UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte KEN CHOW, DANIEL W. GIL, JAMES A. BURKE, DALE A. HARCOURT, MICHAEL E. GARST, LARRY A. WHEELER, and STEPHEN A. MUNK

Appeal 2008-4221
Application 09/948,001
Technology Center 1600

Decided: August 12, 2008

Before ERIC GRIMES, LORA M. GREEN, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a process for the treatment of chronic pain, which the Examiner has rejected as failing to enable the full scope of the claims. We have jurisdiction under 35 U.S.C. § 6(b). We reverse and enter a new ground of rejection.

Background

"Compounds which have adrenergic activity are well known in the art, and are described in numerous United States and foreign patents and in scientific publications" (Spec. 1). The Specification discloses that "pharmaceutical compositions having an adrenergic compound or compounds as the active ingredient are useful for treating glaucoma, chronic pain, nasal congestion, high blood pressure, congestive heart failure and inducing anesthesia" (Spec. 1). The Specification also notes that the "two main families of adrenergic receptor are termed alpha adrenergic receptors and beta adrenergic receptors in the art, and each of these two families is known to have subtypes" (Spec. 1).

Appellants teach that the "adrenergic compounds which act selectively, and preferably even specifically as agonists of the α2B or α2B / α2C . . . receptor subtypes in preference over the α2A receptor subtype, possess desirable therapeutic properties associated with adrenergics but without having one or more undesirable side effects" (Spec. 2).

Statement of the Case

The Claims

Claims 88-113 are on appeal. We will focus on claims 88 and 103 which are representative and read as follows:

> 88. A process for the treatment of chronic pain comprising administering to a host mammal suffering from chronic pain a pharmaceutical composition containing an effective dose of a compound having adrenergic activity wherein said compound is a selective agonist of the α2B

> adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype.
>
> 103. A process for treating or preventing a condition selected form the group consisting of muscle spasticity including hyperactive micturition, diarrhea, diuresis, withdrawal syndromes, pain including neuropathic pain, neurodegenerative diseases including optic neuropathy, spinal ischemia and stroke, memory and cognition deficits, attention deficit disorder, psychoses including manic disorders, anxiety, depression, hypertension, congestive heart failure, cardiac ischemia and nasal congestion without the degree of sedation or depression of heart rate or blood pressure associated with agonism of the alpha 2a receptor comprising administering to said mammal a pharmaceutical composition comprising an effective dose of a compound wherein said compound is a selective agonist of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor receptor subtype(s) as compared to the α2A adrenoceptor receptor subtype.

The rejection as presented by the Examiner is as follows:

Claims 88-113 stand rejected under 35 U.S.C. § 112, first paragraph as being nonenabled for the full scope of the claims (Ans. 3).

35 U.S.C. § 112, first paragraph Enablement rejection

Claims 88-113 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the Specification

> while being enabling for treating chronic pain or elevated intraocular pressure, treating a mammal to lower intraocular pressure, treating muscle spascity.., nasal congestion and a method of selectively agonizing the α2B adrenoceptor adrenoceptor subtype or α2B/ α2C adrenoceptor subtypes without significantly agonizing the α2A adrenoceptor subtype using a compound of the formula I shown on page 6

> of the specification or the specific amino oxazolines, amino imidazolines and imidazolines set forth in the specification does not reasonably provide enablement for treating chronic pain or elevated intraocular pressure, treating a mammal to lower intraocular pressure, treating or preventing muscle spascity.., nasal congestion and a method of selectively agonizing the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtypes without significantly agonizing the α2A adrenoceptor subtype using all compounds which are selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype.

(Ans. 3-4.)

The Examiner reasons that "[a]n undue amount of experimentation is needed to determine which compounds are selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype" (Ans. 5).

Appellants argue that the "patent specification 1) provides explicit disclosure of methods of administering compounds having the claimed selectivity, and b) explicitly describes the synthesis and structure of a representative number of such compounds of 4 different core structures. Given such disclosure, the specification clearly provides such disclosure as enables a person of skill in the art to carry out the claimed method" (App. Br. 5). Appellants note that the "high throughput activity-based receptor screening had, as of the filing date of this application, become routine and commonplace. As such, such methods were not undue experimentation" (App. Br. 6).

