

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 23

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte TODD K. JONES,
MARK E. GOLDMAN,
CHARLOTTE L. F. POOLEY,
DAVID T. WINN,
JAMES P. EDWARDS,
SARAH J. WEST,
CHRISTOPHER M. TEGLEY,
LIN ZHI,
LAWRENCE G. HAMANN,
LUC J. FARMER, and
ROBERT L. DAVIS

Appeal No. 2001-1290
Application No. 08/980,032

ON BRIEF

Before WINTERS, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 16 and 18-28, all of the claims remaining. Claim 16 is representative and is reproduced as an appendix to this opinion.

The examiner relies on the following references:

Liao et al. (Liao) 5,208,263 May 4, 1993

Martin et al. (Martin), Harper's Review of Biochemistry, pp. 497, 499 (1983)

Cook et al. (Cook), "Reversal of activity profile in analogs of the antiprogesterin RU 486: Effect of a 16 α -substituent of progestational (agonist) activity," Life Science, Vol. 52, pp. 155-162 (1993)

Teutsch et al. (Teutsch), "History and perspectives of antiprogesterins from the chemist's point of view," Human Reproduction, Vol. 9, Supp. 1, pp. 12-31 (1994)

Claims 16 and 18-28 stand rejected under 35 U.S.C. § 112, first paragraph, as nonenabled.

We reverse.

Background

"Intracellular receptors (IRs) form a class of structurally-related genetic regulators scientists have named 'ligand dependent transcription factors.' . . . Steroid receptors are a recognized subset of the IRs, including the progesterone receptor (PR), androgen receptor (AR), estrogen receptor (ER), glucocorticoid receptor (GR) and mineralocorticoid receptor (MR). Regulation of a gene by such factors requires both the IR itself and a corresponding ligand which has the ability to selectively bind to the IR in a way that affects gene transcription." Specification, page 1.

"Ligands to the steroid receptor are known to play an important role in health of both women and men. For example, the native female ligand, progesterone, as well as synthetic analogues, such as norgestrel (18-homonorethisterone) . . . are used in birth control formulations, typically in

combination with the female hormone estrogen or synthetic estrogen analogues, as effective modulators of both PR and ER. On the other hand, antagonists to PR are potentially useful in treating chronic disorders, such as certain hormone dependent cancers of the breast, ovaries, and uterus, and in treating non-malignant conditions such as uterine fibroids and endometriosis, a leading cause of infertility in women. Similarly, AR antagonists, such as cyproterone acetate and flutamide have proved useful in the treatment of hyperplasia and cancer of the prostate.” Specification, pages 1-2.

The specification discloses that a number of quinoline derivatives are agonists and/or antagonists for one or more of the PR, AR, ER, GR, and MR steroid receptors. See pages 35 to 249 (disclosing synthesis of exemplary compounds), pages 23 to 33 (listing representative compounds that are agonists or antagonists for various receptors), and pages 255 to 262 (showing results of in vitro and in vivo assays to determine agonistic and antagonistic activity with respect to various receptors). The specification also discloses various conditions or disorders that would be amenable to treatment with the disclosed compounds, depending on their agonistic or antagonistic activity with respect to different receptors. See pages 22-23.

Discussion

The claims are directed to therapeutic methods comprising administering a quinoline derivative corresponding to one of three chemical formulae. See claim 16. The examiner rejected the claims as nonenabled, based on a review of the factors set out in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404

(Fed. Cir. 1988). The examiner found, inter alia, that the prior art contained little data on non-steroidal agonists or antagonists for steroid hormone receptors; that steroid hormone receptors binding involves a high degree of unpredictability; and that the formulae recited in the claims encompass numerous structurally different classes of compounds. See the Examiner's Answer, pages 3-5.

On the other hand, the examiner acknowledged that the level of skill in the art is high; that the specification discloses preparation of over 300 compounds, along with in vitro and in vivo assay procedures; and that the claims were enabled as to "using the selective agonist/antagonist compounds and their structurally related compounds for PR, AR, ER, GR, MR for modulating their respective receptor." Examiner's Answer, pages 4-5.¹ On balance, however, the examiner concluded that the claims were nonenabled. See the Examiner's Answer, page 5: "Since insufficient teaching and guidance have been provided in the specification . . . , one of ordinary skill in the art, even with high level of skill, would not be able to use all the structurally diverse compounds for treating a patient requiring steroid receptor therapy and for treating all the different disease conditions as claimed without undue experimentation."

Appellants argue that the assays disclosed in the specification would enable those skilled in the art to routinely determine the receptor modulator activity of the compounds recited in the claims. See the Appeal Brief, page 4. "While the process of synthesizing compounds within the scope of the generic

¹ The precise meaning of the quoted phrase is unclear. Presumably, the examiner is referring to the exemplary compounds that were actually tested and shown to have activity in in vitro and/or

structures recited in the claims and screening them for activity may be somewhat time-consuming and repetitive, it does not constitute undue experimentation.”

Id., page 5 (citing Wands). Appellants conclude that “[g]iven the extensive guidance and examples provided in the specification and the familiarity of those in the field of medicinal chemistry with the screening approach taught for identifying compounds having the desired steroid receptor modulator activity, practice of the claimed methods is fully enabled by the specification and would not require undue experimentation.” Id., page 6.

