Trials@uspto.gov
571.272.7822

Paper No. 14
Entered: July 1, 2016

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LOWER DRUG PRICES FOR CONSUMERS, LLC,
Petitioner,

v.

FOREST LABORATORIES HOLDINGS LIMITED,
Patent Owner.

Case IPR2016-00379
Patent 6,545,040 B1

Before MICHAEL P. TIERNEY, LORA M. GREEN, and TINA E. HULSE, *Administrative Patent Judges*.

HULSE, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Lower Drug Prices for Consumers, LLC ("Petitioner") filed a Corrected Petition requesting an *inter partes* review of claims 1–6 of U.S. Patent No. 6,545,040 B1 (Ex. 1001, "the '040 patent"). Paper 6 ("Pet."). Forest Laboratories Holdings Limited ("Patent Owner") filed a Preliminary Response to the Petition. Paper 12 ("Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon considering the Petition and Preliminary Response, we conclude that the Petition presents substantially the same art and arguments as those previously presented to the Office, and, therefore, exercise our discretion under 35 U.S.C. § 325(d) to deny the Petition.

A. Related Proceedings

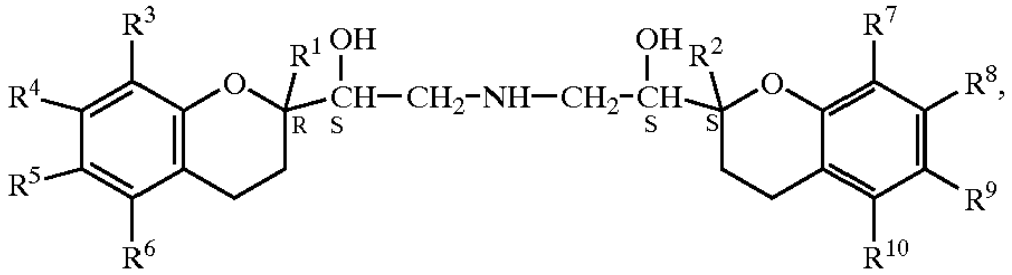
The parties identify several district court proceedings as relating to the '040 patent, all of which are now closed. Pet. 59; Paper 5, 1.

Patent Owner also states the '040 patent was the subject of *ex parte* reexamination proceeding 90/008,356, which is concluded. Paper 5, 2.

B. The '040 Patent

The '040 patent relates to a certain class of isomers of 2,2'-iminobisethanol derivatives having β-adrenergic blocking properties that potentiate the activity of blood pressure reducing agents. Ex. 1001, 1:13–17. The class of compounds is represented by formula (I):

(I)

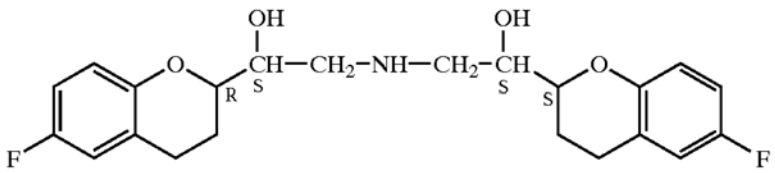


or the pharmaceutically acceptable acid addition salts thereof. *Id.* at 1:21–37.

According to the ’040 patent, the most preferred compound is [2R,αS,2'S, α'S]-α, α'-[iminobismethylene]bis[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol] or a pharmaceutically acceptable acid addition salt thereof. *Id.* at 1:60–63. The Specification states that the compounds of formula (I) potentiate the activity of blood pressure reducing agents and, in particular, potentiate the reduction of blood pressure and heart rate. *Id.* at 4:6–9. The Specification also provides examples of such blood pressure reducing agents, including the SRRR-isomers of the compounds of formula (I). *Id.* at 4:51–55.

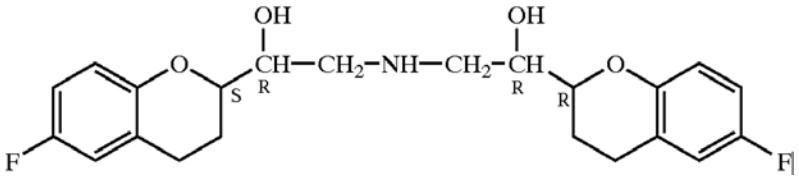
C. Illustrative Claim

Petitioner challenges claims 1–6 of the ’040 patent. Claims 1 and 2 are the only independent claims and are reproduced below:

> 1. A composition consisting of the compound [2R,αS,2'S, α'S]-α, α'-[iminobismethylene]bis[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol] having the formula:
>
> 
>
> or a pharmaceutically acceptable acid addition salt thereof.

