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Paper 21
Date: June 10, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

THORNE RESEARCH, INC.,
Petitioner,

v.

TRUSTEES OF DARTMOUTH COLLEGE,
Patent Owner.

IPR2021-00268
Patent 8,383,086 B2

Before SUSAN L. C. MITCHELL, ROBERT A. POLLOCK, and JOHN E. SCHNEIDER, *Administrative Patent Judges.*

SCHNEIDER, *Administrative Patent Judge*.

DECISION
Granting Institution of *Inter Partes* Review
35 U.S.C. § 314

I. INTRODUCTION

A. Background and Summary

Thorne Research, Inc. ("Petitioner") filed a Petition requesting *inter partes* review of claim 2 of U.S. Patent No. 8,383,086 B2 (Ex. 1001, "the '086 patent"). Paper 2 ("Pet."). The Trustees of Dartmouth College ("Patent Owner") filed a Preliminary Response contending that the Petition should be denied. Paper 10 ("Prelim. Resp."). During a telephone conference held on March 23, 2021, the panel authorized additional briefing regarding the issue of whether certain references were the works "by another" as the term is used in 35 U.S.C. § 102(a).[1] Ex. 1024, 23–24. In accordance with such authorization, on April 30, 2021, Petitioner filed a Reply to Patent Owner's Preliminary Response. Paper 15 ("Pet. Reply"). On May 7, 2021, Patent Owner filed an authorized Sur-Reply. Paper 16 ("Sur-Reply").

B. Real Parties- in-Interest

Throne Research, Inc. identifies itself as the real party-in-interest. Pet. 33. The Trustees of Dartmouth College identify themselves as the real parties-in-interest. Paper 5, 2.

C. Related Matters

Petitioner represents that a petition for *inter partes* review was filed challenging claims 1–5 of the '086 patent in IPR2017-01795 ("the '1795 IPR"). Pet. 33. We issued a final decision holding that all claims were

[1] 35 U.S.C. § 112 was amended by the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284, 287–88 (2011). Because the '086 patent was filed before the effective date of the relevant amendment, the pre-AIA version of §§ 102, 103, and 112 applies.

unpatentable except claim 2. Ex. 1018. That decision was affirmed by the Federal Circuit on March 6, 2020. Ex. 1004.

Petitioner also represents that a petition for *inter partes* review was filed by a third party challenging related patent U.S. Patent No. 8,197,807 in IPR2017-01796. Pet. 34. We denied institution of *inter partes* review of the petition in IPR2017-01796. *Elysium Health, Inc. v. Trustees of Dartmouth College*, IPR2017-01796, Paper 9 (PTAB Jan. 18, 2018).

Patent Owner states that the ’086 patent is the subject of an infringement action in the United States District Court for the District of Delaware in a case captioned *ChromaDex, Inc., et al. v. Elysium Health, Inc.*, Case No. 18-cv-01434 (D. Del.). Paper 5, 3. Patent Owner also states that the ‘086 patent is also subject to a patent misuse counterclaim in *ChromaDex, Inc. v. Elysium Health, Inc.*, Case No. 16-cv-02277-CJC (C.D. Cal.). *Id.* Patent Owner has also recently indicated that it has filed an action against Petitioner for infringement of the ’086 patent and the ’807 patent in *ChromaDex, Inc., et al. v. Thorne Research, Inc*., Case No. 1:21-cv-04241 (S.D.N.Y.). (Paper 19)

D. The ‘086 Patent

The ‘086 patent issued on February 26, 2013 with Charles M. Brenner listed as the inventor. Ex. 1001, codes (45), (75). The ’086 patent issued from an application filed on April 12, 2012 and on its face, claims priority to an application filed April 20, 2006. *Id.* at code (63). As discussed in Section II.D, below, the parties disagree as to whether the ’086 patent is entitled to an earlier priority date of April 25, 2005.

The ’086 Patent relates generally to the production of nicotinamide riboside (“NR”) and compositions containing NR. Ex. 1001, col. 4, ll. 1–16. The ’086 patent also describes the use of compositions containing an

effective amount of NR to treat various disorders stemming from a deficiency in NR. *Id.* at col. 4, ll. 17–29. The compositions can be in the form of a dietary supplement, such as ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, chewing gums, and food. *Id.* at col. 4, ll. 14–16, col. 29, ll. 43–46.

E. Illustrative Claims

Claim 2 is the only challenged claim before us. Claim 2 depends from claim 1 and therefore incorporates all of the limitations of claim 1. 35 U.S.C. § 112 ¶ 4 (2006). Claims 1 and 2 are reproduced below.

> 1. A pharmaceutical composition comprising nicotinamide riboside in admixture with a carrier, wherein said composition is formulated for oral administration.
> 2. The pharmaceutical composition of claim 1, wherein the nicotinamide riboside is isolated from a natural or synthetic source.

Ex. 1001, col. 53, ll. 38–43.

F. Evidence

Petitioner relies on the following references:

Stamler et al., WO 02/055018 A2, published July 18, 2002. ("Stamler") (Ex. 1006).

Brenner, et al., WO 2005/077091 A2, published August 25, 2005. ("Brenner") (Ex. 1007).

