United States Court of Appeals for the Federal Circuit

ALMIRALL, LLC,
Appellant

v.

AMNEAL PHARMACEUTICALS LLC, AMNEAL PHARMACEUTICALS OF NEW YORK, LLC,
Appellees

ANDREW HIRSHFELD, PERFORMING THE FUNCTIONS AND DUTIES OF THE UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE,
Intervenor

2020-2331

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2019-00207, IPR2019-01095.

Decided: March 14, 2022

JAMES TRAINOR, Fenwick & West LLP, New York, NY, argued for appellant. Also represented by ADAM GAHTAN, RICHARD SHEA; ELIZABETH B. HAGAN, Seattle, WA.

DENNIES VARUGHESE, Sterne Kessler Goldstein & Fox, PLLC, Washington, DC, argued for appellees. Also represented by KRISTINA CAGGIANO KELLY, ADAM LAROCK.

ROBERT J. MCMANUS, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, for intervenor. Also represented by BENJAMIN T. HICKMAN, THOMAS W. KRAUSE, FARHEENA YASMEEN RASHEED.

Before LOURIE, CHEN, and CUNNINGHAM, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Almirall, LLC ("Almirall") appeals from the final written decision of the U.S. Patent and Trademark Office Patent Trial and Appeal Board (the "Board") holding that claims 1–8 of U.S. Patent 9,517,219 (the "'219 patent") would have been obvious over the cited prior art at the time the alleged invention was made.[1] *See Amneal Pharms. LLC v. Almirall, LLC*, No. IPR2019-00207, 2020 WL 2833274 (P.T.A.B. May 29, 2020) ("*Decision*"). For the reasons provided below, we affirm.

BACKGROUND

Almirall owns the '219 patent, which relates to methods of treating acne or rosacea with dapsone formulations that include an acrylamide/sodium acryloyldimethyl taurate copolymer ("A/SA") thickening agent and the solvent diethylene glycol monoethyl ether ("DGME"). Dapsone can be used for treating various dermatological conditions.

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[1] Because the challenged claims of the '219 patent have an effective filing date before March 16, 2013, we apply the version of 35 U.S.C. § 103 in effect before the adoption of the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284 (2011).

'219 patent, col. 1 ll. 19–23. DGME allows compositions to be prepared with increased solubilized concentrations of dapsone. *Id.* at col. 2 ll. 48–50. A polymeric viscosity builder such as an A/SA agent can minimize the intensity of yellowing of the composition. *Id.* at col. 2, ll. 54–61. It can also influence dapsone crystallization by reducing the particle size and minimizing a gritty feel upon application. *See id.*

Adapalene is a compound used for treating dermatological conditions, sometimes in combination with dapsone. *See Decision* at *18. The '219 patent includes 62 generalized composition embodiments, '219 patent, col. 6 l. 58–col. 12 l. 40, and eight specific example formulations, *id.* at col. 12 l. 42–col. 15 l. 33. Several of the examples are described as including adapalene.

Independent claims 1 and 6 read as follows:

> 1. A method for treating a dermatological condition selected from the group consisting of acne vulgaris and rosacea comprising administering to a subject having the dermatological condition selected from the group consisting of acne vulgaris and rosacea a topical pharmaceutical composition comprising:
>
> about 7.5% w/w dapsone;
>
> about 30% w/w to about 40% w/w diethylene glycol monoethyl ether;
>
> **about 2% w/w to about 6% w/w of a polymeric viscosity builder comprising acrylamide/sodium acryloyldimethyl taurate copolymer**; and
>
> water;
>
> **wherein the topical pharmaceutical composition does not comprise adapalene**.

Id. at col. 15 l. 40–col. 16 l. 13 (emphases added).

> 6. A method for treating a dermatological condition selected from the group consisting of acne vulgaris and rosacea comprising administering to a subject having the dermatological condition selected from the group consisting of acne vulgaris and rosacea a topical pharmaceutical composition comprising:
>
> about 7.5% w/w dapsone;
>
> about 30% w/w diethylene glycol monoethyl ether;
>
> **about 4% w/w of a polymeric viscosity builder comprising acrylamide/sodium acryloyldimethyl taurate copolymer**; and
>
> water;
>
> **wherein the topical pharmaceutical composition does not comprise adapalene**.

