # 11581.[1]

ANALYSIS

Claim Construction

In a post-grant review, we interpret 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. § 42.200(b); *see also In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1281 (Fed. Cir. 2015) (concluding that "Congress implicitly adopted the broadest reasonable interpretation standard in enacting the AIA"), *aff'd sub nom. Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46 (2016). Under that standard, and absent any special definitions, we assign claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the

[1] Lot # 11578 is a 2.5% phenylephrine hydrochloride ophthalmic solution, manufactured in December 2011, and sold and distributed to an Altaire customer in October 2012. Ex. 1003 ¶¶ 4, 36; Ex. 1007. Lot # 11581 is a 10% phenylephrine hydrochloride ophthalmic solution, manufactured in January 2012, and sold and distributed to another Altaire customer in October 2012. Ex. 1003 ¶¶ 5, 6, 36; Ex. 1009.

art at the time of the invention, in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

In its Response, Patent Owner states that it agrees with our determination in the Institution Decision that no terms require express construction. PO Resp. 14 (citing Dec. 9). Nonetheless, Patent Owner contends that "claim 1 requires storage after six months, between −10 to 10 degrees Celsius, such that the chiral purity after said storage is at least 95% of the initial chiral purity." *Id.* To the extent Patent Owner requests that we limit the method step by adding a six-months-cold-storage requirement, we reject this attempt.

We find no basis to interpret the claims as requiring a step of cold storage of the composition for six months before administering to a patient. The only step of claim 1 recites that the composition is "stored between –10 to 10 degree Celsius prior to administration." Ex. 1001, 12:45–48. It does not specify how long the storage must be at that cold temperature. Patent Owner, however, relies on the preamble, which explicitly recites the chiral purity "is at least 95% of the initial chiral purity *after 6 months*." Ex. 1001, 12:42–44 (emphasis added). This language of the preamble is consistent with the prosecution history, in which the applicants argued, and the examiner agreed, that claim 1 was patentable because the chiral purity remained at least 95% of the initial chiral purity after cold storage for six months. *See* Ex. 1002, 110, 113, 167.

Maintaining at least 95% of the initial chiral purity after six months, however, simply describes a property of the composition to be administered.

The characteristic, defined in the preamble, does not add a limitation on the duration of storage at cold temperatures recited in the "administering" step. This is especially so because the preamble requires that, after the six-month storage, the chiral purity is only at least 90.25% (i.e., "at least 95% of the initial chiral purity," which is already defined in the preamble as "at least 95%"). *See id.* at 12:41–44. In contrast, the step of claim 1 requires "a chiral purity of at least 95% when administered after storage." *Id.* at 12:49–50. In other words, the step of claim 1 defines the chiral purity of the composition at the time of administration after cold storage for an unspecified time period, whereas the preamble defines chiral purity of the composition after six months in relation to the "initial" chiral purity. We, therefore, treat the preamble as a limitation only to the extent that it defines a property of the composition to be administered.[2]

Thus, we reject Patent Owner's interpretation that the administering step of claim 1 requires an active step of cold storage for six months. Instead, we determine that claim 1 is directed to a method of administering a composition—wherein the composition comprises R-phenylephrine hydrochloride that exhibits the property of having at least 95% of the initial chiral purity after six months—as long as the composition is stored in cold temperature before the administration, and is at least 95% R-phenylephrine hydrochloride when administered.

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[2] Neither party has argued that the preamble should be disregarded altogether in our analysis.

Witness Status of Assad Sawaya

In support of its patentability challenge, Petitioner relies on a Declaration of Assad Sawaya, who is the President of Petitioner. Ex. 1003. Patent Owner argues that Petitioner's witness, Mr. Sawaya, is a fact witness, and not an expert. PO Resp. 29. We agree with Patent Owner.

In his declaration in support of the Petition, Mr. Sawaya testifies "based upon [his] personal knowledge of the facts stated [t]herein." Ex. 1003 ¶ 1. Nowhere in that declaration does he explain his "knowledge, skill, experience, training, or education" that would provide the bases for his qualification as an expert. *See* Dec. 14 (quoting Fed. R. Evid. § 702). As such, we find it appropriate to consider Mr. Sawaya as a fact witness, rather than an expert, in this proceeding.