Bieganowski et al., *Discoveries of Nicotinamide Riboside as a Nutrient and Conserved NRK Genes Establish a Preiss-Handler Independent Route to NAD$^+$ in Fungi and Humans*, 117 Cell 495 (May 14, 2005) ("Bieganowski") (Ex. 1008).

Petitioner also relies on the Declaration of Dr. Samie Jaffery, M.D., Ph.D. (Ex. 1002).

G. Asserted Grounds

Petitioner asserts that claim 2 would have been unpatentable on the following grounds:

Claim(s) Challenged	35 U.S.C. §	Reference(s)/Basis
2	102(b)	Stamler
2	103	Stamler
2	102(b)	Bieganowski
2	103	Bieganowski
2	102(b)	Brenner

H. The Prior Proceeding

As noted above, the '086 patent was the subject of a prior IPR proceeding, the '1795 IPR, initiated by Petitioner Elysium Health, Inc. on July 17, 2017. Elysium requested review of original claims 1–5 of the '086 patent on grounds that: (1) claims 1–5 were anticipated under 35 U.S.C. § 102(b) by Goldberger et al., *A Study of the Blacktongue-Preventive Action of 16 Foodstuffs, with Special Reference to the Identity of Blacktongue of Dogs and Pellagra of Man*, 43 Pub. Health Reports 1385 (1928) (Ex. 1011, "Goldberger"); and (2) claims 1–5 were anticipated under § 102(b) by Goldberger and Tanner, *A Study of the Treatment and Prevention of Pellagra*, 39 Pub. Health Reports 87 (1924) (Ex. 1012, "Goldberger and Tanner"). *See* Ex. 1018, 5. We granted Elysium's petition on January 29, 2018. *Id.* at 2.

In our Final Written Decision, we concluded that Elysium had demonstrated by a preponderance of the evidence that claims 1 and 3–5 were unpatentable as anticipated by both Goldberger and Goldberger and Tanner. *Id.* at 42. We also concluded that Elysium had not demonstrated that claim 2 was unpatentable. *Id.* Central to our holding with respect to claim 2 was our finding that Elysium had not demonstrated that the compositions disclosed

in Goldberger and Goldberger and Tanner comprised "isolated" NR, as we construed that claim term. *Id.* at 12–14, 26–27; *see also id.* at 12–15 (construing "isolated" to mean "that the nicotinamide riboside is separated or substantially free from at least some of the other components associated with the source of the molecule such that it constitutes at least 25% (w/w) of the composition").

II. ANALYSIS

A. Discretion Under 35 U.S.C. § 314(a) and 325(d)

Patent Owner argues that we should exercise our discretion under 35 U.S.C. § 314(a) or 325(d) and deny the petition. Prelim. Resp. 50. In support of this argument, Patent Owner points to the weakness of Petitioner's arguments, the prior challenge to the '086 patent, and the pending litigation involving the '086 patent. *Id.* at 51–59.

Petitioner argues that we should not exercise our discretion under Section 314(a) or 325(d). Pet. 17, 23. Applying the factors set forth in *Gen. Plastic Indus. Co. v. Canon Kabushiki Kaisha*, IPR2016-01357, Paper 19 at 9–10 (PTAB Sept. 6, 2017) ("*General Plastic*") (precedential), Petitioner contends that the balance of factors weighs in favor of not using our discretion to deny the petition. *Id.* at 24–25. Petitioner also argues that under the test set forth in *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (PTAB Feb. 13, 2020) (precedential), we should not exercise our discretion to deny the petition under 35 U.S.C. § 325(d).

We have considered the arguments presented by the parties and the evidence of record and decline to exercise our discretion to deny the petition under 35 U.S.C. § 314(a) or 325(d).

In deciding whether to institute, we take into account various considerations. *See* Patent Trial and Appeal Board Consolidated Trial Practice Guide November 2019 ("TPG") at 55–63. We also consider a two-part framework under 35 U.S.C. § 325(d), which first looks at "whether the same or substantially the same art previously was presented to the Office or whether the same or substantially the same arguments previously were presented to the Office," and second, if either of those conditions is met, considers "whether the petitioner has demonstrated that the office erred in a manner material to the patentability of challenged claims." *Advanced Bionics*, IPR2019-01469, Paper 6 at 8. This analysis applies to situations where similar art or arguments were before the Office during a previous IPR. *See id.* at 10. For the first part of the test, the Board may consider non-exclusive *Becton, Dickinson* factors regarding "the similarities" between and "cumulative nature of" the asserted art and the previously-presented prior art, and "the extent of the overlap between the arguments made [previously] and the manner in which petitioner relies on the prior art [or patent owner distinguishes the prior art]." *See id.* at 9–10 (citing *Becton, Dickinson & Co. v. B. Braun Melsungen AG*, IPR2017-01586, Paper 8 at 17–18 (PTAB Dec. 15, 2017) ("*Becton Dickinson*") (precedential in relevant part)).

