



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
**United States Patent and Trademark Office**  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/506,017	02/23/2017	Gary G. Deng	X20396	4924
25885	7590	10/18/2019	EXAMINER	
ELI LILLY & COMPANY PATENT DIVISION P.O. BOX 6288 INDIANAPOLIS, IN 46206-6288			COUGHLIN, MATTHEW P	
			ART UNIT	PAPER NUMBER
			1626	
			NOTIFICATION DATE	DELIVERY MODE
			10/18/2019	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE PATENT TRIAL AND APPEAL BOARD

---

*Ex parte* GARY G. DENG, DANWEN HUANG,  
CYNTHIA DARSHINI JESUDASON, and JOSHUA O. ODINGO<sup>1</sup>

---

Appeal 2019-004604  
Application 15/506,017  
Technology Center 1600

---

BEFORE DONALD E. ADAMS, ERIC B. GRIMES, and RYAN H. FLAX,  
*Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to chemical compounds, which have been rejected based on 35 U.S.C. § 112(d) and obviousness-type double patenting. We have jurisdiction under 35 U.S.C. § 6(b). We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM the rejection based 35 U.S.C. § 112(d) but REVERSE the rejections for double patenting. Thus, we AFFIRM-IN-PART.

---

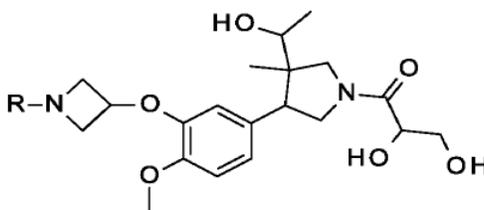
<sup>1</sup> Appellant identifies the real party in interest as Eli Lilly and Company. Appeal Br. 1. We use the word Appellant to refer to “applicant” as defined in 37 C.F.R. § 1.42(a).

### STATEMENT OF THE CASE

The Specification discloses “compounds which are inhibitors of PDE4 [phosphodiesterase 4] and as such, are useful in treatment of overactive bladder.” Spec. 1:28–29.

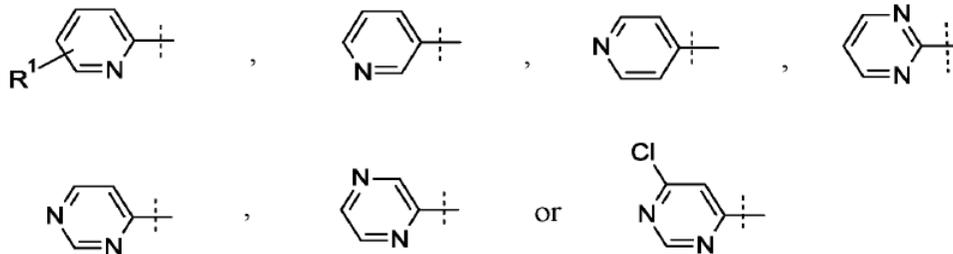
Claims 1–3, 5, and 7–10 are on appeal.<sup>2</sup> Claim 1 is illustrative and reads as follows:

1. A compound of the formula



wherein

R is



R<sup>1</sup> is CH<sub>3</sub>, CD<sub>3</sub>, CN, Cl or CF<sub>3</sub>;

provided when R<sup>1</sup> is CH<sub>3</sub> or CD<sub>3</sub> it is not attached at the 5 position;

or a pharmaceutically acceptable salt thereof.

The claims stand rejected as follows:

Claim 5 under 35 U.S.C. § 112(d) as being in improper dependent form (Ans. 3);

---

<sup>2</sup> Claims 4 and 6 are also pending but are not subject to any outstanding rejection.

