

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS INC.,
Petitioner,

v.

NISSAN CHEMICAL INDUSTRIES, LTD.,
Patent Owner.

Case IPR2015-01069
Patent 5,856,336

Before JACQUELINE WRIGHT BONILLA, SHERIDAN K. SNEDDEN,
and TINA E. HULSE, *Administrative Patent Judges*.

SNEDDEN, *Administrative Patent Judge*.

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

I. INTRODUCTION

Mylan Pharmaceuticals Inc. (“Petitioner”) filed a Petition to institute an *inter partes* review of claims 1 and 2 (Paper 2; “Pet.”) of U.S. Patent No. 5,856,336 B2 (Ex. 1001; “the ’336 patent”). Nissan Chemical Industries, Ltd. (“Patent Owner”) filed a Patent Owner Preliminary Response. Paper 7 (“Prelim. Resp.”).

Upon consideration of the Petition and Patent Owner Preliminary Response, we conclude that Petitioner has not established that there is a reasonable likelihood that it will prevail with respect to at least one of the challenged claims. For the reasons that follow, we do not institute an *inter partes* review.

A. *Related Proceedings*

The parties inform us of the following related litigation between them involving the ’336 patent: *Kowa Company, Ltd. v. Mylan, Inc.*, 1:14-cv-02647 (S.D.N.Y. Apr. 14, 2014). Pet. 1; Paper 5.

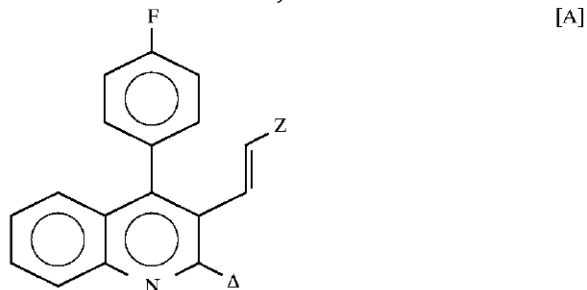
B. *The ’336 patent (Ex. 1001)*

The ’336 patent discloses mevalonolactone derivatives having a quinoline ring and their use as a pharmaceutical for reducing hyperlipidemia, hyperlipoproteinemia or atherosclerosis. Ex. 1001, 1:6–35.

C. Challenged Claims

Challenged claims 1 and 2 are reproduced below:

1. A compound of the formula,



$Z = \text{—CH(OH)—CH}_2\text{—CH(OH)—CH}_2\text{—COO. } \frac{1}{2}\text{Ca.}$

2. A method for reducing hyperlipidemia, hyperlipoproteinemia or atherosclerosis, which comprises administering an effective amount of the compound of formula A as defined in claim 1.

D. Asserted Grounds of Unpatentability

Petitioner challenges claims 1 and 2 of the '336 patent on the following grounds. Pet. 16–60.

Reference[s]	Basis	Claims Challenged
Kathawala, ¹ Kathawala Abstract, ² Hoefle, ³ Roth, ⁴ Anderson, ⁵ Wareing, ⁶ Hansch, ⁷ Suh, ⁸ Berge, ⁹ and Gould ¹⁰	§ 103	1 and 2

¹ U.S. Patent No. 4,739,073, issued Apr. 19, 1988. Ex. 1010.

² Faizulla G. Kathawala, et al., *XU 62-320, An HMG-CoA Reductase Inhibitor, More Potent Than Compactin*, Abstract for American Chemical Society library, July 29, 1987 (hereinafter “Kathawala Abstract”). Ex. 1009.

³ U.S. Patent No. 4,647,576, issued Mar. 3, 1987. Ex. 1016.

⁴ U.S. Patent No. 4,681,893, issued July 21, 1987. Ex. 1019.

⁵ U.S. Patent No. 4,751,235, issued June 14, 1988. Ex. 1020.

⁶ U.S. Patent No. 4,613,610, issued Sept. 23, 1986. Ex. 1018.

Reference[s]	Basis	Claims Challenged
Kathawala, Kathawala Abstract, Hoefle, Roth, Anderson, Wareing, Hansch, Suh, Berge, Gould, Engstrom Abstract, ¹¹ Tobert, ¹² Lee, ¹³ and Picard ¹⁴	§103	1 and 2
Picard	§ 102	1 and 2

Petitioner relies also on the Declaration of Roger Frank Newton, Ph.D. (Ex. 1008) and the Declaration of Dr. David Gortler (Ex. 1015) in support of the proposed grounds of unpatentability.