In deciding whether "efficiency, fairness, and the merits support the exercise of authority to deny institution in view of an earlier trial date in [a] parallel proceeding," the Board's "holistic view" may include consideration of the *Fintiv* factors. *Apple, Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 at 5–6 (PTAB Mar. 20, 2020) (precedential). These *Fintiv* factors include "whether the court granted a stay or evidence exists that one maybe granted if a proceeding is instituted," "proximity of the court's trial date to the Board's projected statutory deadline for a final written decision,"

"investment in the parallel proceeding by the court and the parties," "overlap between issues raised in the petition and in the parallel proceeding," and "other circumstances that impact the Board's exercise of discretion, including the merits." *Id.*

Patent Owner contends that we should deny the present petition on several grounds including the fact that the '086 patent was the subject of the '1795 IPR, the same art and arguments were previously before the Office, the pendency of litigation challenging the validity of the '086 patent, and the weakness of Petitioner's unpatentability arguments. Prelim. Resp. 55. We address each of these arguments in turn.

1. The '1795 IPR

As discussed above, the '086 patent was the subject of the '1795 IPR proceeding. In that case, all of the challenged claims were held unpatentable except claim 2, the sole claim challenged in the present petition.

We begin by noting that the present petition relies on three references, which were not cited in the '1795 IPR. *Compare* Pet. 34–35, *with* Ex. 1018, 5.

We also find that the references are not cumulative of the art cited in the '1795 IPR proceeding. For example, as discussed more fully below, we find that Stamler's disclosure of commercially available NR shows that one skilled in the art would have recognized that isolated NR was known at the time the present invention was made. This teaching was missing from the art considered in the '1795 IPR.

Thus, under the first part of the *Advanced Bionics* framework, we find that the same or substantially the same art or arguments were not previously presented during the '1795 IPR, which weighs against exercising our discretion to deny institution under 35 U.S.C. § 325(d). Because we do not

find that the same or substantially the same prior art previously was presented to the Office with respect to the '1795 IPR, we need not reach the second part of the *Advanced Bionics* framework. *Advanced Bionics* at 8.

2. Art and Arguments Previously Presented to the Office during Prosecution

Patent Owner also contends that Beiganowski was submitted to the Office in an IDS during prosecution and marked as considered by the Examiner, thereby satisfying the first part of the *Advanced Bionics* framework. Prelim. Resp. 57–58. Even though Beiganowksi was cited, , the other two references in the Petition, Stamler and Brenner[2], were not before the Examiner during prosecution. *See* Ex. 1001, code (56). As such, we determine that the combination of prior art references presented in the Petition are not the same or substantially the same as those presented during prosecution. Because we do not find that the same or substantially the same prior art previously was presented to the Office with respect to the prosecution history, we need not reach the second part of the *Advanced Bionics* framework. *Advanced Bionics* at 8. We decline to exercise our discretion to deny institution under 35 U.S.C. § 325(d).

3. Pending Litigation

Patent Owner contends that the pending litigation involving the 086 patent weighs in favor of exercising our discretion to deny the petition. Prelim. Resp. 58–59. Patent Owner contends that the pending case will be

[2] Patent Owner contends that Brenner and Beiganowski are not prior art as they are not the work of another under 35 U.S.C. § 102 (a) or (e). Prelim. Resp. 8. As discussed more fully below, based on the preliminary record before us, we do not agree with Patent Owner's assertion.

decided well before we issue a final decision in this matter and that a stay is unlikely. *Id.* Patent Owner contends that it would be inefficient for this proceeding to proceed, given the fact that the district court will address similar art and challenges well before we issue a decision in this case. *Id.*

We are unpersauded by Patent Owner's argument. While we note the two of the *Finitiv* factors weigh in favor of denying the petition, the remaining factors do not. AS Patent Owner points out the '086 patent is the subject of litigation currently scheduled for trial in September of 2021 and that no stay has been granted in that matter. PO Resp. 58–59. These factors weigh in favor of denying the petition.

With respect to the third factor, Patent Owner has not presented any evidence regarding the investment in the parallel proceeding by the parties and the court. *See Id.* Absent such record evidence, this factor does not weigh in favor of denial.

Patent Owner has not alleged nor has it advanced any evidence that the same or similar evidence regarding isolated NR has been advanced in the district court proceeding. Absent such evidence we cannot say that there is overlap between the issue raised in the parallel proceeding and those raised in the petition.

In addition, the present IPR is limited to a single claim and the issue of whether the references disclose the use of isolated NR. Given the narrow scope of issues before us and the fact that the current references do not appear to be before the district court, we find that the fourth and fifth *Finitiv* factors do not weigh in favor of exercising our discretion.

4. Relative Weakness of Petitioner's Arguments

Patent Owner contends that the weakness of Petitioner's arguments concerning unpatentability of claim 2 weigh in favor of denying the petition.

Prelim. Resp. 59. Patent Owner contends that the Brenner and Bieganowski references are not prior art and that Stamler does not teach all of the elements of the claims, let alone whether NR is isolated. *Id.* Patent Owner contends that Petitioner's unsupported reliance on collateral estoppel demonstrates the weakness of its case. *Id.*

Again, we find Patent Owner's arguments unpersuasive. As discussed below, we find that with respect to Grounds based on Stamler, Petitioner has demonstrated a reasonable likelihood of showing that claim 2 is unpatentable. Moreover, we are not convinced at this stage that Brenner and Bieganowski are not prior art against the '086 patent. In addition, contrary to Patent Owner's arguments, we conclude that estoppel does apply with respect to certain issues.

