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Paper 8
Entered: October 1, 2014

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

TORRENT PHARMACEUTICALS LIMITED,
Petitioner,

v.

MERCK FROSST CANADA & CO.,
Patent Owner.

Case IPR2014-00559
Patent 6,448,274 B2

Before LORA M. GREEN, ERICA A. FRANKLIN, and ZHENYU YANG, *Administrative Patent Judges*.

YANG, *Administrative Patent Judge*.

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

I. INTRODUCTION

Torrent Pharmaceuticals Limited ("Petitioner") filed a Petition for an *inter partes* review of claims 1 and 2 of U.S. Patent No. 6,448,274 ("the '274 patent"). Paper 1 ("Pet."). Merck Frosst Canada & Co. ("Patent Owner") did not file a Preliminary Response. We have jurisdiction under 35 U.S.C. § 314.

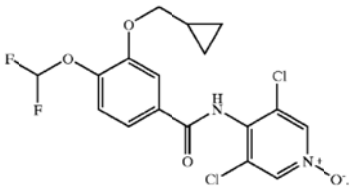
For the reasons provided below, we determine Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of at least one of the challenged claims. Because the Petition fails to meet the threshold requirement set forth in 35 U.S.C. § 314(a), we deny the Petition.

A. The '274 Patent

The '274 patent is directed to N-(3,5-Dichloro-1-oxido-pyridin-4-yl)-4-difluoromethoxy-3-cyclopropylmethoxybenzamide, which is a cAMP phosphodiesterase-4 (PDE4) inhibitor. Ex. 1001, 1:12–15. According to the '274 patent, inhibition of PDE4 "can beneficially affect allergy and inflammation symptoms." *Id.* at 1:46–49.

Claims 1 and 2 read:

1. A compound represented by Formula (I):



2. A pharmaceutical composition comprising a therapeutically effective amount of

the compound according to claim 1 or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier.

B. Asserted Grounds of Unpatentability

Petitioner challenges claims 1 and 2 as anticipated by PCT Publication No. WO 94/02465 (published on February 3, 1994) (Ex. 1002, "Fenton"). Pet. 13. Petitioner also alleges that Fenton, together with PCT Publication No. WO 92/12961(published on August 6, 1992) (Ex. 1003, "Ashton") and a skilled artisan's general knowledge, renders claims 1 and 2 obvious. *Id.* Both Fenton and Ashton were published more than one year before the priority date (May 25, 2000) of '274 patent and thus, qualify as art under 35 U.S.C. § 102(b).

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, the Board interprets a claim term in an unexpired patent according to its broadest reasonable construction in light of the specification of the patent in which it appears. 37 C.F.R. § 42.100(b). Under this standard, we assign claim terms their ordinary and customary meaning, as understood by a person of ordinary skill in the art, in the context of the entire patent disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

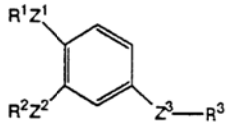
Petitioner proposes a construction for the chemical formula recited in claim 1. Pet. 10. Petitioner also asks us to construe the terms "pharmaceutical composition comprising a therapeutically effective amount" and "pharmaceutically acceptable carrier." *Id.* at 10–11. Petitioner does not explain how the constructions of these terms are material to our decision of whether to institute a trial, and we conclude that such constructions are not

necessary at this time. Thus, we decline to construe these terms expressly for purposes of this Decision.

B. Prior Art

1. Fenton

Fenton teaches compounds in the following formula:



wherein

R^1 is lower alkyl;

R^2 is alkyl, alkenyl, cycloalkyl, cycloalkenyl, cyclothioalkyl or cyclothioalkenyl;

R^3 is aryl or heteroaryl;

Z, Z^1, and Z^2 are independently oxygen or sulfur;

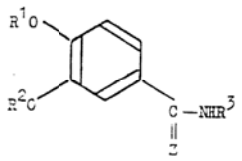
Z^3 is -CH=CH-, -C≡C-, -CH2-CZ-, -CZCH2-, -CZ-CZ-, -CH2-NH-, -CH2-O-, -CH_2-S-, -CX_2-O-, -CZNH-,.-NH-CH_2-, -O-CH_2-, -SCH_2-, -$SOCH_2$-, -SO_2CH_2-, -O-CX_2-, -O-CZ-, -NH-CZ-, -N=N-, -NH-SO_2-, -SO_2-NH- , -CZ-CZ-NH-, -NH-CO-O-, -O-CO-NH- or -NH-CO-NH-; and

X is halo.

