NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

IN RE: INSTITUT PASTEUR,
Appellant

2022-1896

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 14/730,396.

Decided: December 13, 2023

SALVATORE J. ARRIGO, III, Arrigo, Lee, Guttman & Mouta-Bellum LLP, Washington, DC, argued for appellant. Also represented by HARRY JOEL GUTTMAN.

KAKOLI CAPRIHAN, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, argued for appellee Katherine K. Vidal. Also represented by AMY J. NELSON, MAUREEN DONOVAN QUELER, FARHEENA YASMEEN RASHEED.

Before TARANTO, CLEVENGER, and STOLL, *Circuit Judges*.

CLEVENGER, *Circuit Judge*.

Institut Pasteur ("Pasteur") appeals from a decision of the Patent Trial and Appeal Board ("Board") affirming an examiner's rejection of claims 35–53 of U.S. Patent Application No. 14/730,396 ("'396 Application") for obviousness-type double patenting. For the reasons set forth below, we *affirm*.

BACKGROUND

Pasteur filed the '396 Application on June 4, 2015. The '396 Application relates to "peptides derived from human Basic Proline-rich Lacrimal Protein (BPLP), notably opiorphin." '396 Application, Abstract.

Following amendments during prosecution, an independent Claim 17 for the '396 Application recited:

> 17. A method for treating pain comprising administering a dose of 10-300 mg/day of a peptide consisting of the sequence Gln-Arg-Phe-Ser-Arg (SEQ ID NO:2) or Glp-Arg-Phe-Ser-Arg (SEQ ID NO:55) for 7 days.

J.A. 327.

The examiner rejected pending claims 17–29 on the ground of obviousness-type double patenting over "claims 1, 3, 5, 6, 8, 10, 11 and 14 of U.S. Patent No. 9,403,871." J.A. 234, 325.

U.S. Patent No. 9,403,871 ("'871 Patent") was filed by Pasteur on May 19, 2014, and is titled "Methods for treating pain by administering peptides derived from human basic proline-rich lacrimal protein." The '871 Patent relates to "diagnostic and therapeutic uses of human BPLP protein, [and] peptides derived therefrom." '871 Patent, col. 1, ll. 24–26. Claim 1 and 6 of the '871 Patent recite:

> 1. A method for treating pain comprising administering an effective amount of an isolated peptide consisting of up to 15 amino acids to a human subject,

> wherein the peptide comprises the sequence Glu-Arg-Phe-Ser-Arg (SEQ ID NO: 3) or Glp-Arg-Phe-Ser-Arg (SEQ ID NO: 7),
>
> wherein the peptide exhibits an inhibitory property against a neutral endopeptidase or an aminopeptidase and
>
> wherein the peptide has the same amino acid sequence as that found within human Basic Proline-rich Lacrimal Protein (SEQ ID NO:2) or differs from the amino acid sequence found within SEQ ID NO:2 by two or less amino acid substitutions.
>
> . . .
>
> 6. The method of claim 1, comprising administering a dose of 10-100 mg of the peptide.

'871 Patent, col. 41, l. 27–col. 42, l. 27.[1]

In the rejection based on the '871 Patent, the examiner explained that it would have been "obvious for one of ordinary skill in the art to treat chronic pain by the methods of claims 1, 3, 5, 6, 8, 10, 11 and 14 of U.S. Patent No. 9,403,871, which would require treatment for several days, 7 included." J.A. 234.

Pasteur appealed the obviousness-type double patenting rejection to the Board. The Board affirmed and agreed with the examiner that "the '871 patent's claim term 'pain' . . . includes at least 'acute pain' and 'chronic inflammatory pain such as arthritis or inflammatory bowel disease.'" *Ex Parte Rougeot*, No. 2018-007103, 2019 WL 6208056, at *5 (P.T.A.B. Oct. 4, 2019) ("First Decision") (quoting '871 Patent, col. 18, ll. 15–17). The Board also found that the '871

---

[1] A certificate of correction replaced "Glu" with "Gln" in Claim 1 of the '871 Patent.

Patent's claim term "'effective amount of an isolated peptide' includes within its scope . . . a therapeutic mixture including about 0.0001 to 100 milligrams of the peptide, or, most preferably, 10–100 milligrams per dose, and that '[m]ultiple doses can be administered.'" *Id.* (quoting '871 Patent, col. 16, ll. 49–57).