According to Appellants regarding a correlation between compounds which meet the functional requirement of claim 88 and their ability to treat the conditions listed in claim 88, the "Examiner has provided absolutely no evidence supporting the contention that there is no such correlation. In the absence of any such evidence the Applicants' assertion that such correlation does exist must be presumed to be accurate." (App. Br. 8).

In view of these conflicting positions, we frame the enablement issue before us as follows:

Would it have required undue experimentation to identify additional compounds which are selective antagonists of the α2B adrenoceptor subtype or α2B/ α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype which function to treat conditions including chronic pain?

Findings of Fact (FF)

Breadth of the Claims

1. Claim 1 is not limited to the specific compounds disclosed in the specification but is open to any compound meeting the functional requirements (*see* Claim 1).

Presence of Working Examples

2. The Specification discloses "over 80 compounds, the majority of which are disclosed to have the selectivity required by claim 88" (App. Br. 4).

Amount of Direction or Guidance Presented

3. The Specification teaches a specific assay to identify compounds which have the selectivity required by claim 88 (Spec. 81:25 to 83:20).

4. The Specification teaches 84 different structures (Spec. 83-105).

5. The Specification teaches techniques to measure compound effects on intraocular pressure and cardiac side effects (Spec. 105-111).

6. The Specification teaches "a rodent model of neuropathic pain that is known to be predictive of clinical activity" (Spec 114:22-23).

State of the Prior Art and Unpredictability of the Art

7. The Examiner states that "there is unpredictability in the art" (Answer 4) but made no factual findings demonstrating unpredictability in the art.

Quantity of Experimentation necessary

8. The Examiner made no factual findings regarding the quantity of experimentation necessary to carry out the invention.

9. Appellants state that the "high throughput activity-based receptor screening had, as of the filing date of this application, become routine and commonplace. As such, such methods were not undue experimentation" (App. Br. 6).

Discussion of 35 U.S.C. § 112, first paragraph Enablement rejection

"The essential question here is whether the scope of enablement … is as broad as the scope of the claim[s]." *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991).

We agree with the Appellants that the Examiner has not provided sufficient evidence to show that it would have required undue experimentation to practice of the full scope of the claimed invention.

Other than breadth of the claims, the other *Wands* factors favor Appellants, particularly "the amount of direction or guidance presented", "working examples" and "quantity of experimentation"," *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Even the factor of "the predictability or unpredictability of the art" weighs in favor of Appellants, since the Examiner made no factual findings that identification of compounds meeting the selectivity requirements of claim 88 would be unpredictable.

> It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Angstadt*, 537 F.2d 498, 502-03 [] (CCPA 1976). However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill in the art how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility.

In re Vaeck, 947 F.2d 488, 496 (Fed. Cir. 1991). In the instant fact pattern, there is significant disclosure of methods for making and screening selective antagonists of the α2B adrenoceptor subtype or α2B/ α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype which function to treat conditions (*see* FF 1-9).

We are not persuaded by the Examiner's argument that "[w]hile applicants have described assays to teach a person of skill in the art how to find additional compounds with the desired selectivity it only enables treatment of the claimed conditions with the compounds in the specification" (Ans. 7). The Examiner has the initial burden to establish a reasonable basis

to question the enablement provided for the claimed invention and no such evidence or scientific reasoning is present in the instant rejection. *See In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993) (Examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure).

We also do not find persuasive the Examiner's argument that "[n]one of the examples in the specification teach how to prevent the conditions set forth in claims 103 to 113. The conditions such as hypertension, psychoses, pain and congestive heart failure are treatable but not preventable" (Ans. 7). We note that claim 103 claims the alternatives of "treating or preventing" and the Examiner admits that these conditions are treatable. The Examiner has provided no reason or evidence to support the position that the stated conditions are not preventable and therefore has failed to establish a reasonable basis to question the enablement.

We reverse the rejection of claims 88-113 under 35 U.S.C. § 112, first paragraph, enablement.

New ground of rejection

Under the provisions of 37 C.F.R. § 41.50(b), we enter the following new ground of rejection.

Claims 88-113 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Findings of Fact

10. Claims 88-113 encompass compounds which are not described in the Specification since the claim encompasses any compounds which are selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype but the Specification only discloses four core structures and 84 total compounds (*see* Claims 88-113, Specification 6-12).