This is so even though later, in its Reply, Petitioner argues that Mr. Sawaya qualifies as an expert witness. *See* Reply 2–3. As support, Petitioner submits another declaration by Mr. Sawaya, accompanied by his curriculum vitae, detailing his experience in the pharmaceutical industry.[3] *See* Ex. 1025. Petitioner fails to appreciate that the issue here is not whether Mr. Sawaya qualifies as an expert witness in the abstract; rather, it is whether Petitioner has properly qualified Mr. Sawaya as an expert witness with respect to the testimony he has provided *in this proceeding*. We determine Petitioner has not.

[3] Substantively, the Reply Declaration of Mr. Sawaya does not include any testimony to support Petitioner's patentability challenge.

A reply may only respond to arguments raised in the corresponding patent owner response. 37 C.F.R. § 42.23(b). As we previously explained, "respond," in the context of this Rule, does not permit Petitioner to depart from the positions originally taken in the Petition and embark in a new direction with a new approach. Paper 38, 1. Here, Petitioner intends to revise the witness status of Mr. Sawaya from a lay person to an expert. This change would affect what subjects on which Mr. Sawaya may testify competently. For example, under Federal Rule of Evidence 602, a witness may testify only to a matter of which he has personal knowledge. In contrast, "[a]n expert may base an opinion on facts or data in the case that the expert has been made aware of or personally observed." Fed. R. Evid. § 703. As a result, while an expert may testify on certain topics, such as prior art teachings or the level of ordinary skill, a lay witness may not do so. Because retroactively qualifying Mr. Sawaya as an expert at the time of the Reply would impact our treatment of the testimony he provided in support of the Petition, and because Patent Owner did not have the opportunity to consider and respond to Mr. Sawaya's prior testimony in that capacity, we decline to do so at this late stage.

Our approach is consistent with those of federal courts, which generally do not consider new evidence presented at the end of a briefing schedule when the other party no longer has an opportunity to respond. *See, e.g.*, *Stamps.com Inc. v. Endicia, Inc.*, 437 F. App'x 897, 909 (Fed. Cir. 2011) (holding that the district court acted within its discretion when it did

not consider supplementary declarations submitted for the first time in a reply brief because the other party did not have an opportunity to respond).

In sum, we reject Petitioner's belated attempt and decline to consider the new Sawaya declaration because it is improper reply evidence. Petitioner has failed to timely qualify Mr. Sawaya as an expert witness in this proceeding. Thus, we accord no weight to his opinion in that capacity.

Obviousness over Altaire's Product

Petitioner argues that claims 1–13 of the '623 patent are unpatentable as obvious over Altaire's Product. Pet. 33–45.

Petitioner relies on two lots of Altaire's phenylephrine hydrochloride ophthalmic solution products: Lot # 11578 and Lot # 11581. Pet. 34. We explained in the Decision to Institute that Petitioner has shown that these products were "in public use, on sale, or otherwise available to the public" before November 14, 2013, the effective filing date of the challenged claims. *See* Dec. 10 (citing 35 U.S.C. § 102(a)(1)). Patent Owner does not dispute this finding. Having considered the complete record developed at trial, we see no reason to change our conclusion that Lot # 11578 and Lot # 11581 qualify as prior art.

Petitioner points out that Altaire's Product contains R-phenylephrine hydrochloride and an aqueous buffer, as claim 1 requires. Pet. 38 (citing Ex. 1018, 1). The package insert directs the user to place one drop of the solution in each eye for pupil dilation, also as claim 1 requires. *Id.* at 37 (citing Ex. 1018, 1), 39 (citing Ex. 1018, 2). Furthermore, the package insert instructs that the Altaire's Product should be stored at 2–8 degree Celsius,

within the temperature range recited in claim 1. *Id.* at 40 (citing Ex. 1018, 2). Patent Owner does not dispute Petitioner's assertions regarding these limitations. Based on the full record developed at trial, we are persuaded that Altaire's Product meets these limitations of claim 1.