Id. at col. 16 ll. 23–36 (emphases added).

Amneal filed a petition for *inter partes* review of claims 1–8 of the '219 patent. J.A. 120. Amneal argued that claims 1–8 would have been obvious over Int'l Patent Pub. WO 2009/061298 ("Garrett") and Int'l Patent Pub. WO 2010/072958 ("Nadau-Fourcade"). J.A. 117–18. Amneal also argued that claims 1–8 would have been obvious over Garrett and a publication titled "Characterization and Stability of Emulsion Gels Based on Acrylamide/Sodium Acryloyldimethyl Taurate Copolymer" ("Bonacucina").[2] *Id.*

Garrett describes topical dapsone treatments for treating dermatological conditions including acne and rosacea. Garrett states that the dapsone may exist in "a microparticulate form, a dissolved form, or both." J.A. 1475. Garrett

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[2] Giulia Bonacucina, *et al., Characterization and Stability of Emulsion Gels Based on Acrylamide/Sodium Acryloyldimethyl Taurate Copolymer*, 10(2) AAPS PHARMSCITECH 368–75 (2009).

does not disclose any formulations that include adapalene. For example, Garrett identifies a commercial product, Aczone®, that lacks adapalene. J.A. 1482.

Garrett's formulations include thickening agents. J.A. 1486. Garrett describes suitable thickening agents as including polymer thickeners such as hydrophilic gelling agents used in the cosmetic and pharmaceutical industries. J.A. 1485. Garrett explains that a gelling agent preferably comprises between about 0.2% to about 4% by weight of the composition. *Id.* Garrett identifies Carbopol® as a preferred thickening agent. *Id.* Carbopol® is one of numerous cross-linked acrylic acid polymers that are given the name "carbomer." *Id.* Garrett's preferred compositional weight percent range for Carbopol® is between about 0.5% to about 2%.

Garrett discloses a preferred embodiment that "includes about 0.5% to 4.0% carbomer . . .; about 53.8% to 84.2% water; about 10% to 30% ethoxydiglycol [i.e., DGME]; about 0.2% methylparaben; about 5% to 10% dapsone in a microparticulate and dissolved state; and about 0.1% to 2% sodium hydroxide solution." *Decision* at *5 (citing J.A. 1476). But Garrett also contemplates adjustments for optimization. "The relative percentages for each of the reagents used . . . may vary depending upon the desired strength of the target formulation, gel viscosity, and the desired ratio of microparticulate to dissolved dapsone. Unless otherwise designated, all reagents listed . . . are commonly known by one of ordinary skill in the art and are commercially available from pharmaceutical or cosmetic excipient suppliers." *Id.* at *6 (citing J.A. 1490, 1495).

Nadau-Fourcade describes topical pharmaceutical compositions with a water-sensitive active pharmaceutical ingredient in dissolved form. J.A. 1529. The compositions are for dermatologic use for conditions including acne and rosacea. J.A. 1578. Nadau-Fourcade's compositions may include a hydrophilic gelling agent. J.A. 1574. Nadau-

Fourcade lists exemplary thickeners including carbomers (e.g., Carbopol® products) and A/SA agents (e.g., Sepineo® or Simulgel® products) in a range of concentrations, but preferentially ranging from 0.01% to 5%. J.A. 1574–75. Two formulations shown in Examples 6 and 13 utilize similar components but different gelling agents. J.A. 1587, 1589 (containing carbomer 0.1% and Simulgel® 600 0.20%, respectively).

Bonacucina presents research on Sepineo® P 600, a concentrated dispersion of acrylamide/sodium acryloyldimethyl taurate copolymer in isohexadecane. J.A. 1688. Bonacucina reports that Sepineo® P 600 has self-gelling and thickening properties that are effective for topical administration. J.A. 1688–89 (explaining that "the possibility of obtaining stiff and stable gelled phases with this polymer makes it a good candidate for the formulation of emulsion gels"). Testing revealed that Sepineo® P 600 "thickens and gels well, a property that depends strongly on polymer concentration." J.A. 1694. Bonacucina's gels included a Sepineo® P 600 concentration of 0.5% to 5%. J.A. 1694; *see also* J.A. 1690 (Table I, showing examples with 0.5%, 1%, 3%, and 5% (w/w) Sepineo®).