Claims 1–3, 5, and 7–10 on the basis of nonstatutory obviousness-type double patenting based on claims 1–6 of U.S. Patent 9,034,864 (“‘864 Patent”), by itself or combined with Hood<sup>3</sup> (Ans. 5);

Claims 1–3, 5, and 7–10 on the basis of nonstatutory obviousness-type double patenting based on claims 1–4 of U.S. Patent 9,266,859 (“‘859 Patent”) (Ans. 10); and

Claims 1–3, 5, and 7–10 on the basis of nonstatutory obviousness-type double patenting based on claims 3 and 4 of U.S. Patent 9,604,967 (“‘967 Patent”), by itself or combined with Hood (Ans. 15).

## OPINION

### *Improper Dependent Form*

The Examiner has rejected claim 5 under 35 U.S.C. § 112(d) “as being of improper dependent form” because “[t]he last option in claim 5 provides for a -CD<sub>3</sub> group at the 5-position of a pyridyl ring, which is excluded from claim 1 by provision.” Ans. 3.

Appellant did not dispute the merits of this rejection in the Appeal Brief. With the Reply Brief, Appellant filed an amendment “to specifically address said rejection.” Reply Br. 6.

However, amendments filed after the appeal brief may only be admitted “to cancel claims, where such cancellation does not affect the scope of any other pending claim in the proceeding, or . . . [t]o rewrite dependent claims into independent form.” 37 C.F.R. § 41.33(b). “All other

---

<sup>3</sup> Hood et al., *Common theme for drugs effective in overactive bladder treatment: Inhibition of afferent signaling from the bladder*, International Journal of Urology 20:21–27 (2013).

amendments filed after the date of filing an appeal . . . will not be admitted except as permitted by §§ 41.39(b)(1), 41.50(a)(2)(i), and 41.50(b)(1),” none of which apply here. 37 C.F.R. § 41.33(c).

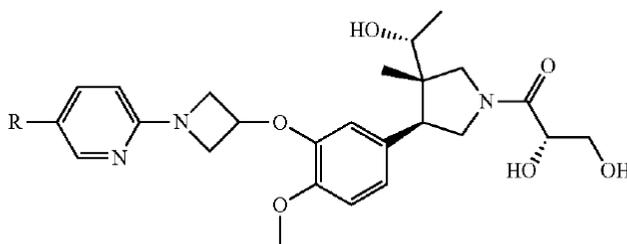
We therefore affirm the rejection of claim 5 under 35 U.S.C. § 112(d).

#### *Obviousness-type Double Patenting*

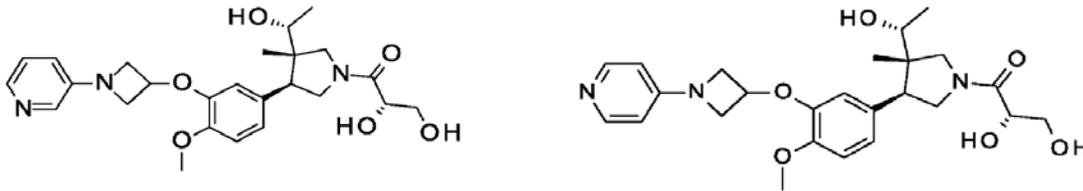
The Examiner has rejected claims 1–3, 5, and 7–10 for obviousness-type double patenting, based on: (1) the '864 Patent, by itself or combined with Hood; (2) the '859 Patent; and (3) the '967 Patent, by itself or combined with Hood. Ans. 5, 10, 15. The Examiner's reasoning is substantively the same for each of the rejections, and Appellant relies on the same arguments with respect to all of the rejections, so we will address them together.

We will focus on the rejection based on the '864 Patent. Hood is cited only with respect to claim 10 (which requires combining the claimed compound with tadalafil), and therefore is not relevant to the dispositive issue.