5. Conclusion

Based on the foregoing we decline to deny the Petition on the basis of discretion under either 35 U.S.C. § 314(a) or 325(d).

B. Collateral Estoppel

Petitioner contends that Patent Owner is collaterally estopped from relying on the limitations of claim 1 to support the patentability of claim 2 based on the Board's determination that claim 1 was unpatentable in the earlier '1795 IPR. Pet. 2. Petitioner cites to *MaxLinear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1377 (Fed. Cir. 2018) to support this contention. *Id.*

Patent Owner contends that Petitioner's collateral estoppel argument is unsupported in that Petitioner failed to make the requisite showing for collateral estoppel to apply, citing *United Access Techs., LLC v. CenturyTel Broadband Servs. LLC*, 778 F.3d 1327, 1331 (Fed. Cir. 2015). Prelim. Resp.

31–32. Patent Owner also contends that the Federal Circuit's holding is not as limiting as asserted by Petitioner. *Id.* at 33.

We have considered the arguments presented by the parties and find that Petitioner has the better positon.

As Patent Owner points out, the application of collateral estoppel requires that (1) the previous determination was necessary to the decision; (2) the identical issue was previously litigated; (3) the issue was actually decided in a decision that was final, valid, and on the merits; and (4) the party being precluded from relitigating the issue was adequately represented in the previous action. *United Access Techs.*, 778 F.3d at 1331. Each of these factors is present in the instant case.

In the '1795 IPR, we determined that claim 1 was anticipated by both Goldberger and Goldberger and Tanner. Ex. 1018, 42. An essential part of that decision was that all of the elements of claim 1 were found in the references. Ex. 1018, 16–25, 32–37. Thus the finding that the elements of claim 1 were in the prior art was an essential part of the ruling, and the same issue is present in the instant case.

As Petitioner points out, Patent Owner first appealed the decision in the '1795 IPR, but then withdrew that appeal, rendering our decision final, valid, and on the merits. Pet. 2 (citing Exs. 1021, 1022).

Finally, Patent Owner was represented by the same counsel as in this proceeding and has not argued or suggested that it was not adequately represented in the '1795 IPR. *See* Prelim. Resp. 31–34.

Patent Owner contends that the issue in the present case is different from the '1795 IPR as different references have been asserted in this proceeding. *See* Prelim. Resp. 32–33. Patent Owner contends that Petitioner must show that the new references teach or disclose each of the elements of

claim 1 as well as the limitation of claim 2. *Id.* We are not persuaded by Patent Owner's argument.

We find that our reviewing court's decision in *MaxLinear* is controlling in this case. In *MaxLinear* the issue before the court was what effect collateral estoppel had on a determination of the validity of dependent claims where the independent claims had been found unpatentable in a prior IPR. *MaxLinear,* 880 F.3d at 1377. As in the present proceeding, the finding of unpatentability in the prior IPR was based on a different set of references than those asserted in the case on appeal. Our reviewing court held collateral estoppel precluded relitigation of the patentability of the independent claims. *Id.* In remanding the case for consideration of the patentability of the dependent claims, the court directed the board to decide whether the remaining claims "present materially different issues that alter the question of patentability, making them patentably distinct from [the independent claims]." *Id.* at 1377–78.

Applying *MaxLinear* to the present case, we find our review of claim 2 is limited to the issue of whether claim 2 presents a materially different issue regarding patentability from the unpatentable claim 1, from which it depends. As we found in the '1795 IPR, the sole distinction between these two claims is the requirement that the NR be isolated. Thus our review is limited to that issue.

C. Legal Standards

1. Burden of Proof

At this stage of the proceeding, the burden rests on the petitioner to establish a reasonable likelihood that it will prevail in showing that at least one of the challenged claims is unpatentable. 35 U.S.C. § 314(a) (2018).

2. Anticipation[3]

"Under 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim." *Gechter v. Davidson*, 116 F.3d 1454, 1457 (Fed. Cir. 1997). "[U]nless a prior art reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102." *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1371 (Fed. Cir. 2008).

3. Obviousness

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) where in evidence, so-called secondary considerations. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). 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, the claim is unpatentable under 35 U.S.C. § 103(a). *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 406 (2007).

A proper § 103 analysis requires "a searching comparison of the claimed invention—including all its limitations—with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995).

[3] As noted above, the pre-AIA provisions of 35 U.S.C. apply to the '086 patent.

"Obviousness requires more than a mere showing that the prior art includes separate references covering each separate limitation in a claim under examination." *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011). "Rather, obviousness requires the additional showing that a person of ordinary skill at the time of the invention would have selected and combined those prior art elements in the normal course of research and development to yield the claimed invention with a reasonable expectation of success." *Id.*

D. Effective Filing Date of the '086 Patent

Petitioner contends that the '086 patent is entitled to a priority date of April 20, 2006, the filing date of U.S. Application No. 11/912,400. ("the '400 application"). Pet. 6. Petitioner contends that operation of both the Paris Convention and the Patent Cooperation Treaty ("PCT") precludes any claim of priority earlier than that date because the priority chain of the '086 patent includes two PCT applications. *Id.* at 7–14.