Relevant to this appeal, the Board's decision hinged on whether a person of ordinary skill in the art would have found it obvious to substitute an A/SA agent taught by Nadau-Fourcade or Bonacucina for the carbomer gelling agent in Garrett's formulations to arrive at the claimed composition. *See Decision* at *16. Garrett does not teach using an A/SA agent as its polymeric viscosity builder. *Id.* Instead, Garrett identifies five other preferred gelling agents, including Carbopol®. J.A. 1485.

First, the Board determined that Garrett and Nadau-Fourcade in combination teach or suggest every claim limitation and that a person of ordinary skill in the art would have been motivated, with a reasonable expectation of success, to incorporate Nadau-Fourcade's A/SA gelling agent

into Garrett's dapsone formulations. *Id.* at *30. Specifically, the Board determined that it would have been obvious to substitute Nadau-Fourcade's Sepineo® for Garrett's Carbopol®. *Id.* at *16. The Board found that the class of hydrophilic gelling agents and the specific examples in the concentrations disclosed in Garrett overlap with the gelling agents taught by Nadau-Fourcade. *Id.* Nadau-Fourcade pairs Carbopol® and Sepineo® in a small set of especially preferred gelling agents. *Id.* at *17. The Board also relied on expert testimony explaining that a person of skill would have been able to immediately appreciate that Carbopol® and Sepineo® "perform the same function and are interchangeable" and that "such a substitution was routine and predictable because such thickening agents were known for use in topical compositions with water insoluble drugs." *Id.*

Second, the Board determined that Garrett and Bonacucina in combination also teach or suggest every claim limitation and that a person of ordinary skill in the art would have been motivated, with a reasonable expectation of success, to incorporate Bonacucina's A/SA gelling agent into Garrett's dapsone formulations. *Id.* at *30. Specifically, the Board determined that it would have been obvious to substitute Bonacucina's Sepineo® for Garrett's Carbopol®. *Id.* at *20.

The Board found that a person of ordinary skill would have had good reasons to pursue a replacement for Carbopol®. The Board relied on expert testimony that Garrett's Carbopol® was known to have drawbacks, for example, requiring neutralization to achieve maximum viscosity and producing grittiness and possible agglomeration. *Id.* at *21. The Board also credited expert testimony in finding that Sepineo®'s advantages would have motivated a person of skill to replace Carbopol® with Sepineo®. For example, Sepineo® is self-gelling, is pre-neutralized, and reduces grittiness. *Id.*

The Board also found that a skilled artisan would have had a reasonable expectation of successfully replacing Garrett's gelling agents with Bonacucina's Sepineo®, in the same amounts, to arrive at the composition recited in the claims. *Id.* The Board determined that overlapping ranges support the conclusion that a person of ordinary skill in the art would have been expected to successfully replace Carbopol® with equal amounts of Sepineo® in Garrett's formulations. *Id.* The Board concluded that replacing Garrett's Carbopol® with Bonacucina's Sepineo® would have been a mere substitution of one gelling agent for another known in the field, and that each component of the Garrett-Bonacucina combination, once Sepineo® was substituted for Carbopol®, was used for the same function it is known to perform. *Id.*

The Board also agreed with Amneal that Garrett teaches the negative adapalene claim limitation. *Id.* at *18. The Board found that "there is ample evidence of record supporting the conclusion that Garrett's dapsone formulations for treating acne neither inherently included nor implicitly required adapalene." *Id.* at *25. The Board explained that "it is not Garrett's mere silence as to the presence of adapalene, but its disclosure of complete dapsone formulations to treat acne in its absence that suggests that adapalene is not included in Garrett's formulations." *Id.* at *18. The Board noted that "the commercial Aczone® 5% product referenced in Garrett did not include adapalene." *Id.* Relying on Garrett's teachings and expert testimony, the Board determined that Almirall failed to show that a person of ordinary skill in the art would have viewed adapalene as included in Garrett's dapsone formulations. *Id.*

The Board ultimately concluded that Amneal demonstrated by a preponderance of the evidence that claims 1–8 of the '219 patent are unpatentable. *Id.* at *33. Almirall appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

Almirall raises two challenges on appeal. First, Almirall contends that the Board erred in presuming obviousness based on overlapping ranges. Second, Almirall argues that the Board's obviousness determinations were unsupported by substantial evidence.