“When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.” In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

In this case, we conclude that the examiner has not carried the initial burden of showing prima facie nonenablement. The examiner seems to focus on the lack of predictability involved in ligand/steroid hormone receptor binding and the breadth of the claims. See the Examiner’s Answer, pages 3-5, and the examiner’s conclusion on page 5: “[O]ne of ordinary skill in the art, even with

in in vivo assays as agonists or antagonists for various steroid hormone receptors. See the specification, pages 255-262.

high level of skill, would not be able to use all the structurally diverse compounds for treating a patient requiring steroid receptor therapy and for treating all the different disease conditions as claimed without undue experimentation.”

Predictability, however, is not the only factor to consider, nor is the amount of experimentation. In this case, the examiner’s concession that the specification provides over 300 exemplary compounds is evidence of the routine nature of making compounds within formulae recited in the claims. Likewise, the specification discloses the results of testing numerous exemplary compounds in an in vitro assay, suggesting that such testing would also be routine to those of skill in the art, especially given the concededly high level of skill in the art. Thus, the lack of predictability in the art is ameliorated by the apparently routine nature of making and testing other compounds encompassed by the claims.

The examiner also appears to be concerned with the skilled artisan “be[ing] able to use all the structurally diverse compounds for treating a patient requiring steroid receptor therapy and for treating all the different disease conditions as claimed.” Examiner’s Answer, page 5 (emphasis added). Thus, the examiner’s concern may be that the formulae recited in the claims encompass compounds that will be inoperative therapeutically.

By itself, however, the presence of inoperative embodiments in the claim does not support a conclusion of nonenablement. See Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 414 (Fed. Cir. 1984): “Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. ‘It is not a function of the claims to specifically

exclude * * * possible inoperative substances * * * *” (quoting In re Dinh-Nguyn, 492 F.2d 856, 858-59, 181 USPQ 46, 48 (CCPA 1974)). It is only “if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, [that] the claims might indeed be [nonenabled].” Id. The examiner has not shown that the number of potential inoperative embodiments is so high that an undue amount of experimentation would be expected.

Summary

The examiner has not adequately shown that the balance of the Wands factors favor a conclusion of nonenablement. Since the examiner bears the initial burden of showing nonenablement, and since that burden has not been carried here, we reverse the rejection under 35 U.S.C. § 112, first paragraph.

REVERSED

Sherman D. Winters)
Administrative Patent Judge)
)
)
) BOARD OF PATENT
Toni R. Scheiner)
Administrative Patent Judge) APPEALS AND
)
) INTERFERENCES
)
Eric Grimes)
Administrative Patent Judge)

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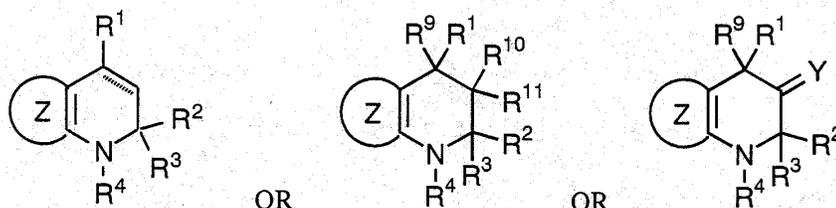
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APPENDIX

16. A method of treating a patient requiring steroid receptor therapy comprising administering to a patient an effective amount of a compound that modulates the activity of a steroid receptor, which compound is of the formula:



wherein:

R¹ through R³ each independently are hydrogen, a C₁ - C₆ alkyl, optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, or heteroaryl;

R⁴ is hydrogen, a C₁ - C₆ alkyl, or R⁵C=O, OR⁶, or NR⁶R⁷, where R⁵ is hydrogen, a C₁ - C₆ alkyl, optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, or heteroaryl, and wherein R⁶ and R⁷ each independently are hydrogen, a C₁ - C₆ alkyl, optionally substituted allyl, arylmethyl, aryl, or heteroaryl;

R⁹ through R¹⁰ each independently are hydrogen, a C₁ - C₆ alkyl, optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, or heteroaryl;

R¹¹ is hydrogen, a C₁ - C₆ alkyl, OR⁶ or optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, or heteroaryl, where R⁶ has the same definition given above, or R¹ and R², R² and R³, R¹ and R⁹, R¹⁰ and R¹¹, R¹ and R¹⁰ and/or R¹¹ and R² when taken together can form a three- to seven-membered ring optionally substituted with hydrogen, F, OR⁶ or NR⁶R⁷, where R⁶ through R⁷ have the definitions given above, provided, however, that R¹, R², R¹⁰ and R¹¹ cannot form more than two three- to seven-membered rings at a time;

Y is O, CHR⁶ or NR⁶, where R⁶ has the same definition given above; and

Z is a polycyclic aryl or a monocyclic or polycyclic heteroaryl group, optionally substituted at one or more positions with hydrogen, a C₁ - C₆ alkyl, optionally substituted

allyl, arylmethyl, alkynyl, alkenyl, aryl, heteroaryl, F, Cl, Br, I, CN, $R^5C=O$, $R^6R^7NC=O$, $R^6OC=O$, perfluoroalkyl, haloalkyl, a $C_1 - C_6$ straight-chain hydroxy alkyl, $HOCHR^5R^8$, nitro, R^6OCH_2 , R^6O , NH_2 , or R^6R^7N , where R^5 through R^7 have the definitions given above and where R^8 is hydrogen, a $C_1 - C_6$ alkyl or optionally substituted allyl, arylmethyl, alkynyl, alkenyl, aryl, or heteroaryl.