Patent Owner contends that the recited provisions of the Paris Convention and PCT are not applicable to the '086 patent as the claim of priority arises under 35 U.S.C. § 120 and not 35 U.S.C. § 119. Prelim. Resp. 17–20. Patent Owner contends that the '086 patent meets the requirements of 35 U.S.C. § 120. *Id.* at 22–24. Patent Owner contends that the priority date of the '086 patent is April 25, 2005 which is the filing date of U.S. Application No. 11/113,701. ("the '701 application"). *Id.* at 25.

We have considered the arguments presented by the parties and the evidence of record and conclude, at this stage, that Patent Owner has the better argument.

As Patent Owner points out, the relevant portions of the Paris Convention and the PCT are found in 35 U.S.C. § 119. Prelim Resp. 17.

Section 119 relates to claims to foreign priority and is not applicable to the instant case. *See* 35 U.S.C. § 119(a), (c) (2018); *Return Mail, Inc. v. U.S. Postal Serv.*, 139 S. Ct. 1853, 1864 n.5 (2019).

The '086 patent claims priority to domestic applications involving either US patent applications or a PCT application designating the United States. *See* Ex. 1001, col. 1, ll. 7–13.

> Under § 120, a patent is entitled to the priority date of an earlier filed application if (1) the written description of the earlier filed application discloses the invention claimed in the later filed application sufficient to satisfy the requirements of § 112; (2) the applications have at least one common inventor; (3) the later application is filed before the issuance or abandonment of the earlier filed application; and (4) the later application contains a reference to the earlier filed application.

In re NTP, Inc., 654 F.3d 1268, 1277 (Fed. Cir. 2011); *see also* 35 U.S.C. § 120 (2018). Patent Owner contends that the priority claim for the '086 patent meets these requirements. Prelim. Resp. 22. We agree based on the record before us.

On this record, we find that the relevant portions of the '086 patent that support claim 2 can be found in the '086 Specification, as well as the '400 application, the '495 PCT application, and the '701 application. *See* Exs. 1001, 2004, 2005, and 2006. The '086 patent and all three applications just mentioned list Dr. Brenner as the inventor. *Id.* There was co-pendency for applications. For instance, the '086 patent was filed on April 12, 2012, before the issuance of the '400 application as the '807 patent on June 12, 2012. *See* Ex. 1001, code (22); Ex. 2004, code (45). And the '400 application is a national stage entry of the '495 PCT, which was filed on April 20, 2006, before the abandonment of the '701 application on

December 28, 2006. *See* Ex. 2004, code (22), (86); Ex. 2005, code (22); Ex. 2006, 336–37. Finally, the '086 patent specifically identifies the earlier applications to which priority is claimed. Ex. 1001, col. 1, ll. 7–13.

Based on the foregoing, we conclude on this record that the '086 patent is entitled to a filing date of April 25, 2005.

E. Level of Ordinary Skill in the Art

The level of ordinary skill in the art is a factual determination that provides a primary guarantee of objectivity in an obviousness analysis. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 1324 (Fed. Cir. 1999) (citing *Graham v. John Deere Co*., 383 U.S. 1, 17–18 (1966); *Ryko Mfg. Co. v. Nu-Star, Inc.*, 950 F.2d 714, 718 (Fed. Cir. 1991)).

Petitioner contends that the definition of a person of ordinary skill in the art offered by Patent Owner in the '1795 IPR should apply to this proceeding, namely "someone with a Ph.D. in biochemistry or similar field in the pharmaceutical sciences, with familiarity and experience with pharmacokinetics." Pet. 33. At this stage of the proceeding, and without opposition from Patent Owner at this time, we determine that Petitioner's description of the level of ordinary skill in the art is supported by the current record. *See* Ex. 1002 ¶ 59. For purposes of this Decision, therefore, we adopt Petitioner's description.

We also note that the applied prior art reflects the appropriate level of skill at the time of the claimed invention and supports Petitioner's definition. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

F. Claim Construction

We interpret a claim "using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b)." 37 C.F.R. § 42.100(b) (2020). Under this standard, we construe the

claim "in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent." *Id.* Furthermore we need only construe the claims to the extent necessary to determine the patentability of the challenged claims. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017) ("[W]e need only construe terms 'that are in controversy, and only to the extent necessary to resolve the controversy . . . .'" (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc*., 200 F.3d 795, 803 (Fed. Cir. 1999))).

The parties have proposed constructions for three terms: "Pharmaceutical composition comprising nicotinamide riboside"; "carrier"; and "isolated." We address each of these terms in turn.

1. Pharmaceutical Composition

Both Petitioner and Patent Owner argue that we should adopt the same construction for this term as we did in the '1795 IPR. Pet. 35–36; Prelim. Resp. 28.[4] Absent any argument or evidence to the contrary, we apply the same construction in this proceeding that we applied in the '1795 IPR for the reasons set forth in that proceeding: "a composition, including a food composition, which contains NR as an active agent in an amount effective for the treatment or prevention of a disease or condition associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis." Ex. 1018, 10–11.