In evaluating the "7 days" limitation, the Board considered "the type of pain disclosed and claimed as being treated in the '871 patent [to] include[] chronic pain, which by its very persisting or reoccurring nature may last several days." *Id.* The Board then concluded that "one of ordinary skill in the art would have found it obvious to treat such pain for 7 days (and more) because of its persistent nature." *Id.* The Board also agreed with the reasoning of the examiner that "'[i]t is reasonable to interpret that treatment "administering a dose of 10-100 mg of the peptide" occurs at intervals necessary to alleviate pain, starting with daily administration' and if pain persists, chronically, to a second day, treatment should likewise extend to the second day, and so on to the claimed 7 days (or beyond)." *Id.*

After the First Decision, Pasteur filed a Request for Continued Examination to modify the independent claim to recite:

> 17. [] A method for treating pain <u>in a human patient</u> comprising administering a dose of <u>1 mg/kg to 2mg/kg</u> <u>at</u> 10-300 mg/day of a peptide consisting of the sequence Gln-Arg-Phe-Ser-Arg (SEQ ID NO:2) or Glp-Arg-Phe-Ser-Arg (SEQ ID NO:55) <u>to the patient</u> for 7 days <u>without inducing pharmacodependence or tolerance in the patient</u>.

J.A. 335. This claim was later renumbered to be Claim 35 and is representative for the purposes of this appeal. J.A. 371.

The examiner again rejected the amended claims based on obviousness-type double patenting because of the '871 Patent. The examiner noted Pasteur's argument regarding the difference in dosages and duration of treatment reflected by the claim language of claims 1 and 6 of the '871 Patent and claim 17 of the '396 Application, and responded that Pasteur's argument has been fully considered and answered in the previous rejection, which had been affirmed by the Board and not appealed to this court. J.A. 385–86. With respect to the "1 mg/kg to 2 mg/kg" addition, the examiner explained "that 1 mg/kg to 2 mg/kg per day equals to 80 mg to 160 mg per day[for the] average weight of 80 kg." J.A. 383. The examiner also explained that adding "without inducing pharmacodependence or tolerance in the patient" did not create patentability because "[t]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." J.A. 383–84 (quoting *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999)).

After the Non-Final Rejection on the amended claims, Pasteur filed a Declaration from Catherine Rougeot. Ms. Rougeot is a "visiting researcher" at Pasteur and is also the named inventor on the '396 Application. J.A. 19, 444. Ms. Rougeot declared that "opioid receptor agonists, such as morphine" are the "most efficient drugs to alleviate severe pain" but their "clinical usefulness has been limited by the development of tolerance and dependence that occurs after long-term treatment." J.A. 446 ¶¶ 15–16.

Ms. Rougeot also declared that "[i]t was known in 2008 that human opiorphin at systemically equi-analgesic morphine doses (1-2 mg/kg, i.v.) inhibits nociception in standard morphine-sensitive pain models." J.A. 447 ¶ 23. Further, Ms. Rougeot declared that "it was expected that opiorphin could induce tolerance and dependence – just as morphine does" and "opiorphin's lack of the detrimental side effects of opioids – tolerance and dependence – was

surprising and unexpected." J.A. 448 ¶ 25, 449 ¶ 36. Ms. Rougeot also declared that "opiorphin fulfils a long-felt need for efficient pain-controlling compounds without the detrimental side effects of opioids – tolerance and dependence." J.A. 449 ¶ 35.

The examiner again rejected the amended claims. In addressing the Rougeot Declaration, the examiner noted that the "Declaration states that administration of 1-2 mg/kg of opiorphin to alleviate pain was known, and . . . [the Declaration] contemplates that the expected physiological mechanism of action of opiorphin would prohibit its use over extended period, such as for 7 days or 11 days." J.A. 479. The examiner then recognized that the "Declarant explains . . . that the further research found opirphin [sic] to have a minimal adverse morphine-associated effect and to produce analgesic potency, and concludes that this effect was surprising and unexpected." J.A. 479.

The examiner found that the arguments presented in the Rougeot Declaration were not persuasive. The examiner explained that "the Declaration acknowledges that the instant method of treatment of pain uses the same drug and the same dose as taught by the '871 patent," and so "[t]he only remaining disputed difference between the scope of the instant claims and the claims of the '871 patent is the duration of the treatment." J.A. 479. The examiner explained that this issue was previously before the Board and that "the treatment of pain of the '871 patented claims encompasses treatment of chronic pain . . . even if the full understanding of the mechanism of pharmacopedendence [sic] of the drug was not appreciated at the time." J.A. 479–80. The examiner decided that "Applicant's further research of the subject matter and discovering new properties of opiorphin does not render the instant claims patentable." J.A. 480.