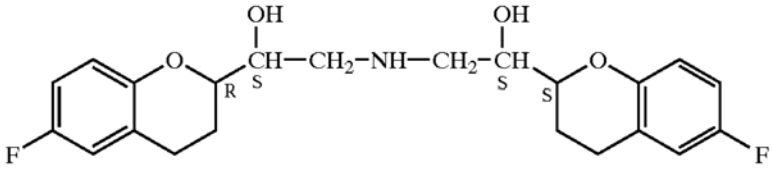
2. A pharmaceutical composition consisting of a pharmaceutically acceptable carrier and, as active ingredients:

(a) the blood pressure reducing compound [2S,αR,2'R, α'R]-α, α'-[iminobismethylene]bis[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol] having the formula:



or a pharmaceutically acceptable acid addition salt thereof; and

(b) the compound [2R,αS,2'S, α'S]-α, α'-[iminobismethylene]bis[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol] having the formula:



D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–6 of the '040 patent on the following grounds:

References	Basis	Claim(s) challenged
Van Lommen[1] in view of Handbook of Chromatography[2]	§ 103	2–6
Van Lommen and Handbook of Chromatography in view of Okamoto[3]	§ 103	1

[1] Van Lommen et al., US 4,654,362, issued Mar. 31, 1987 (Ex. 1004).
[2] HANDBOOK OF CHROMATOGRAPHY, Vol. II (Gunter Zweig, Ph.D. & Joseph Sherma, Ph.D. eds. 1972) (Ex. 1005).
[3] Okamoto et al., *Optical Resolution of β-Blockers by HPLC on Cellulose Triphenylcarbamate Derivatives*, CHEMISTRY LETTERS 1237–40 (1986) (Ex. 1006).

References	Basis	Claim(s) challenged
Van Lommen and Handbook of Chromatography in view of Armstrong[4]	§ 103	1

Petitioner also relies on the testimony of Ronald W. Millard, Ph.D. (Ex. 1052) and Daniel W. Armstrong, Ph.D. (Ex. 1050).

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 100(b); *Cuozzo Speed Techs., LLC v. Lee*, No. 15–446, 2016 WL 3369425, at *12 (U.S. June 20, 2016) (upholding the use of the broadest reasonable interpretation standard). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *See In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

The claims recite a composition "consisting of" the claimed compound. The parties agree that the transitional phrase "consisting of" is a term of art in patent law that "closes" the claim and excludes other elements, steps, or ingredients not specified in the claim. Pet. 29–30; Prelim. Resp. 23.

[4] Armstrong et al., *Separation of Drug Stereoisomers by the Formation of β-Cyclodextrin Inclusion Complexes*, 232 SCIENCE 1132–35 (1986) (Ex. 1007).

The use of "consisting of" does not exclude the presence of ordinary and expected impurities or additional components or steps that are unrelated to the invention. *Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1360 (Fed. Cir. 2006). Accordingly, we determine that the term "consisting of" does not exclude the presence of ordinary expected impurities or the presence of additional components that are unrelated to the invention.

B. 35 U.S.C. § 325(d)

Under 35 U.S.C. § 325(d), the Board has discretion to reject a petition for *inter partes* review because "the same or substantially the same prior art or arguments previously were presented to the Office." *Id.* Under the facts and circumstances of this proceeding, we exercise our discretion to deny the Petition under § 325(d).

1. Prosecution History of the '040 Patent

During prosecution, the Examiner repeatedly rejected the pending claims on several grounds, including as obvious over Van Lommen. Ex. 1002, 73–75 (Office Action mailed Nov. 10, 1992), 88–90 (Office Action mailed May 14, 1993), 114–16 (Final Office Action mailed Feb. 15, 1994). The rejected claims mirror the issued claims of the '040 patent, except the rejected claims used the transitional phrase "consisting essentially of" rather than the narrower phrase "consisting of," as recited in the patented claims. *Compare id.* at 158–60 (claims 21, 22, 24–26), *with* Ex. 1001, 11:22–12:35 (claims); *see also* Prelim. Resp. 9 (comparing side-by-side the rejected claims with the '040 patent claims).