[4] In its discussion of each of the terms, Patent Owner also cited to the construction given to the terms by the district court. *See, e.g.*, Prelim Resp. 28. Patent Owner then states that, for this proceeding, it is applying the construction from the '1795 IPR. *Id.*

2. Carrier

Both Petitioner and Patent Owner argue that we should adopt the same construction for this term as we did in the '1795 IPR. Pet. 36; Prelim. Resp. 29. Absent any argument or evidence to the contrary, we apply the same construction in this proceeding that we applied in the '1795 IPR for the reasons set forth in that proceeding: "[A] liquid or solid filler, diluent, excipient, or solvent encapsulating material, [that] is involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be acceptable in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient." Ex. 1018, 14–15.

3. Isolated

Both Petitioner and Patent Owner argue that we should adopt the same construction for this term as we did in the '1795 IPR. Pet. 36–38; Prelim. Resp. 30–31. Absent any argument or evidence to the contrary, we apply the same construction in this proceeding that we applied in the '1795 IPR for the reasons set forth in that proceeding: "the nicotinamide riboside is separated or substantially free from at least some of the other components associated with the source of the molecule such that it constitutes at least 25% (w/w) of the composition." Ex. 1018, 14.

G. Ground 1 – Anticipation by Stamler

Petitioner contends that claim 2 is anticipated by Stamler. Pet. 38. Patent Owner disagrees. Prelim Resp. 34.

1. Stamler

Stamler discloses a method for modulating nitric oxide bioactivity in a patient by inhibiting the enzyme glutathione-dependent formaldehyde dehydrogenase. Ex. 1006, 1–2; Ex. 1002 ¶ 48. Stamler discloses that

inhibiting glutathione-dependent formaldehyde dehydrogenase benefits patients with breathing disorders (*e.g.*, asthma, cystic fibrosis, and ARDS), heart disease, hypertension, ischemic coronary syndromes, atherosclerosis, glaucoma, diseases characterized by angiogenesis (*e.g.*, coronary artery disease), disorders where there is a risk of thrombosis or restenosis occurring, chronic inflammatory diseases (*e.g.*, AIDS, dementia, and psoriasis), diseases where there is risk of apoptosis occurring (*e.g.*, heart failure, atherosclerosis, degenerative neurologic disorders, arthritis and liver injury (ischemic or alcoholic)), impotence, obesity caused by eating in response to craving for food, stroke, reperfusion injury (*e.g.*, traumatic muscle injury in heart or lung or crush injury), and disorders where preconditioning of heart or brain for nitric oxide ("NO") protection against subsequent ischemic events is beneficial. Ex. 1006, 13–14.

Stamler teaches that NR can act as an inhibitor of glutathione-dependent formaldehyde dehydrogenase and that NR and related nicotinamide-based inhibitors "are available commercially or their synthesis is described in or obvious from the literature." *Id.* at 3–4, 13; Ex. 1002 ¶¶ 52, 74. Stamler discloses that a therapeutically effective amount of an inhibitor of glutathione-dependent formaldehyde dehydrogenase ranges from 1 μg to 10 g/kg and often ranges from 10 μg to 1 g/kg, or 10 μg to 100 mg/kg body weight of the patient. Ex. 1006, 15; Ex. 1002 ¶ 50. Stamler discloses that oral administration of a glutathione-dependent formaldehyde dehydrogenase is preferred. Ex. 1006, 15; Ex. 1002 ¶ 51.

2. Analysis of Claim 2

Claim 2 depends from claim 1. As we have previously found for purposes of this decision, *see supra* Section II.B., collateral estoppel applies to prevent Patent Owner from challenging our previous determination in the

'1795 IPR that claim 1 is unpatentable. Thus, we apply the reasoning and findings that we set forth in our final written decision in the '1795 IPR for why claim 1 is unpatentable. Ex. 1018, 16–25, 32–37.

Therefore, we will determine whether Petitioner has shown a reasonable likelihood that claim 2 is unpatentable by first addressing whether the additional limitations recited in claim 2 are taught by the prior art.[5] Claim 2 adds the limitation that the NR be isolated from a natural or synthetic source.

a) Is isolated from a natural or synthetic source

Petitioner contends that Stamler discloses this limitation. Pet. 40. Petitioner contends that Stamler discloses that the NR is commercially available or that its synthesis is described or obvious from the literature. *Id.* (citing Ex. 1006, 13; Ex. 1002 ¶ 74). Petitioner contends that one skilled in the art would understand that synthetic and commercially available NR is isolated from a natural or synthetic source, thus meeting the limitation of claim 2. Pet. 40 (citing Ex. 1002 ¶¶ 75–76).

Patent Owner contends that Stamler does not teach this limitation. Prelim. Resp. 38–40. Patent Owner contends that the reference to commercially available or synthetically produced NR does not meet the definition of "isolated" as we have construed the term and the reference does not indicate the purity of the NR. *Id.*

We have considered the arguments presented by the parties and the evidence of record and conclude that Petitioner has the better argument.

[5] As discussed above, collateral estoppel prevents Patent Owner from relitigating whether the art teaches the limitations of claim 1.