With regard to the chiral-purity limitations of claim 1, Petitioner refers to Exhibits 1012, 1016, and 1019.[4] *Id.* at 35–39. Exhibits 1016 and 1019 refer to data from certain High Performance Liquid Chromatography (HPLC) experiments. Exhibit 1012 refers to certain optical rotation data obtained using an optical polarimeter.

HPLC Data (Exhibits 1016 and 1019)

Petitioner argues that, in Exhibit 1016, the HPLC data showed no S-form of phenylephrine was detected in either Lot # 11578 or Lot # 11581 after storage under room temperature for 37 months. Pet. 35–37. Petitioner also asserts that, in Exhibit 1019, the HPLC data showed no S-form of phenylephrine was detected in Lot # 11581 after cold storage for over six months. *Id.* at 37, 39. According to Petitioner, because the chiral purity of R-phenylephrine hydrochloride remained undiminished after over six months of storage under either cold or room temperature, the initial chiral purity must have been essentially 100%. *Id.* at 35–39. Thus, Petitioner concludes that Altaire's Product meets the limitations of claim 1, requiring

[4] Petitioner also refers to Exhibit 1017. *See* Pet. 24–26, 36. The results shown in that exhibit, however, are from a "fresh preparation of" sample, and not Lot # 11578 or Lot # 11581. Thus, we do not consider the data in Exhibit 1017 in rendering this Decision.

"an initial chiral purity of at least 95%" and the chiral purity to be "at least 95% of the initial chiral purity after 6 months." *Id.*

In its Response, Patent Owner maintains that the USP standard HPLC does not reliably detect chiral impurity.[5] PO Resp. 38–42. According to Patent Owner, because the USP standard HPLC method is incapable of separating R- and S- form of phenylephrine, Petitioner cannot use the method to show that Altaire's Product meets the chiral-purity limitations of the challenged claims. *Id.* at 42–43.

In its Reply, Petitioner does not address the USP standard HPLC method. Rather, it asserts that, instead of the "*publicly* available" USP standard HPLC method, Petitioner "relies on its proprietary HPLC procedure <TMQC-247> (ref.:Validation Report STU0346)." Reply 8. According to Petitioner, "Patent Owner did not conduct its own testing to show that Petitioner's products do *not* meet the limitations of the challenged claims." Reply 9. Petitioner argues that "because Patent Owner failed to provide affirmative test results to the contrary, it is more likely than not that Petitioner's HPLC testing data is reliable and accurate." *Id.* at 9–10. Petitioner is mistaken.

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[5] On this issue, at the institution stage, we were not persuaded by the record available then, wherein Patent Owner relied upon a declaration submitted during the prosecution ("the Witham Declaration"). Dec. 12. During trial, Patent Owner provides additional evidence to support its position. *See* Exs. 2021, 2040.

In a post-grant review, as in an *inter partes* review, the burden of persuasion is on the petitioner to prove unpatentability, and that burden never shifts to the patentee. *See* 35 U.S.C. § 326(e); *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). In addition, "[w]here, as here, the only question presented is whether due consideration of the four *Graham* factors renders a claim or claims obvious, no burden [of production] shifts from the patent challenger to the patentee." *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1376 (Fed. Cir. 2016).

Further, while we may institute a post-grant review if the petition demonstrates it is "more likely than not" that at least one challenged claim is unpatentable (*see* 35 U.S.C. § 324(a)), the petitioner must prove unpatentability by a preponderance of the evidence (*see* 35 U.S.C. § 326(e)). Thus, in this proceeding, our only inquiry is whether Petitioner has met its burden of proving obviousness by a preponderance of the evidence. And we conclude Petitioner has not done so.

Petitioner contends that, in the Decision to Institute, we "relied on Patent Owner's representations that Petitioner used the HPLC method published by the USP Guidelines." Reply 8 n.3. In fact, however, we also relied on Petition's representation that "Altaire's HPLC method for chiral purity testing was validated pursuant to established United States Pharmacopeia guidelines (USP <1225> Validation of Compendial Procedures)." *See* Pet. 36 n.10. Petitioner argues that, notwithstanding footnote 10 in the Petition, the only HPLC methodology referred to therein is TMQC-247, Petitioner's proprietary method. Tr. 10:23–11:13; *see also*

Reply 9 (arguing that the Validation of Compendial Procedures monograph "does not set forth a method of conducting HPLC testing, nor does it require a method to follow the USP published HPLC method to obtain validation"). According to Petitioner, Mr. Sawaya's declaration confirmed the usage of the proprietary methodology. Tr. 11:21–23; Reply 8. We are not persuaded.