According to the examiner, Van Lommen teaches the claims' designated compounds, "includ[ing] all position isomers inherent in the claimed compound." *See, e.g.*, Ex. 1002, 114. The examiner then stated that "a skilled artisan would have known that various isomers would exhibit

biological activity at various levels." *Id.* "Absent information to the contrary, the skilled artisan would have seen optical isomer separation as a routine procedure leading to the compounds claimed herein." *Id.*

In response to the rejections, the applicants offered a declaration from the inventor, Dr. Raymond M. Xhonneux, supporting their unexpected results argument. *Id.* at 41–45. Dr. Xhonneux described the results of a study published in the EUROPEAN JOURNAL OF PHARMACOLOGY regarding the potentiating activity of RSSS-nebivolol with SRRR-nebivolol. *Id.* (referring to Ex. 1043[5]). Dr. Xhonneux concluded that the results of the study indicate that "the (RSSS)-compound potentiates the antihypertensive effects of the (SRRR)-compound, but not the bradycardiac [e]ffects of the (SRRR)-compound." *Id.* at 44.

The examiner, however, was not persuaded by the applicants' evidence of unexpected results. *See, e.g.*, *id.* at 114–16. The examiner stated that "[a]ny information proffered to demonstrate unexpected benefits residing in any isomer must be compared to the natural racemic mixture." *Id.* at 114. The examiner also stated that the differences in biological activity between the different isomers is a difference in degree, and not patentably distinct differences in kind. *Id.* at 116.

The applicants appealed the rejection to our predecessor, the Board of Patent Appeals and Interferences. *Id.* at 137–57. In its decision, the panel reversed the examiner's rejection of the pending claims. The panel recognized that Van Lommen discloses "compound 84," a mixture of four of

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[5] Xhonneux et al., *The l-Enantiomer of Nebivolol Potentiates the Blood Pressure Lowering Effect of the d-Enantiomer*, 181 EUR. J. OF PHARM. 261–65 (1990) (Ex. 1043).

the ten possible isomers of nebivolol, and that Van Lommen states that "[p]ure stereochemically isomeric forms of the compounds . . . may be obtained by the application of art-known procedures." *Id.* at 198–99. The panel also acknowledged the examiner's argument that Van Lommen teaches the claimed compound and that a skilled artisan would have seen optical isomer separation as a routine procedure leading to the compounds claimed. *Id.* at 199.

For purposes of the appeal, the panel "accept[ed], without deciding, that the examiner has established a prima facie case of obviousness against claims 21, 22, and 24–26." *Id.* The panel then considered the Xhonneux declaration, finding that it "presents evidence supporting a conclusion that the RSSS stereoisomer, unlike its enantiomer, SRRR, 'only minimally affects blood pressure when administered alone' but significantly 'potentiates the antihypertensive effects of the (SRRR)-compound, but not the bradycardiac affects [sic] of the (SRRR)-compound.'" *Id.* at 200. The panel also found that the examiner "does not propose any reason why a person having ordinary skill in the art would have expected the RSSS stereoisomer to have such properties. Nor does the examiner contend that the potentiating property, described in the declaration, is insignificant." *Id.* Accordingly, the panel reversed the rejection under § 103 "on the strength of appellants' rebuttal evidence establishing that the claimed subject matter possesses unexpectedly superior results." *Id.*

On remand, the applicants canceled the pending claims and added new, narrower claims using the phrase "consisting of" instead of "consisting essentially of." *Id.* at 210–12. The applicants also submitted the declaration of Alain Gilbert Dupont, who provided further evidence, including several journal articles, regarding the unexpected properties of the RSSS isomer. *Id.*

at 214–16; 219–30 (Dupont Decl.). The examiner subsequently allowed the amended claims. *Id.* at 248.

2. Analysis

Patent Owner asserts that we should exercise our discretion to deny the Petition under § 325(d) because Petitioner's obviousness challenge is based on (i) the same primary reference addressed during prosecution, including by the Board in an appeal; and (ii) the same arguments regarding that primary reference and how it allegedly would have been modified. Prelim. Resp. 56–60. Upon reviewing the Petition, Preliminary Response, and the prosecution history of the '040 patent, we agree.

During prosecution, the examiner rejected the claims as obvious over Van Lommen. Here, Petitioner also relies primarily on Van Lommen to argue the claims are obvious. We, therefore, find that substantially the same prior art was previously presented to the Office.

We also find that substantially the same arguments were previously presented to the Office, including to the Board. Petitioner argues that a person of ordinary skill in the art would have selected Compound 84 of Van Lommen as a base compound for investigation and would have been motivated to stereochemically separate the stereoisomers of Compound 84 using the chromatography techniques disclosed in the secondary prior art references. Pet. 33. As Patent Owner notes, however, the examiner repeatedly stated that "the skilled artisan would have seen optical isomer separation as a routine procedure leading to the compounds claimed herein." Prelim. Resp. 57 (citing Ex. 1002, 48, 73, 88, 113). Thus, Petitioner asserts substantially the same argument that the examiner asserted during prosecution.