Ex. 1002, 7. Fenton also teaches "an N-oxide thereof or a pharmaceutically acceptable salt thereof." *Id.* According to Fenton, these compounds, through their ability to inhibit PDE4, are useful in treating inflammatory and autoimmune diseases. *Id.*

2. Ashton

Ashton teaches benzamide derivatives depicted in the following formula:



"wherein R^1 represents alkyl, R^2 represents alkyl or mono-, bi- or tricycloalkyl, R^3 represents an optionally substituted phenyl, naphthyl or heterocyclyl group, and Z represents oxygen or sulphur."[1] Ex. 1003, Abstract, 1–2. Ashton also teaches the N-oxides of the compounds "when said heterocyclyl groups contain one or more nitrogen ring atoms." *Id.* at Abstract, 2. According to Ashton, compositions containing these compounds, and their pharmaceutically acceptable salts, are useful, for example, as bronchodilators and asthma-prophylactic agents, in treating conditions that can be ameliorated by administering a PDE inhibitor. *Id.* at 10.

Ashton discloses that "[e]specially important compounds" include those wherein at least one of R^1, R^2, and R^3 is selected from the following:

(i) R^1 represents a methyl group;
(ii) R^2 represents a propyl, butyl, nonyl, dodecyl, cyclohexyl, 8,9,10-trinorbornyl or, more especially, cyclopentyl group; and/or
(iii) R^3 represents an optionally substituted pyrazinyl, pyrimidinyl, isoxazolyl, preferably pyridyl group, or an N-oxide thereof, or an optionally substituted phenyl group.

Id. at 3.

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[1] According to the Petition, R^1 in Ashton and R^1 in Fenton correspond to the same position. Pet. 26. Similarly, R^2 and R^3 in the two references correspond to the same respective positions. *Id.* Further, -CZNH- in Ashton corresponds to Z^3 in Fenton. *Id.* at 26–27.

C. Anticipation

Referring to various excerpts in Fenton that teach preferred classes of substituents at the positions of R^1, R^2, R^3, Z^1, Z^2, and Z^3, Petitioner asserts that Fenton discloses each and every limitation of claims 1 and 2 "arranged as claimed," and thus, anticipates the challenged claims. Pet. 13–23. We disagree.

For example, according to Petitioner, challenged claim 1 has difluorinated methyl at the position corresponding to R^1 in Fenton. *Id.* at 16. Petitioner asserts that Fenton discloses "lower alkyl substituted by halo" as preferred R^1 (*id.* at 16 (citing Ex. 1002, 12:17–21, 12:36–37, 13:7–10)), with lower alkyl being "about 1 to about 4 carbon atoms in the chain which may be straight or branched" (Ex. 1002, 8:9–10).[2] Petitioner also points out that Fenton discloses:

> Compounds of the invention wherein R^1 is substituted by halo, preferably fluoro, are preferred. It is also preferred that the halo substitution is on positions of the R^1 that are adjacent to the position of R^1 that is attached respectively to Z^1.

Pet. 16 (citing Ex. 1002, 14:1–4). Based on these disclosures, Petitioner concludes "Fenton prefers [R^1] as a fluorinated methyl group – including difluoro – as recited in [the challenged] claim 1." *Id.*

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[2] Petitioner cites Ex. 1002, 8:27–28 for the proposition that "Fenton discloses R^1 as a lower alkyl (lower alkyls are about 1–4C)." Pet. 16. The cited portion of Fenton, however, in its entirety, reads "'Cycloalkyl' means a non-aromatic mono- or multicyclic ring system of about 3 to about 10 carbon atoms. Preferred monocyclic cycloalkyl rings," and thus, does not support Petitioner's statement. *See* Ex. 1002, 8:27–28.

Through similar analyses, Petitioner argues that Fenton prefers cyclopropylmethyl at the R^2 position (*id.* at 17); 3,5-dihalopyrid-4-yl N-oxide at R^3 (*id.* at 18); oxygen at both Z^1 and Z^2 (*id.* at 19–20); and -CZNH- (where Z is O) at Z^3 (*id.* at 21–22). A combination of these preferred substituents at these positions, according to Petitioner, results in the same formula as the compound recited in challenged claim 1. *Id.* at 14.

Petitioner's argument runs afoul of well-settled law on anticipation. To anticipate, a prior art reference "must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim.'" *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008) (quoting *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)).

Fenton, the purported anticipatory reference, does not satisfy this requirement. It does not show the specific combination as illustrated in the challenged claim 1, but only demonstrates classes of possible substituents at various positions. Ex. 1002, 9–16. Fenton does teach certain subclasses of substituents as preferred; but the scope and content of these subclasses are not so specific as to be deemed a disclosure of the claimed combination. In particular, Fenton does not present so short and selective a list of these subclasses that a person of ordinary skill would, as Petitioner asserts, "at once envisage" the claimed compound. Pet. 23; *see Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1376 (Fed. Cir. 2006).