The Examiner finds that the '864 Patent claims two compounds, of the following formula:

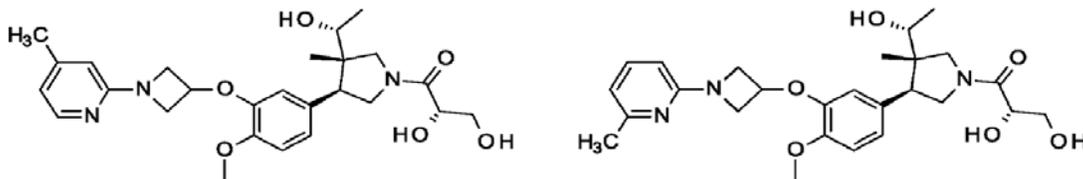


wherein R is hydrogen or methyl. Ans. 5 (citing '864 Patent, claim 2). The Examiner finds that the rejected claims of the instant application encompass the following compounds:



*Id.* at 6. The Examiner finds that these compounds “differ from the patented compound where R is H based on the point of attachment on the pyridine ring.” *Id.* at 7.

The Examiner also finds that the rejected claims of the instant application encompass the following compounds:



*Id.* The Examiner finds that these compounds “differ from the patented compound where R is CH<sub>3</sub> based on the location of methyl substitution on the pyridine ring.” *Id.*

The Examiner concludes that “[t]he instant claims encompass obvious variations of the patented compounds (and by extension the same compositions and methods thereof).” *Id.* at 6. The Examiner reasons that

[i]t is well established that position isomers are *prima facie* structurally obvious even in the absence of a teaching to modify. The isomer is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers.

*Id.* at 7.

The Examiner also reasons that the latter two compounds reproduced above (with H<sub>3</sub>C- substituents on the left side) “could similarly be said . . . [to be] homologs of the patented compound with R is H” because “[t]he

compounds above differ from the patented compound based on the replacement of hydrogen with methyl.” *Id.* at 8.

The Examiner finds that a skilled artisan “would expect that the compounds could be prepared by the same method as taught by the patent and have the same utility as the compounds taught by the patent.” *Id.* at 9. “[T]he replacement of hydrogen for an alkyl group falls under the well-established doctrine of homology, which assumes that homologous compounds are likely to have similar properties.” *Id.* at 10.

Appellant argues that the “claims cited in the rejections are . . . limited to wherein R is only hydrogen or methyl, and further to wherein R is only limited to the five position of the pyridinyl group, which is only attached to the backbone at the two position.” Appeal Br. 10. Appellant argues that “the Examiner has not provided a reasoned explanation, based on any teaching of the prior art for these particular compounds, to establish that a skilled artisan would have been lead [sic] to start from the cited claims . . . and then arrive at the presently claimed compounds, with a reasonable expectation of success.” *Id.* at 11.

Appellant disagrees that “general propositions such as homologs or positional isomers are legally sufficient to establish obviousness.” *Id.* “Applicants specifically reject the allegation that positional isomers are prima facie obvious based only on general assumptions,” and “the rejection does not provide a reasoned basis for this conclusory finding.” *Id.* at 12, citing *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007).

Appellant argues that the rejection is based on the “type of misreading and misapplication of the recited cases [that] was clearly addressed in *In re Grabiak*, 769 F2d 729 (Fed. Cir. 1985),” which stated that “generalization should be avoided insofar as specific chemical structures are alleged to be prima facie obvious one from the other.” Reply Br. 12. Appellant argues that “[t]he Office’s assertion that ‘that ring-walking a methyl group or replacing hydrogen with methyl’ would be predictable is exactly the type of generalization forbidden by *Grabiak*,” *id.* at 13, and “[t]he Office has provided no prior art reference which provides the motivation to make such modifications to the two compounds of claim 2 in U.S. Patent No. 9,034,864.” *Id.* at 15.

We agree with Appellant that the double patenting rejections are not supported by a preponderance of the evidence. Specifically, the cited evidence does not adequately show that, at the time the instant application was filed, a person of ordinary skill in the art would have had a reason to modify the claimed compounds in the specific manner required to produce the instantly claimed compounds, with a reasonable expectation that the new compounds would retain the activity of inhibiting PDE4.