While we agree with Patent Owner that Stamler does not expressly mention NR that has been isolated from a natural or synthetic source, Stamler does disclose that the glutathione-dependent formaldehyde dehydrogenase inhibitors such as NR "are available commercially or their synthesis is described or obvious from the literature." Ex. 1006, 13. Dr. Jaffery testified that one skilled the art would understand this statement to mean that the inhibitors would be isolated from a natural or synthetic source and would be substantially pure. Ex. 1002 ¶¶ 74–75. In addition, as Dr. Jaffery testified, one skilled in the art would understand that NR isolated from a natural or synthetic source would be at least 25% of the composition. *Id.* ¶¶75–76. Although not necessary to our decision on institution, we note that Petitioner's argument is underscored by the '086 patent's admission that synthetically-sourced NA, for example, is "commercially available from most large chemical companies including Merck, Glaxo, Bristol Meyers Squibb, Monsanto/Searle, Eli Lilly and Pharmacia." Ex. 1001 26:64–67.

While Patent Owner argues that Stamler does not disclose the use of NR that is isolated, Patent Owner offers no evidence to support its contentions. *See* Prelim. Resp. 38–40. "Attorneys' argument is no substitute for evidence." *Johnston*, 885 F.2d, 1574, 1581 (Fed. Cir. 1989).

At this stage of the proceeding we find that Stamler discloses this limitation. Therefore, we find that Petitioner has shown a reasonable likelihood that claim 2 is unpatentable.

Although we do not need to reach Patent Owner's arguments for which we find on this record that it is collaterally estopped from raising, for completeness and as an alternative basis for granting the petition, we address them here. Patent Owner challenges whether Stamler teaches "a

pharmaceutical composition comprising nicotinamide riboside" or teaches whether NR is "in admixture with a carrier." Prelim. Resp. 34–38.

b) A pharmaceutical composition comprising nicotinamide riboside

Petitioner contends that Stamler discloses this claim element. Pet. 38–39. Petitioner contends that Stamler discloses a method of treating a patient by administering an effective amount of a glutathione-dependent formaldehyde dehydrogenase inhibitor to treat certain disorders. *Id.* (citing Ex. 1006, 13–17; Ex. 1002 ¶ 70). Petitioner contends that Stamler discloses that NR can be a glutathione-dependent formaldehyde dehydrogenase inhibitor thus teaching a pharmaceutical composition comprising NR. *Id.* (citing Ex. 1006, 3–4; Ex. 1002 ¶¶ 70–71).

Patent Owner contends that Stamler fails to disclose this limitation. Prelim Resp. 35–36. Patent Owner contends that Stamler does not disclose a specific composition comprising NR. *Id.* Patent Owner also contends that Petitioner has not shown that the compositions of Stamler inherently contain NR. *Id.* Patent Owner contends that Petitioner improperly relies on collateral estoppel to contend that Patent Owner is estopped from arguing that Stamler fails to teach this limitation. *Id.* at 31–34.

For purposes of this decision we find that Petitioner has made a sufficient showing that Stamler discloses this limitation.

Stamler discloses the use of inhibitors of glutathione-dependent formaldehyde dehydrogenase to treat patients with breathing disorders (*e.g.*, asthma, cystic fibrosis, and ARDS), heart disease, hypertension, ischemic coronary syndromes, atherosclerosis, glaucoma, diseases characterized by angiogenesis (*e.g.*, coronary artery disease), disorders where there is a risk of thrombosis or restenosis occurring, chronic inflammatory diseases (*e.g.*, AIDS, dementia, and psoriasis), diseases where there is risk of apoptosis

occurring (*e.g.*, heart failure, atherosclerosis, degenerative neurologic disorders, arthritis and liver injury (ischemic or alcoholic)), impotence, obesity caused by eating in response to craving for food, stroke, reperfusion injury (*e.g.*, traumatic muscle injury in heart or lung or crush injury), and disorders where preconditioning of heart or brain for NO protection against subsequent ischemic events is beneficial. Ex. 1006, 13–14. Stamler discloses that NR is an inhibitor of glutathione-dependent formaldehyde dehydrogenase, which is "available commercially or [whose] "synthesis is described in or obvious from the literature." *Id.* at 4, 13. Given that Stamler discloses the use of NR for "treatment or prevention of a disease or condition associated with the nicotinamide riboside kinase pathway of NAD+ biosynthesis," , at this stage of the proceeding, we find that Stamler discloses a "pharmaceutical composition comprising nicotinamide riboside."

c) In admixture with a carrier

Petitioner contends that Stamler discloses this limitation. Pet. 38–39. Petitioner contends that the disclosure in Stamler that the NR can be administered orally in the amounts recited in Stamler would lead one skilled in the art to the understanding that the NR is mixed with a carrier. *Id.* at 39 (citing Ex. 1006, 15; Ex. 1002 ¶¶ 72–73).

Patent Owner contends that Stamler does not disclose this limitation. Prelim. Resp. 36–38. Patent Owner contends that Stamler does not disclose any form of carrier either explicitly or inherently. *Id.* at 37. Patent Owner argues that Petitioner improperly relies on what one skilled in the art would have understood Stamler to disclose and improperly relies on the disclosure of the '086 patent. *Id.* at 37–38.

We have considered the arguments presented by the parties and the evidence of record and conclude that Petitioner has the better argument.