⁷ Corwin Hansch et al., “*Aromatic*” *Substituent Constants for Structure-Activity Correlations*, 16 J. MED. CHEM. 1207–1216 (1973) (hereinafter “Hansch”). Ex. 1024.

⁸ John T. Suh et al., *Angiotensin-Converting Enzyme Inhibitors New Orally Active Antihypertensive (Mercaptoalkanoyl)- and [(Acylthio)alkanoyl]glycine Derivatives*, 28 J. MED. CHEM. 57–60 (1985) (hereinafter “Suh”). Ex. 1029.

⁹ Stephen M. Berge et al., *Pharmaceutical Salts*, 66 J. PHARM. SCI. 1–19 (1977) (hereinafter “Berge”). Ex. 1027.

¹⁰ Philip L. Gould, *Salt Selection for Basic Drugs*, 33 INT. J. PHARM. 201–217 (1986). Ex. 1028.

¹¹ R. G. Engstrom et al., *Hypolipoproteinemic Effects of a Potent HMG-CoA Reductase Inhibitor*, IX International Symposium on Drugs Affecting Lipid Metabolism, Florence (Italy), Oct. 22-25, 1986 (hereinafter “Engstrom”). Ex. 1011.

¹² Jonathan A. Tobert, *New Developments in Lipid-Lowering Therapy: The Role of Inhibitors of Hydroxymethylglutaryl-Coenzyme A Reductase*, 76 CIRCULATION 534–538 (1987). Ex. 1012.

¹³ Ta-Jyh Lee, *Synthesis, SARs and Therapeutic Potential of HMG-CoA Reductase Inhibitors*, 8 TRENDS PHARMACOL. SCI. 442–446 (1987). Ex. 1013.

¹⁴ U.S. Patent No. 4,761,419, issued Aug. 2, 1988. Ex. 1021.

II. ANALYSIS

A. Claim Interpretation

We interpret claims using the “broadest reasonable construction in light of the specification of the patent in which [they] appear[.]” 37 C.F.R. § 42.100(b); *see also* Office Patent Trial Practice Guide, 77 Fed. Reg. 48,756, 48,766 (Aug. 14, 2012); *In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1278–79 (Fed. Cir. 2015) (“Congress implicitly approved the broadest reasonable interpretation standard in enacting the AIA,”¹⁵ and “the standard was properly adopted by PTO regulation.”). Under the broadest reasonable construction standard, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). “Absent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaim[s] the broader definition.” *In re Bigio*, 381 F.3d 1320, 1325 (Fed. Cir. 2004). “Although an inventor is indeed free to define the specific terms used to describe his or her invention, this must be done with reasonable clarity, deliberateness, and precision.” *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

We determine that explicit construction of any specific claim term is not necessary to determine whether to institute a trial in this case. *See, e.g., Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011) (“[C]laim terms need only be construed ‘to the extent necessary to resolve

¹⁵ The Leahy-Smith America Invents Act, Pub. L. No. 112–29, 125 Stat. 284 (2011) (“AIA”).

the controversy.’”) (quoting *Vivid Techs., Inc. v. Am. Sci. & Eng’g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999)).

B. Petitioner’s Asserted Obviousness Grounds

We generally follow a two-part inquiry to determine whether a new chemical compound would have been obvious over particular prior art compounds. *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1291–93 (Fed. Cir. 2012). First, we determine “whether a chemist of ordinary skill would have selected the asserted prior art compounds as lead compounds, or starting points, for further development efforts.” *Id.* at 1291. Second, we analyze whether there was a reason to modify a lead compound to make the claimed compound with a reasonable expectation of success. *Id.* at 1292. Establishing that a chemical compound would have been obvious over a structurally similar compound requires “a showing that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention.” *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007) (internal quotations omitted).

In the instant case, Petitioner contends that Kathawala discloses fluvastatin, which would have been a lead compound as it was known to possess “excellent *in vitro* activity and demonstrated relatively high activity for *in vivo* cholesterol biosynthesis inhibition.” Pet. 7. Petitioner argues that a “[person of ordinary skill in the art] would have considered the logical structural avenues available to further optimize [fluvastatin]” in order to achieve the compound encompassed by the claims of the ’336 patent, referred to in the Petition as pitavastatin. *Id.* at 8–9. Such “optimization”

would require, *inter alia*, adding a single carbon to the indole ring of the fluvastatin core to arrive at the quinoline ring structure of pitavastatin, relocating the isopropyl group on the nitrogen of the indole ring of the fluvastatin core to a carbon on the 2 position of the quinoline ring, and modifying the isopropyl group to a cyclopropyl group. *Id.* 8–10; 28–43. Petitioner contends that such modifications would have been routine to a person of ordinary skill in the art. *Id.*