The Petition refers to Altaire's allegedly proprietary HPLC method TMQC-247 three times, none of which addresses the chiral purity of Altaire's Product. *See* Pet. 20, 49–50, 61. Indeed, according to the Petition, "Altaire performed Chiral HPLC studies using its proprietary and validated HPLC procedure <TMQC-247> (ref.: Validation Report STU0346) to determine the impact of storage at room temperature upon" the "Akorn product." *Id.* at 20. In addition, "Altaire tested five lots of the API manufactured by Syn-Tech – more than one year prior to the '623 patent's filing date – using Altaire's HPLC method (Altaire test method TMQC-247)." *Id.* at 49–50; *see also id.* at 61 (the same). Mr. Sawaya's testimony on this issue is substantially the same as these two statements. *See* Ex. 1003 ¶¶ 21, 47.

In contrast, when discussing the HPLC method to determine the chiral purity of Altaire's Product, Petitioner neither describes it as proprietary nor refers to it as TMQC-247. *See, e.g.,* Pet. 35 (stating "HPLC analysis of lot # 11578 for chiral purity"), 36 (stating a freshly prepared lot was "analyzed by HPLC for chiral purity"). Thus, we cannot verify, based on the Petition and the accompanying evidence, that the HPLC data of Altaire's Product

Petitioner relies on were generated using its allegedly proprietary HPLC method TMQC-247, and not the USP standard HPLC method.

Moreover, even if we accept Petitioner's assertion that it generated the data using its allegedly proprietary HPLC method TMQC-247, we still would not be persuaded to rule in Petitioner's favor. This is because, as Patent Owner correctly points out, the tests and data submitted with the Petition do not meet the requirements of 37 C.F.R. § 42.65. *See* PO Resp. 31–38.

Our Rule requires that:

> If a party relies on a technical test or data from such a test, the party must provide an affidavit explaining:
> (1) Why the test or data is being used;
> (2) How the test was performed and the data was generated;
> (3) How the data is used to determine a value;
> (4) How the test is regarded in the relevant art; and
> (5) Any other information necessary for the Board to evaluate the test and data.

37 C.F.R. § 42.65(b). Here, Petitioner relies on the HPLC data to show that Altaire's Product meets the chiral-purity limitations of claim 1. The Sawaya Declaration (Ex. 1003)—the only declaration submitted with the Petition—however, fails to explain, among others, how the test was performed and how the data was generated.

During the hearing, Petitioner argued that Exhibit 1020 provides all necessary HPLC information. Tr. 12:3–10. Exhibit 1020 shows the detection of S- and R- isomers in the drug substance used in manufacturing Altaire's Product, i.e., the active ingredient from Syn-Tech. Pet. 50; Tr. 8:3–

14. The note of the exhibit reads: "S(+)-isomer concentration was determined by HPLC using a Chiralpak 4.6x250mm, 5µm column at 270nm as per Altaire test method TMQC-247." Ex. 1020. According to Petitioner, this note shows that "all of the information that was necessary for the HPLC methodology to be run or to be tested against was provided within the petition." Tr. 12:8–10. We are not persuaded.