We review the Board's legal determinations *de novo*, *In re Elsner*, 381 F.3d 1125, 1127 (Fed. Cir. 2004), but we review the Board's factual findings underlying those determinations for substantial evidence, *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). A finding is supported by substantial evidence if a reasonable mind might accept the evidence as adequate to support the finding. *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938).

I

We first consider Almirall's challenge to the Board's determination that "Garrett discloses a range for each of the various components of the composition that either fully encompasses or overlaps/abuts the ranges and amounts for those components recited in the challenged claims, and this is sufficient to create a presumption of obviousness as to the claimed amounts." *Decision* at *14.

Almirall argues that the Board erred in presuming obviousness based on overlapping ranges because no single reference discloses all of the claimed ranges. First, Almirall argues that Garrett's ranges for its polymeric viscosity builders do not create a presumption of obviousness because Garrett only discloses ranges for carbomer thickeners, not A/SA thickeners as claimed. Second, Almirall argues that the Board erred by looking to the overlapping range for the A/SA element in Nadau-Fourcade and Bonacucina to provide that missing limitation. Almirall argues that Nadau-Fourcade and Bonacucina cannot be used in combination with Garrett to establish a presumption of obviousness because the presumption applies only

when a single reference discloses all claimed ranges. *See* Appellant's Br. 27–28 (citing *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317 (Fed. Cir. 2004)).

Amneal responds that the Board did not err in applying a presumption of obviousness of overlapping ranges. First, Amneal argues that Garrett's disclosure of carbomer thickener ranges is sufficient to support the rejection because disclosure of the precise, claimed composition is not necessary to show obviousness. Citing *Valeant* and *Anacor*, Amneal asserts that ranges for structurally and functionally similar compounds can establish a *prima facie* case of obviousness. *See* Appellee's Br. 24–26 (citing *Valeant Pharms Int'l Inc. v. Mylan Pharms Inc.*, 955 F.3d 25 (Fed. Cir. 2020); *Anacor Pharms., Inc. v. Iancu*, 889 F.3d 1372 (Fed. Cir. 2018)). Second, Amneal argues that the Board did not err in looking to Nadau-Fourcade and Bonacucina because the obviousness inquiry is flexible and does not require that all elements be shown in a single reference.

"A *prima facie* case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003) (citing *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997)); *see also E.I. du Pont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018); *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004). "The point of our overlapping range cases is that, in the absence of evidence indicating that there is something special or critical about the claimed range, an overlap suffices to show that the claimed range was disclosed in—and therefore obvious in light of—the prior art." *E.I. du Pont*, 904 F.3d at 1008. A presumption of obviousness does not shift the burden of persuasion to the patentee to prove nonobviousness, but a presumption establishes that, "absent a reason to conclude otherwise, a factfinder is justified in concluding that a disclosed range does just that—discloses the entire range." *Id.*

We agree with Amneal that the Board did not err in applying a presumption of obviousness of overlapping ranges. The Board's decision sets forth factual findings of similarity between carbomers and A/SA agents that support its conclusion that "Garrett discloses a range for each of the various components of the composition that either fully encompasses or overlaps/abuts the ranges and amounts for those components recited in the challenged claims, and this is sufficient to create a presumption of obviousness as to the claimed amounts." *Decision* at *14. For example, Amneal's expert explained that Garrett's gelling agents and Nadau-Fourcade's gelling agents have overlapping characteristics. *Id.* at *17. The Board also credited expert testimony that a person of ordinary skill in the art would have been able to immediately appreciate that the carbomers and A/SA agents at issue perform the same function and are interchangeable. *Id.* Moreover, there was no evidence that A/SA agents would have different interactions with the other ingredients of the compositions relative to carbomer. Indeed, the Board credited expert testimony that a skilled artisan "would not have expected any incompatibilities in substituting" the gelling agents. *Id.* Thus, the Board found that Garrett's gelling agents and A/SA agents are "used in very similar concentrations for similar formulations." *Id.*

The Board also found that the presumption was not overcome because Almirall's evidence of unexpected results and failure of others was unpersuasive. We find those conclusions supported by substantial evidence.