11. The Specification provides a functional definition for the desired compounds, but the claims impose no structural requirements whatsoever (*see* Claims 88-113, Spec. 3:15-26).

12. The Specification fails to identify which region, or regions, within the four disclosed core structures are involved in adrenergic receptor binding (*see* Spec. 1-20).

Discussion

Describing a claim to a method requires describing the compounds used in the method:

> the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods. As the district court observed, "[t]he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment."

University of Rochester v. G.D. Searle & Co., 358 F.3d 916, 926 (Fed. Cir. 2004).

Claims 88-113 require the use of a compound which, when administered to a host, will be capable of both treating a condition and functional as a selective agonist of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype. The Specification therefore must adequately describe that genus of compounds.

The written description requirement can be met by disclosing "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002).

In this case, the Specification provides the complete structure of four core structures (*see* FF 10). The Specification provides no information on what structural elements of the disclosed compounds causes the adrenergic activity (*see* Spec. 4:3-18, where only functional activity is assayed).

The Specification does not describe any of the specific structural features of adrenergic receptors which give rise to the function that permits compounds to act as selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype. In fact, the Specification fails to identify which region, or regions, within the four disclosed core structures are involved in adrenergic receptor binding (FF 12).

The present case is therefore analogous to *Rochester*. In *Rochester*, the patent claimed a method of selectively inhibiting the enzyme PGHS-2

(also known as COX-2) by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product to a human." *Rochester*, 358 F.3d at 918. The patent "describes in detail how to make cells that express either COX-1 or COX-2, but not both . . ., as well as 'assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.'" *Rochester*, 358 F.3d at 927.

The court held that "[e]ven with the three-dimensional structures of enzymes such as COX-1 and COX-2 in hand, it may even now not be within the ordinary skill in the art to predict what compounds might bind to and inhibit them." *Rochester*, 358 F.3d at 925. There is no evidence of record in the Specification that prediction of compounds which bind to adrenergic receptors was within the ordinary skill in the art at the time this invention was filed.

As in *Rochester*, the present application discloses the assay for screening for compounds that act as selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype but fails to provide any mode of identification other than trial and error.

> As the district court pointed out: Tellingly, . . . what plaintiff's experts' [sic] do not say is that one of skill in the art would, from reading the patent, understand what compound or compounds-which, as the patent makes clear, are necessary to practice the claimed method-would be suitable, nor would one know how to find such a compound except through trial and error . . . . Plaintiff's experts opine that a person of ordinary skill in the art

> would understand from reading the ’850 patent what method is claimed, but it is clear from reading the patent that one critical aspect of the method-a compound that selectively inhibits PGHS-2 activity-was hypothetical, for it is clear that the inventors had neither possession nor knowledge of such a compound.

Rochester, 358 F.3d at 925-926.

Just as in *Rochester*, it is hypothetical and unknowable which compounds will share the claimed activity as selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype.

As *Enzo* notes, written description may be met with "*functional characteristics when coupled with a known or disclosed correlation between function and structure*, or some combination of such characteristics." *Enzo Biochem, Inc. v. Gen-Probe Inc*., 323 F.3d 956, 964 (Fed. Cir. 2002). It is the absence of any knowledge of structural elements for compounds which function as selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype that fails the *Enzo* description test.

The Specification lacks possession of any method, other than trial and error, to determine whether structural alterations will impact the binding to adrenergic receptors (FF 10-11).

With no structural guidance, the ordinary artisan is left to trial and error screening on how to distinguish which of the virtually infinite possible compounds which exist would be useful in the claimed screening assay. The disclosure of four core structures does not provide description of an entire

undescribed genus of compounds which function as selective agonists of the α2B adrenoceptor subtype or α2B/α2C adrenoceptor subtype(s) as compared to the α2A adrenoceptor subtype. *See Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997)("These cases do not compel the conclusion that a description of a species always constitutes a description of a genus of which it is a part.")

CONCLUSION

This decision contains new grounds of rejection pursuant to 37 C.F.R. § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 C.F.R. § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that the Appellants, *WITHIN TWO MONTHS FROM THE DATE OF THE DECISION*, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the Examiner, in which event the proceeding will be remanded to the Examiner. . . .
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

<u>REVERSED, 37 C.F.R. § 41.50(b)</u>

Ssc:

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