Dr. Gojko Lalic, the expert witness for Patent Owner, testifies that in an HPLC test, "[t]he elution profile for a given sample is dependent on experimental conditions," such as the "solid packing material in the column, mobile phase (solvent), flow rate, and temperature." Ex. 2016 ¶ 26. Petitioner's own documents (Exs. 1027, 1028)[6] appear to confirm Dr. Lalic's testimony. Indeed, the protocol for TMQC-247 is ten pages long, in contrast to the one-sentence note in Exhibit 1020. The protocol provides information about the standards and samples preparation as well as the procedures for running the test. For chromatographic parameters, the protocol lists not only the column and wavelength as shown in Exhibit 1020, but also includes the flow rate, column temperature, injection volume, and run time. Petitioner, however, did not submit the protocol until filing its Reply, when Patent Owner no longer has an opportunity to respond. Tr. 11:14–20. As a result, we do not consider Exhibits 1027 and 1028. *See* 77 Fed. Reg. 48612, 48620

[6] We previously granted Petitioner's Motion to seal Exhibits 1027 and 1028 in their entirety. *See* Paper 46. In rendering this Decision, although we refer to the sealed exhibits, we do not rely on the substantive information therein.

(Aug. 14, 2012) ("Reply evidence . . . must be responsive and not merely new evidence that could have been presented earlier.").

Petitioner asserts that Patent Owner has waived its challenge of Petitioner's evidence, including the HPLC data supporting the Petition, because Patent Owner failed to timely object pursuant to 37 C.F.R. § 42.64(b)(1). Reply 4–5. According to Petitioner, had Patent Owner followed the rules, "Petitioner could have, if deemed necessary, served supplemental evidence or sought leave to file supplemental information to address Patent Owner's concerns." *Id.* at 5. We are not persuaded.

First, Patent Owner's contention regarding Petitioner's HPLC data is directed to the sufficiency of the evidence, rather than its admissibility.[7] As a result, the time limit provided for evidentiary objections in § 42.64(b)(1) does not apply. Second, as Petitioner recognizes, it could have sought leave to file supplemental information after we instituted trial. Filing supplemental information, however, does not depend on any objection from Patent Owner. *See* 37 C.F.R. § 42.123. Thus, we conclude that Patent Owner has not waived its challenge of the sufficiency of Petitioner's evidence, including the HPLC data.

[7] Patent Owner also asserts that Mr. Sawaya lacks personal knowledge in testifying on the HPLC and polarimetry tests that Petitioner relies on. PO Resp. 30–31. To the extent these arguments relate to the admissibility of Petitioner's evidence, we do not consider Patent Owner's assertions in rendering this Decision.

Petitioner also argues that Patent Owner is, and has been, in possession of the details of Petitioner's test method TMQC-247. Reply 5. That might well be so; yet, it does not relieve Petitioner from meeting the requirements of § 42.65(b). After all, it is the Board, and not Patent Owner, who must evaluate the patentability of the challenged claims. In this post-grant review, an adversarial proceeding, while each party should conduct itself in a civil manner, Patent Owner has no duty to first bring to our attention, and then thoroughly address, evidence to support Petitioner's case. Without the necessary information prescribed in § 42.65(b), we cannot determine whether the evidence Petitioner relies on is credible.

In short, regarding the HPLC data, Petitioner does not point to any credible evidence accompanying the Petition that meets the requirements of § 42.65(b). Thus, even if we accept Petitioner's assertion that the HPLC data of Altaire's Product were generated using its allegedly proprietary HPLC method TMQC-247, we give no weight to those data.

Optical-Rotation Data (Exhibit 1012)

Petitioner further relies on Exhibit 1012, which reports the optical-rotation data from an identification test by polarimetry. Ex. 1012, 3. Exhibit 1012 uses "Phenylephrine Hydrochloride R (-) Sigma Aldrich lot P6126" as the control to determine if the phenylephrine hydrochloride in Altaire's product is in R- or S- form. *Id.* Exhibit 1012 shows the specific rotation of Lot # 11578 is 101.5% of the control. *Id.* at 8–9. In other words, the chiral purity of Altaire's product Lot # 11578 was over 100%. Pet. 10. Because the chiral purity of Lot # 11578 after cold storage for over six months was

essentially 100% of R-phenylephrine, Petitioner contends, the initial chirality of the product would have been essentially 100%. *Id.* at 36–39.