Petitioner also argues that the prosecution is "devoid of any discussion as to whether a POSITA would have selected Compound 84 of [Van Lommen] as a base compound for investigation, or whether a POSITA would have been motivated and able to stereochemically separate Compound 84 to create the claimed purified enantiomers using chromatography." Pet. 57. We disagree. The Board specifically referred to compound 84 in its decision, noting that it was acknowledged in the brief and at oral argument that compound 84 is an unresolved mixture of four of the ten isomers of nebivolol. Ex. 1002, 198–99. Regardless, the panel assumed the examiner established a prima facie case of obviousness and found the evidence of unexpected results was sufficient to rebut the prima facie case. *Id.* at 199–200.

Petitioner also asserts that the evidence of unexpected results should be disregarded because the declarations discuss laboratory testing that occurred after the priority date of the '040 patent. Pet. 55. We are not persuaded because the law permits consideration of evidence of unexpected results even if it was obtained after the patent's filing or issue date. *See Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1307 (Fed. Cir. 2011).

Petitioner further argues that Patent Owner did not present evidence with a sufficient nexus to the claims. Pet. 55–56. In particular, Petitioner asserts that Patent Owner did not submit evidence that the claimed compounds showed unexpected properties or results as compared to the prior art base compound (Compound 84). *Id.* at 56. The examiner made a similar argument in the Examiner's Answer to the Board, stating "[a]ny information proffered to demonstrate unexpected benefits residing in any isomer must be compared to the natural racemic mixture." Ex. 1002, 169.

The Board, however, was not persuaded by the examiner's argument, concluding the applicants' evidence of unexpected results sufficient, and implicitly finding a sufficient nexus between the evidence and the claimed invention. *See In re Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) ("For objective evidence of secondary considerations to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the *claimed invention*.") (quoting *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1246 (Fed. Cir. 2010)).

Finally, Petitioner argues that it has submitted "ample evidence" that the compounds of claims 1 and 2 would be the intended and expected result of combining the asserted references, and that claims 3–6 would not be an unexpected result of the suggested combination. Pet. 56 (citing Ex. 1050 ¶¶ 50, 56, 66, 73, 74, 81, 93, 106; Ex. 1052 ¶¶ 60–68, 93, 100). But Petitioner's cited evidence relates to how a person of ordinary skill in the art would have considered separating and studying the stereoisomers of compound 84 to be ordinary and routine. *See, e.g.*, Ex. 1050 ¶ 73 ("A POSITA at the time would have had an expectation that this stereochemical resolution could be easily achieved using known and commercially available techniques, without undue experimentation."); Ex. 1052 ¶ 93 ("[I]t is my opinion that a POSITA at the time of the '040 Patent's priority date, would have been motivated to carry out standard new-drug investigation on each of the purified stereochemical forms in order to determine the effectiveness of each stereochemical form, to determine whether the drug could be administered as a racemic mixture or whether a purified enantiomer was required, to determine the interactions between stereoisomers if administered together, and to determine the effective amounts of each compound necessary for treatment of hypertension."). The Board, however, assumed

this to be true in its prior decision by accepting, without deciding, that the examiner established a prima facie case of obviousness. Ex. 1002, 199. Nevertheless, the Board still found the unexpected results evidence presented by the applicants to be sufficient.

Finally, although the prior panel expressly set forth the deficiencies in the examiner's position with respect to the evidence of unexpected results, the Petition is silent as to those deficiencies. In particular, Petitioner has not offered sufficient evidence to show why an ordinary artisan "would have expected the RSSS stereoisomer to have such [potentiating] properties" or to show "that the potentiating property, described in the declaration, is insignificant." *See* Ex. 1002, 200. Because Petitioner has not addressed these issues, we are not inclined to reconsider the Board's prior decision. Accordingly, under the facts and circumstances of this case, we find that readjudicating substantially the same prior art and arguments as those presented during prosecution would not be an efficient use of Board resources.

III. CONCLUSION

We find that the same prior art and substantially the same arguments were presented to the Office previously. We, therefore, exercise our discretion and deny the Petition under 35 U.S.C. § 325(d).

IV. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner's request for an *inter partes* review of claims 1–6 of the '040 patent is *denied*.

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PETITIONER:
Barry Bumgardner
barry@nelbum.com
Brent Bumgardner
brent@nelbum.com

PATENT OWNER:
Jeffrey Kushan
IPRNotices@sidley.com