But even if we agreed with Almirall that the presumption does not apply in this case, the outcome would be the same. Ultimately, despite Almirall's attempts to argue otherwise, this case does not depend on overlapping ranges. It is simply a case of substituting one known gelling agent for another. Each may be effective at a different concentration in different formulations, but that is just a

property of the particular known material, subject to conventional experimentation.

It is undisputed that Nadau-Fourcade and Bonacucina each separately disclose an A/SA thickener within the claimed range. As further discussed below, despite determining that there was a presumption of obviousness, the Board also analyzed whether a person of ordinary skill in the art would have been motivated to combine Garrett with Nadau-Fourcade or Bonacucina to arrive at the claims with a reasonable expectation of success.

II

We therefore next consider Almirall's arguments that the Board erred in determining that claims 1–8 would have been obvious over Garrett and Nadau-Fourcade (Ground 1), as well as over Garrett and Bonacucina (Ground 2).

As a preliminary matter relevant to both obviousness grounds, Almirall argues that the Board failed to account for the negative adapalene claim limitation. Almirall argues that although Garrett does not indicate that any of its formulations include adapalene, more is needed for a disclosure of a negative claim limitation. Amneal responds that substantial evidence supports the Board's finding that Garrett effectively teaches the negative adapalene claim limitation.

We agree with Amneal. Almirall's argument is contrary to our precedent. "[A] reference need not state a feature's absence in order to disclose a negative limitation." *AC Techs., S.A. v. Amazon.com, Inc.*, 912 F.3d 1358, 1367 (Fed. Cir. 2019). Instead, it was reasonable for the Board to find that, in the context of Garrett, a skilled artisan would recognize that the reference discloses a complete formulation—excluding the possibility of an additional active ingredient. *See, e.g.*, *Novartis Pharms. Corp. v. Accord Healthcare, Inc.*, 21 F.4th 1362, 1373 (Fed. Cir. 2022)

(recognizing that for negative limitations, "the disclosure must be read from the perspective of a person of skill in the art"). It is undisputed that Garrett discloses dapsone formulations that lack adapalene. The Board thus did not err in concluding that Garrett discloses the negative adapalene claim limitation.

Ground 1: Garrett and Nadau-Fourcade

Almirall argues that the Board's holding that claims 1–8 would have been obvious over Garrett and Nadau-Fourcade was unsupported by substantial evidence.

First, we consider Almirall's argument that the Board failed to require evidence of a motivation to combine Garrett with Nadau-Fourcade. The presence or absence of a motivation to combine references in an obviousness determination is a question of fact. *See In re Gartside*, 203 F.3d at 1316. Almirall argues that the Board erred by substituting the alleged interchangeability of Sepineo® and Carbopol® for evidence of a motivation to combine Nadau-Fourcade with Garrett. Amneal responds that the Board properly placed the burden on Amneal to show that the prior art provided reasons to combine the references.

The record amply supports the Board's conclusion that a person of ordinary skill in the art would have been motivated to replace Garrett's gelling agent with an A/SA copolymer. The Board relied on prior art and expert testimony in determining that a person of ordinary skill would have recognized Carbopol® and Sepineo® as closely related gelling agents that could be interchangeably used in dapsone formulations in the same concentration range. The Board did not rely on a conclusory rationale of "design choice" as sufficient to find that a skilled artisan would have combined the references; on the contrary, it reviewed the context-specific evidence for the soundness of Amneal's rationale. In explaining why a person of ordinary skill would have made the choice to use an A/SA copolymer, the Board relied on Garrett and Nadau-Fourcade's teachings

as well as expert testimony. For example, the Board credited Amneal's expert's testimony that "such a substitution was routine and predictable because such thickening agents were known for use in topical compositions with water insoluble drugs" and that a person of ordinary skill "would not have expected any incompatibilities." *Decision* at *17.

We conclude that the Board's rationale for the combination was sufficient to support its obviousness determination. The Board noted that Garrett explicitly states that "[p]olymer thickeners that may be used include those known to one skilled in the art, such as hydrophilic and hydroalcoholic gelling agents frequently used in the cosmetic and pharmaceutical industries." *Id.* (citing J.A. 1485). The record demonstrates that A/SA copolymers would have been predictable design choices that a person of ordinary skill would have considered for development of topical dapsone formulations. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007) ("When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp."); *id.* at 416 ("[W]hen a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result."); *id.* at 417 ("If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.").