The Examiner cites several cases for the proposition that “position isomers are *prima facie* structurally obvious even in the absence of a teaching to modify.” Ans. 7. Similarly, the Examiner cites cases for the proposition that replacing a hydrogen on a known compound with a methyl group is obvious because “the replacement of hydrogen [with] an alkyl group falls under the well-established doctrine of homology, which assumes that homologous compounds are likely to have similar properties.” *Id.* at 10.

The Examiner's position, however, is not supported by precedent. As Appellant pointed out, the *Grabiak* court cautioned that "generalization should be avoided insofar as specific chemical structures are alleged to be *prima facie* obvious one from the other." 769 F.2d at 731. In that case, the court held that "there must be adequate support in the prior art for the ester/thioester change in structure, in order to complete the PTO's *prima facie* case." *Id.* at 731–32. "The PTO cited no pertinent reference showing or suggesting to one of ordinary skill in the art the change of a thioester for an ester group," and the court reversed the rejection. *Id.* at 732.

The court has characterized *Grabiak* as holding that, "[i]n addition to structural similarity between the compounds, a *prima facie* case of obviousness also requires a showing of 'adequate support in the prior art' for the change in structure." *Takeda*, 492 F.3d at 1356. The *Takeda* court noted that *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995), stated that a known compound may suggest its homolog or isomer because such compounds often have similar properties. 492 F.3d at 1356. The court noted that *Deuel* "clarified, however, that in order to find a *prima facie* case of unpatentability in such instances, a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention' was also required." *Id.*

Thus, the instantly claimed compounds cannot be rejected as obvious variants of the patented compounds based on structural similarity by itself. That conclusion also requires a showing that, based on what was known at the time, a skilled artisan would have had a reason to make the specific molecular modifications required; i.e., to attach a methyl group at the 4 or 6

position of the pyridine ring (rather than at the 5 position), or to attach the (unsubstituted) pyridine ring at a carbon other than the 2 position.

The Examiner points out that the patented claims encompass “two compounds that differ by the presence [or] absence of a methyl group on a pyridine ring (for the variable R),” both of which “have similar utility.” Ans. 23. That is, the R group can be either hydrogen or methyl in the patented compounds, and both compounds inhibit PDE4. The Examiner concludes that “[i]f the claims of the patent demonstrate anything it is that hydrogen/methyl variation on the pyridine ring is tolerated.” *Id.*

As Appellant has pointed out, however, “this is the only structural change taught in U.S. Patent No. 9,034,864, and this change occurs only in the para position [i.e., position 5]. No other substitutions on this ring are taught in U.S. Patent No. 9,034,864.” Reply Br. 11.

We agree with Appellant that the two patented compounds, which differ only by having either hydrogen or methyl at position 5 of the pyridine ring, do not provide an adequate basis for the rejections. That is, the two compounds might support a conclusion that limited variation at the 5 position of the pyridine ring is unlikely to affect PDE4 inhibitor activity. They do not, however, show the effect of any variations at different positions of the pyridine ring, or the effect of varying the point of attachment of the pyridine ring to the rest of the molecule.

Thus, the evidence relied on in support of the rejections does not adequately show that—without the later disclosure that certain structurally related compounds also inhibit PDE4—a skilled artisan would have had a reason to make the specific molecular modifications to the patented

compounds that are required by the claims on appeal, with a reasonable expectation that they would have similar activity. We therefore reverse all of the rejections for obviousness-type double patenting.

### DECISION SUMMARY

In summary:

<b>Claims Rejected</b>	<b>35 U.S.C. §</b>	<b>Basis</b>	<b>Affirmed</b>	<b>Reversed</b>
5	112(d)	Improper Dependent Form	5	
1-3, 5, 7-10		Obviousness-type Double Patenting; '864 Patent, Hood		1-3, 5, 7-10
1-3, 5, 7-10		Obviousness-type Double Patenting, '859 Patent		1-3, 5, 7-10
1-3, 5, 7-10		Obviousness-type Double Patenting, '967 Patent, Hood		1-3, 5, 7-10
<b>Overall Outcome</b>			5	1-3, 7-10

### TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED-IN-PART