We are not convinced that the steps needed to go from fluvastatin ultimately to pitavastatin constituted routine optimization. The process of modifying fluvastatin to pitavastatin would have required a number of chemical alterations, each having a number of possible combinations. Rather, we find that the process of modifying fluvastatin to pitavastatin would have required significant guesswork and variation of a number of parameters to achieve the end result. Prelim. Resp. 26–46. For example, if we focus on the modification of the isopropyl group to a cyclopropyl group alone, the prior art does not clearly direct a person of ordinary skill in the art to a cyclopropyl group, let alone the placement of a cyclopropyl group at the 2 position of a quinoline ring. As provided in the Petition,

Kathawala [] compounds of Formula I include compounds in which one of R_o and R is a substituted phenyl (such as 4-fluorophenyl), and the other is primary or secondary C₁₋₆alkyl not containing an asymmetric carbon atom, **C₃₋₆ cycloalkyl**, or phenyl(CH₂)_m.

Pet. 37 (emphasis in original). Petitioner contends that the C₃₋₆ cycloalkyl group contains a small number of compounds including cyclopropyl. *Id.* (citing Ex. 1008 ¶¶ 111–112). Kathawala formula I, however, describes a genus of compounds that are distinct from pitavastatin, and we find no

teaching in Kathawala directing us specifically to the use of cyclopropyl. Nonetheless, relying on Roth, for example, Petitioner contends that one of ordinary skill in the art “would have been motivated to try modifications at the 2 position with substituents similar to isopropyl” because Roth “disclosed the substitution of a trifluoromethyl group for isopropyl at the 2 position.” *Id.* at 36 (citing Roth Table 1; Ex. 1008 ¶¶ 86–99). Petitioner then contends that, as “there were a finite number of compounds that had similar size and chemistry to isopropyl, cyclopropyl would have been obvious to try.” *Id.* at 43.

Such information does not make a persuasive case that knowledge in the prior art was specific enough to identify the specific compound of the claims. *See Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1089 (Fed. Cir. 2008) (upholding the district court’s finding of non-obviousness where there were a “wide range of possible outcomes” and a “relative unlikelihood” that the desired results would be obtained); *cf. Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1367 (Fed. Cir. 2007) (“[T]he prior art provided not only the means of creating acid addition salts but also predicted the results, which Pfizer merely had to verify through routine testing.”). Rather, we conclude that the information set forth in the Petition offers an impermissible “obvious to try” situation, where the prior art provides only general guidance with regard to a line of experimentation to pursue. *See Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 997 (Fed. Cir. 2009) (“[P]atents are not barred just because it was obvious ‘to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.’”) (quoting

In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988)).

In view of the above, we are not persuaded that there is a reasonable likelihood that Petitioner would prevail at trial with respect to at least one claim of the '336 patent on either of their obviousness challenges.

C. Petitioner's Asserted Anticipation Ground

Petitioner asserts that “the genus disclosed in [Picard] clearly includes pitavastatin calcium.” Pet. 58 (citing Ex. 1021, 2:9–3:1, 9:61–68; Ex. 1008 ¶ 168). Patent Owner contends that Picard discloses a genus of thousands of compounds based on a quinoline core. Prelim. Resp. 56, (citing Ex. 1021, 2:10–3:2, 17:67–20:15).

We agree with Patent Owner. The Petition fails to explain adequately why the genus of Picard meets the test for a genus-to-species anticipation. *See Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006) (“It is well established that the disclosure of a genus in the prior art is not necessarily a disclosure of every species that is a member of that genus.”). For example, Petitioner has not established a “pattern of preferences” in Picard that points to the pitavastatin calcium species of the claims. *See Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1377 (Fed. Cir. 2006) (requiring the genus disclosure to disclose a “pattern of preferences” that reads onto the species claim in order for anticipation to be found). Accordingly, we are not persuaded that there is a reasonable likelihood that Petitioner would prevail at trial with respect to at least one claim of the '336 patent, based on anticipation of claims 1 and 2 by Picard.

III. CONCLUSION

The Petition does not persuade us that there is a reasonable likelihood that at least one of the challenged claims is unpatentable based on the asserted grounds. We deny the petition for *inter partes* review and decline to institute trial on any of the asserted grounds as to any of the challenged claims.

IV. ORDER

In consideration of the foregoing, it is hereby ORDERED that the petition is *denied* as to all challenged claims and no trial is instituted.

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