Second, we consider Almirall's argument that a person of ordinary skill would not have had a reasonable expectation of success in incorporating Nadau-Fourcade's A/SA copolymer into Garrett's formulations. Almirall argues that the evidence fails to show that Sepineo® and Carbopol® are interchangeable. Almirall asserts that a person of ordinary skill could not substitute an A/SA copolymer at the same amount and concentration as a carbomer. Almirall

contends that Nadau-Fourcade's Examples 6 and 13 demonstrate that different formulations require different thickeners at different concentrations. Amneal counters that the Board relied on expert testimony in correctly determining that Nadau-Fourcade teaches that Sepineo® is interchangeable with Carbopol® as a gelling agent in topical pharmaceutical formulations containing water-insoluble drugs.

We agree with Amneal. A finding of a reasonable expectation of success does not require absolute predictability of success. *See OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019). The Board's reasonable expectation of success analysis is supported by substantial evidence. The Board credited Amneal's expert's testimony that a person of ordinary skill would have understood that use of Nadau-Fourcade's A/SA gelling agents in Garrett's formulation would have been routine and predictable because the agents were known for use in topical compositions with water insoluble drugs. Furthermore, the Board found that a person of ordinary skill would not have expected any incompatibilities. The Board analyzed the record evidence and found that Carbopol® and Sepineo® were recognized to be interchangeable and equivalent gelling agents that could be used in topical formulations containing dapsone, and that they could be used in the same concentration range. We are therefore not persuaded that the Board erred in analyzing the evidence provided by Amneal and its impact on whether a skilled artisan would have had a reasonable expectation of success in combining these prior art teachings to achieve the claimed invention.

Ground 2: Garrett and Bonacucina

Almirall argues that the Board's holding that claims 1–8 would have been obvious over Garrett and Bonacucina was unsupported by substantial evidence.

First, we consider Almirall's argument that Amneal failed to provide evidence of a motivation to combine

Garrett with Bonacucina. Almirall argues that Bonacucina does not suggest which active pharmaceutical ingredients or excipients may be compatible with Sepineo®. Almirall contends that mitigating grittiness and eliminating a neutralization step were not motivating factors, because grittiness was not a concern for Garrett's formulations and that A/SA copolymers still require neutralization. Amneal counters that the Board relied on expert testimony in correctly determining that a person of ordinary skill would have been motivated to use Bonacucina's A/SA copolymer because of its advantages.

We agree with Amneal that the Board's analysis was supported by substantial evidence. The evidence supports the finding that dapsone compositions with carbomer could be gritty and require neutralization. Bonacucina teaches that Sepineo®, in contrast, forms stiff and stable compositions and is pre-neutralized. We find no error in the Board's determination that Bonacucina suggests Sepineo® as a gelling agent for topical applications like Garrett's dapsone formulations.

Second, we consider Almirall's argument that a person of ordinary skill would not have had a reasonable expectation of success in incorporating Bonacucina's A/SA copolymers into Garrett's formulations. Almirall argues that Bonacucina fails to suggest that Sepineo® could successfully replace a carbomer in any formulation. Amneal counters that the Board relied on expert testimony in correctly determining that a person of ordinary skill would have had a reasonable expectation of success because Bonacucina taught using Sepineo® at overlapping concentrations and because carbomers had known drawbacks which were resolved by Sepineo®.

We again agree with Amneal. The Board's reasonable expectation of success analysis was supported by substantial evidence. The Board found that "[t]he reasonable expectation of success for using Sepineo[®] as a gelling agent

in Garrett's dapsone formulations stems from the fact that Sepineo[®] was a well-known gelling agent that had been successfully used for other similar topical formulations." *Decision* at *27. We are not persuaded that the Board erred in analyzing the evidence provided by Amneal and its impact on whether a skilled artisan would have had a reasonable expectation of success in combining these prior art teachings to achieve the claimed invention.

CONCLUSION

We have considered Almirall's remaining arguments, but we find them unpersuasive. The Board's decision was supported by substantial evidence and not erroneous as a matter of law. For the foregoing reasons, the decision of the Board is affirmed.

AFFIRMED