In sum, Petitioner has not shown Fenton discloses all of the limitations of claim 1 "arranged or combined in the same way as in the claim." *Net MoneyIN*, 545 F.3d at 1370. Therefore, we conclude Petitioner

has not established a reasonable likelihood that it would prevail in showing Fenton anticipates claims 1 or 2.

D. Obviousness

Petitioner asserts that claims 1 and 2 would have been "obvious over Fenton, including in view of Ashton, and a [skilled artisan's] general knowledge." Pet. 25. Petitioner's argument is unpersuasive.

Petitioner bases its asserted obviousness ground on the structural similarities between the claimed compound and the prior art compounds. *See id.* at 25–31. Generally, in such cases, to establish obviousness of a claimed compound, a challenger of the claim needs to identify some reason that would have led a skilled artisan to select and then modify a known compound. *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). The requisite motivation can come from any number of sources, and need not necessarily be explicit in the art. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008).

Petitioner repeats that Fenton's "hierarchy of preferred substituents" at the positions of R^1, R^2, R^3, Z^1, Z^2, and Z^3 would have led one skilled in the art to the exact compound recited in claim 1. Pet. 25. In addition, Petitioner contends, "Ashton would have solidly reinforced Fenton's teaching." *Id.* For example, as discussed above, Petitioner asserts that Fenton prefers "a fluorinated methyl group – including difluoro" as R^1. *See supra* Section II.C. Petitioner also observes that the exemplary compounds in Ashton exclusively have methyl as R^1. Pet. 30. According to Petitioner, one skilled in the art "would thus favor this methyl moiety, but make the fluorine substitutions that Fenton favors." *Id.* Through similar analyses, Petitioner contends that "using Fenton and Ashton," a skilled artisan would have

chosen the claimed substituents as "the most promising moieties" and "would easily and directly arrive at the claimed N-Oxide compound." *Id.* at 28–31.

Petitioner's arguments are tenuous at best. In order to illustrate our reasoning, however, we treat them as if they were correct. Even with such a head start, Petitioner cannot meet its burden. A proper obviousness inquiry analyzes the differences between the prior art and the claimed invention as a whole. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1383 (Fed. Cir. 1986) ("Focusing on the obviousness of substitutions and differences instead of on the invention as a whole . . . was a legally improper way to simplify the difficult determination of obviousness."). Here, even assuming, as Petitioner contends, one skilled in the art would have chosen, *separately*, difluoromethyl at R^1, cyclopropylmethyl at R^2, 3,5-dihalopyrid-4-yl N-oxide at R^3, oxygen at both Z^1 and Z^2, and CONH- at Z^3, Petitioner has not sufficiently explained why one skilled in the art would have selected the claimed substituents at each of the six independent positions *all at once*. In other words, Petitioner has not shown some objective teaching in the prior art or some general knowledge in the art that would have led one of ordinary skill to combine the relevant teachings of the references to arrive at the claimed invention. *See In re Johnston*, 435 F.3d 1381, 1385 (Fed. Cir. 2006).

Petitioner also argues that secondary considerations do not render the challenged claims unobvious. Pet. 3, 33–48. Because Petitioner has not shown that one of ordinary skill would have had a reason or motivation to modify the Fenton and/or Ashton prior art compounds, we need not examine the argument on secondary considerations. Nevertheless, we note that

Petitioner directs our attention to two compounds expressly listed in Fenton: DI (3-cyclopentylmethoxy-N-(3,5-dichloropyrid-4-yl)-4-methoxybenzamide) and DJ (3-cyclopropylmethoxy-N-(3,5-dichloropyrid-4-yl)-4-methoxybenzamide). Pet. 40. Petitioner appears to argue that the N-oxides of these two compounds are the closest prior art compounds. *Id.* Assuming, without deciding, that is the case, Petitioner fails to explain how a skilled artisan would have identified those two compounds from the list of 147 exemplary compounds (A through EQ) as the lead compounds, especially because Fenton does not identify either DI or DJ in its list of 16 "[p]referred compounds." *See* Ex. 1002, 26. Moreover, Petitioner does not provide any evidence or reasoning as to why a skilled artisan would have modified those two compounds to arrive at the claimed compound.

In sum, Petitioner has failed to advance some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). Therefore, we conclude Petitioner has not established a reasonable likelihood that it would prevail in showing Fenton and Ashton would have rendered claims 1 or 2 obvious.

III. CONCLUSION

Petitioner has failed to establish a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim of the '274 patent.

IV. ORDER

Accordingly, it is

ORDERED that the Petition is *denied*.

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