While we agree with Patent Owner that Stamler does not expressly disclose NR in admixture with a carrier, Petitioner has presented unrebutted evidence that one skilled in the art would understand that the compositions disclosed in Stamler would inherently include a carrier. Ex. 1002 ¶ 73. *See Eli Lilly and Co. v. Los Angeles Biomedical Res. Inst. at Harbor-UCLA Med. Ctr.*, 849 F.3d 1073, 1074–75 (Fed. Cir. 2017)(The anticipation inquiry takes into account the prior art's literal teachings, and inferences the ordinarily skilled person would draw from it.)

At this stage of the proceeding we find that Petitioner has shown sufficiently that Stamler discloses this limitation.

d) Formulated for oral administration

Petitioner contends that Stamler discloses this limitation. Pet. 38–39. Petitioner contends that Stamler discloses that oral administration is preferred. *Id.* (citing Ex. 1006, 15; Ex. 1002 ¶ 72).

Patent Owner does not address this limitation. *See* Prelim. Resp. 32–40.

At this stage of the proceeding, we find that Petitioner has shown sufficiently that Stamler discloses this limitation.

e) Conclusion

Based on the foregoing and for purposes of this decision, we conclude that Petitioner has demonstrated a reasonable likelihood of showing that claim 2 is unpatentable as anticipated by Stamler.

3. Ground 2 – Obviousness based on Stamler

Petitioner contends that the subject matter of claim 2 would have been obvious to one of ordinary skill in the art at the time the invention was made over Stamler. Pet. 40–43. Petitioner reiterates its contentions that Stamler

teaches a pharmaceutical composition containing NR that can be administered orally. Pet. 41–42. With respect to the limitation calling for the NR to be in admixture with a carrier, Petitioner contends that if Stamler is not viewed as teaching the use of a carrier, it would have been obvious to use a carrier to facilitate administration of NR to a patient. *Id.* Petitioner also contends that one skilled in the art reading Stamler's reference to obtaining NR commercially or by using standard methods would have been lead to use NR that is isolated as the term has been construed. *Id.* at 42.

Patent Owner contends that Petitioner has failed to show that each of the limitations of claim 2 is taught by Stamler. Prelim. Resp. 41. Patent Owner also contends that Petitioner has failed to show a motivation to modify Stamler, nor has Petitioner established that one skilled in the art would have had a reasonable expectation of success in modifying Stamler. *Id.*

We have considered the arguments presented by the parties and the evidence of record and find that Petitioner has the better position.

As with Ground 1 above, Petitioner has presented evidence to support its contentions, particularly citations to Stamler and the testimony of Dr. Jaffery concerning each element of claim 2. Pet. 25–27; Ex. 1002 ¶¶ 79–86. For example, Dr. Jaffery testified "[t]o the extent that Stamler does not expressly identify a carrier for oral administration, it would have been obvious to do so given the well-known use of carriers to facilitate administration of pharmaceutical compositions containing an active agent, such as nicotinamide riboside, to a patient." Ex. 1002 ¶ 82 (citing Ex. 1001, 28:49–60). Similarly, Dr. Jaffery testified that it was known in the art at the time the invention of claim 2 was made to prepare synthetic NR with a purity of 45%, thus meeting the requirement that the NR be isolated from a

natural or synthetic source. *Id.* ¶ 84 (citing Ex. 1010 (Franchetti article on NR synthesis)).

Dr. Jaffery also provides a motivation to modify the product of Stamler, noting that the addition of a carrier would have facilitated the administration of the active ingredient. *Id.* ¶ 82.

In response, Patent Owner has not presented any evidence to support its contentions, relying only on attorney argument. Again, attorney argument is insufficient.

Based on the foregoing we conclude that, for purposes of this decision, Petitioner has demonstrated a reasonable likelihood of showing that claims 2 is unpatentable as obvious over Stamler.

H. Grounds 3–5

At this stage of the proceeding, Patent Owner has chosen to limit its response to Grounds 3–5 to the issue of whether the references advanced in the grounds are prior art and has not otherwise addressed the merits of Petitioner's contentions. *See* Prelim. Resp. 6–25. Having found that that Petitioner has demonstrated a reasonable likelihood of prevailing with respect to both grounds based on Stamler for claim 2, we need not address Petitioner's arguments with respect to the remaining grounds.

The Supreme Court has held that a final written decision in an *inter partes* review must decide the patentability of all claims challenged in the corresponding petition. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348 (2018). The USPTO has also provided guidance on implementing *SAS*. *See* Guidance on the Impact of SAS on AIA Trial Proceedings (Apr. 26, 2018), https://www.uspto.gov/patents-application-process/patent-trial-andappealboard/trials/guidance-impact-sas-aia-trial ("As required by [SAS] decision, the PTAB will institute as to all claims or none," and "[a]t this

time, if the PTAB institutes a trial, the PTAB will institute on all challenges raised in the petition."); TPG at 5–6.

We therefore grant the Petition and institute trial as to claim 2 of the '086 patent on all grounds asserted.

III. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that, pursuant to 35 U.S.C. § 314(a), a inter partes review is instituted on all challenges raised in the Petition; and

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of trial commencing on the entry of this Decision.

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