The examiner next addressed Pasteur's arguments regarding objective indicia of nonobviousness. The examiner

said that the claims were "not patentably distinct from the invention claimed in the U.S. Patent No. 9,403,871 because it encompasses [an] identical process of administering the same drug to treat the same pathology, which is expected to produce identical results." J.A. 481. The examiner added that "all the adjustments – dose to be administered as well as daily dose, [and] treatment for 7 days or longer . . . – represent a finite number of identified, predictable solutions, and one of ordinary skill in the art would have recognized that the results of this adjustment are predictable." J.A. 481. The examiner concluded that "the results of practicing the treatment regime are reasonably expected to produce identical effect, absent evidence to the contrary." J.A. 481.

Pasteur again appealed the rejection to the Board. In an oral hearing, the Administrative Patent Judge and Pasteur had the following exchange regarding the disputed rejection:

> JUDGE FLAX: So it's -- I think that we all agree that it's reciting the same peptide that is the therapeutic compound of the present claims. I think that we're all --
>
> MR. ARRIGO: Yes. That is correct.
>
> JUDGE FLAX: -- we all agree on that. And I think that we all agree that it's disclosing a dose of 10 to 100 milligrams, which is within that claimed range. And so the new thing that I think you're arguing is that claimed result if you use it for seven days, you don't get the dependence and you don't build up a tolerance.
>
> MR. ARRIGO: Right.

J.A. 575–76.

In the Board's decision regarding the amended claims, the Board again affirmed the examiner and adopted the

examiner's findings of fact. The Board cited its First Decision and repeated its conclusion that "the '871 patent's claims embrace treating chronic pain." *Ex Parte Rougeot*, No. 2021-005009, 2022 WL 1199280, at *4 (P.T.A.B. Apr. 12, 2022) ("Second Decision"). In addressing the Pasteur's arguments with respect to the "without inducing pharmacodependence or tolerance in the patient," the Board first reiterated that "there is no dispute here that the '871 patent's claims teach treating chronic pain with the same drug, at the same dose, for the same duration as presently claimed." *Id.* at *6. The Board then said it was not persuaded by Pasteur's arguments based on the Rougeot Declaration and held that "[t]he fact that performing this prior art method would produce a result, surprising or not, that the treated patient would not experience tolerance or pharmacodependence is, as in *Baxter*, mere recognition of a latent property in an obvious method of treating pain with the same peptide." *Id.* (citing *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991)). The Board also rejected the argument regarding a long-felt need for a "morphine replacement that does not share morphine's potential for tolerance and pharmacodependence, [because] this need would have been satisfied by the subject matter claimed in the '871 Patent, which precedes the present claims." *Id.* at *7.

Pasteur timely appealed the Board's Second Decision, and we have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

The ultimate determination of whether an invention would have been obvious under 35 U.S.C. § 103(a) is a legal conclusion based on underlying findings of fact. *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000). Therefore, the Board's ultimate determination of obviousness is reviewed without deference, and the Board's underlying factual findings are reviewed for substantial evidence. *Id.*; *PersonalWeb Techs., LLC v. Apple, Inc.*, 917 F.3d 1376,

1381 (Fed. Cir. 2019). The underlying factual findings include "objective indicia of nonobviousness." *Ariosa Diagnostics v. Verinata Health, Inc.*, 805 F.3d 1359, 1364 (Fed. Cir. 2015). Additionally, "[t]he inherent teaching of a prior art reference is a question of fact." *Par Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014) (citation omitted).

On appeal, Pasteur challenges the Board's obviousness analysis. Pasteur argues that the Board did not have substantial evidence for its factual determinations and that parts of the Second Decision erred as a matter of law.