Patent Owner counters that because of their variability, "optical rotation measurements are considered unsatisfactory as a tool for determining chiral purity." PO Resp. 37 (citing Ex. 2016 ¶¶ 44, 45; Ex. 2022, 1073). According to Patent Owner, the optical-rotation method merely determines the purity of a test sample as relative to a control. *Id.* at 44 (citing Ex. 2016 ¶ 42). Thus, Patent Owner argues, the optical-rotation study Petitioner relies on is "of no value because, rather than quantitating chiral purity, it merely compares the Lot #11578 sample to a control sample of unknown chiral purity." *Id.* at 43 (citing Ex. 2016 ¶¶ 42, 43, 46, 47). We find Patent Owner's argument more persuasive.

First, as Patent Owner points out, the control sample used in Exhibit 1012 does not appear to be analytical grade. *See* PO Resp. 45. Indeed, while Sigma Aldrich provides certain R-phenylephrine hydrochloride as "analytical standard," Sigma-Aldrich P6126, the control sample Petitioner used, is merely labeled as "powder." Ex. 2037, 1.

Second, in Exhibit 1012, the control sample was assigned a purity factor of 1.00. Ex. 1012, 3. Petitioner does not, however, explain how the chiral purity of the control was determined. Instead, Petitioner points to the catalog page of Sigma-Aldrich P6126, evidence submitted by Patent Owner, which states that the purity is ≥99%. Reply 10 (citing Ex. 2019). We agree with Petitioner that there is no reason to doubt this representation by Sigma-Aldrich. *See id.* at 11. The same catalog page, however, qualifies this

representation as made "at the time of the quality release or subsequent retest date." Ex. 2019. It further suggests that the recommended retest period is three years. *Id.* Petitioner does not point to any credible evidence to show the lot number of the phenylephrine hydrochloride P6126 it used as control, when the lot was manufactured, or how long after the manufacturing date Petitioner used it as the control. Indeed, for the optical-rotation data, as for the HPLC data, Petitioner has not provided any affidavit in compliance with 37 C.F.R. § 42.65(b). Thus, while P6126 was ≥99% pure R-phenylephrine hydrochloride at the time Sigma-Aldrich tested it, Petitioner has not sufficiently shown that the chiral purity remained the same at the time it was used as the control in the polarimetry test of Exhibit 1012.

We acknowledge that Exhibit 1012 shows the specific rotation of 25 mg/mL control solution is -46.3º. Ex. 1012, 6. According to Petitioner, a specific rotation within the -42º to -47.5º range indicates that the phenylephrine hydrochloride tested is in the R-form. *Id.* at 3. We also acknowledge that the USP Monograph reports the same range for a sample of 50 mg/mL of R-phenylephrine hydrochloride. Ex. 2020, 1. Nonetheless, Patent Owner has presented sufficient evidence to challenge the accuracy of estimating enantiomer purity based on the specific rotation. For example, it is recognized that:

> Values of [specific rotation] are affected by many variables, among which are wavelength, solvent, concentration, temperature, and presence of soluble impurities.
>
> * * *

> The cumulative effect of the above-mentioned variables on [the specific-rotation value] is potentially very large. A practical consequence is that precise reproduction of published rotation values, from laboratory to laboratory, or even from day to day in the same laboratory, is difficult to achieve.

Ex. 2022, 1073.

Lastly, the specific rotation of Altaire's Product is over 100% of the control. Ex. 1012, 8. This further casts doubt into either the purity of the control, or the accuracy of the optical-rotation methodology. In sum, we are not persuaded that Petitioner's optical-rotation data amount to a preponderance of the evidence to show that Altaire's Product meets the chiral-purity limitations of the challenged claims.

Real Party in Interest

Patent Owner urges that we dismiss the Petition because Petitioner fails to identify additional real parties in interest with respect to the Petition. PO Resp. 14–28. Because we determine that Petitioner has not shown, by a preponderance of the evidence, the unpatentability of the challenged claims, we need not reach the real-party-in-interest issue.

CONCLUSION

After considering the complete record developed at trial, we determine that Petitioner has not shown in this proceeding, by a preponderance of the evidence, that claims 1–13 of the '623 patent would have been obvious over Altaire's Product.

ORDER

Accordingly, it is

ORDERED that claims 1–13 of the ’623 patent have not been shown to be unpatentable;

FURTHER ORDERED that, because this is a final written decision, parties to this proceeding seeking judicial review of our Decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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