PRIMA FACIE OBVIOUSNESS

Pasteur argues that the Board disregarded differences between the claims of the '871 Patent and the dose and duration limitations of the '396 Application. However, in its obviousness analysis in the Second Decision, the Board cited its First Decision which had previously addressed how these limitations were obvious in light of the claims of the '871 Patent.[2] *Second Decision*, 2022 WL 1199280, at *4. The Board also reiterated how the examiner and its First Decision explained that the "7 days" limitation was obvious because the '871 Patent's claims "embrace[d] treating chronic pain [and] it would have been obvious to administer the therapy for seven days (which is the length of time recited in appealed claim 35), as chronic pain may endure for such a time." *Id.* Additionally, the Board explained that the "1 mg/kg to 2mg/kg at 10-300 mg/day" limitation would be obvious in light of claim 8 of the '871 Patent which claims "a dose of 10-100 mg of the peptide." *Id.* at *5.

The record shows that the Board had substantial evidence for the conclusions regarding the dose and duration limitations in light of the '871 Patent. The Board's findings

---

[2] Pasteur did not appeal the First Decision of the Board to this court.

are reinforced by Pasteur's concessions at its oral hearing before the Board that the '871 Patent disclosed the "same peptide" and "a dose of 10 to 100 milligrams, which is within that claimed range" of the '396 Application and that the "new thing" Pasteur was arguing was "that claimed result if you use it for seven days, you don't get the dependence and you don't build up a tolerance." J.A. 575–76.

Pasteur also challenges the Board's determination regarding the "without inducing pharmacodependence or tolerance in the patient" limitation. After finding all other limitations obvious in light of the '871 Patent, the Board adopted the examiner's finding that the '871 Patent "encompasse[d an] identical process of administering the same drug to treat the same pathology, which is expected to produce identical results." *Second Decision*, 2022 WL 1199280, at *5. The Board determined that "[t]he fact that performing this prior art method would produce a result . . . is . . . mere recognition of a latent property in an obvious method of treating pain with the same peptide." *Id.* at *6 (citing *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002)).

The Board had substantial evidence with respect to its finding regarding the "without inducing pharmacodependence or tolerance in the patient" limitation. Pasteur has not shown that this limitation would not be inherent when practicing the prior art method of the '871 Patent as described by the Board.

Pasteur also argues that the Board misapplied the law in its prima facie obviousness analysis. We disagree. In contrast to Pasteur's characterization, the Board did not merely find that '871 Patent claims "dominat[ed]" the '396 Application but instead explained why each claim limitation was obvious in light of the '871 Patent claims. The Board also did not err with respect to its use of inherency in its obviousness analysis. It is settled that inherency may supply a missing claim limitation in an obviousness

analysis. *See Hospira, Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1332 (Fed. Cir. 2020).

OBJECTIVE INDICIA OF NONOBVIOUSNESS

The Board also had substantial evidence regarding its determinations related to the objective indicia of nonobviousness. Pasteur argues that the Board "improperly dismissed" the objective indicia evidence presented in the Rougeot Declaration. While Pasteur provided some evidence of the expectations of a skilled artisan based on the effect of a similar treatment using morphine, the Board did not find this evidence sufficient to overcome the prima facie case of obviousness. The Board had substantial evidence for this finding as Pasteur did not prove that the claimed benefits are unexpected as compared to the closest prior art. *See Baxter*, 952 F.2d at 392 ("[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.").

Pasteur also argues that the Board's handling of unexpectedness erred as a matter of law under *Honeywell Int'l Inc. v. Mexichem Amanco Holding S.A. DE C.V.*, 865 F.3d 1348, 1355 (Fed. Cir. 2017). However, we clarified in *Couvaras* that "*Honeywell* held that 'unexpected properties may cause what may appear to be an obvious composition to be nonobvious,' not that unexpected mechanisms of action must be found to make the known use of known compounds nonobvious." *See In re Couvaras*, 70 F.4th 1374, 1380 (Fed. Cir. 2023) (quoting *Honeywell*, 865 F.3d at 1355). Similarly, *Honeywell* does not necessitate a finding of nonobviousness here simply because one limitation was found satisfied through inherency.

Pasteur also disagrees with the Board's handling of the Rougeot Declaration with respect to long-felt need. The Board rejected the argument regarding a long-felt need for a "morphine replacement that does not share morphine's potential for tolerance and pharmacodependence,

[because] this need would have been satisfied by the subject matter claimed in the '871 patent, which precedes the present claims." *Second Decision*, 2022 WL 1199280, at *7. This factual conclusion is supported by the substantial evidence for similar reasons as above.

CONCLUSION

After full review of the record and Pasteur's arguments, we conclude that the Board's Decision was supported by substantial evidence and that Pasteur has not identified any incorrect legal conclusions by the Board.

AFFIRMED