

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

Paper No. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MICHAEL L. VAZQUEZ, RICHARD A. MUELLER,
JOHN J. TALLEY, DANIEL P. GETMAN,
GARY A. DECRESCENZO and ERIC T. SUN

Appeal No. 1998-2010
Application No. 08/542,861

ON BRIEF

Before WINTERS, ADAMS, and MILLS Administrative Patent Judges.

MILLS, 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 1, 5, 7-11, 17-25, 27-30 and 32 to 37, which are the subject of this appeal. Claim 38 is also pending and has been indicated by the examiner to contain allowable subject matter.

We affirm.

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Claims 1, 5, 7, 9, 11, 17 and 27 are illustrative of the claims on appeal and are reproduced in the appendix to the Appeal Brief (attached).

The reference relied upon by the examiner is:

Kayegama et al. (Kayegama), "In vitro inhibition of human immunodeficiency virus (HIV) type 1 replication by C₂ symmetry-based HIV protease inhibitors as single agents or in combinations," Antimicrobial Agents and Chemotherapy, Vol. 36, No. 5, pp. 926-933 (1992)

Grounds of Rejection

Claims 1, 5, 7-11, and 17-25 stand rejected under the judicial doctrine of being drawn to an improper Markush group.

Claims 1, 5, 7-11, 17-25, 27-30 and 32 to 37 stand rejected under 35 U.S.C. § 112, first paragraph as based on a disclosure which does not enable the invention as claimed.

Grouping of Claims

In the Appeal Brief, pages 4-5, appellants include a section entitled "Grouping of Claims." Although that section is not entirely clear, we believe that appellants request consideration of product claims separate from method claims and indicate that the claims do not stand or fall together. Beyond that, appellants have not presented clear alternative

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or defined groupings of claims. For our part, we have considered the claims separately, including the composition and method claims. 37 CFR §1.192(c)(7) (1996).

Background

The subject matter of the present claims relates to compounds which act as inhibitors of retroviral protease. Claims 1, 17 and 27. The claimed invention also encompasses pharmaceutical compositions (e.g., claim 5); methods of inhibiting retroviral protease (e.g., claim 7); methods of treating retroviral infection (e.g., claim 9); and methods of treating AIDS (e.g., claim 11).

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied reference, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

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35 U.S.C. § 112, first paragraph

Claims 1, 5, 7-11, 17-25, 27-30 and 32-37 stand rejected under 35 U.S.C.

§ 112, first paragraph as based on a disclosure which does not enable the invention as claimed. The examiner indicates that the specification fails to disclose both how to make and use compounds within the claim scope.

"To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'"

[Emphasis added.] Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42

USPQ2d 1001, 1004 (Fed. Cir.1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27

USPQ2d 1510, 1513 (Fed. Cir. 1993)). Conversely, the first paragraph of Section 112

requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification.

In addition, analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contains sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure. In

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re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Morehouse, 545 F.2d 162, 165, 192 USPQ 29 32 (CCPA 1976). The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement.

In considering the enablement rejection before us for review, we find the following passage from PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996) to be instructive.

In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. See, e.g., In re Goodman, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993); Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991); In re Vaeck, 947 F.2d at 496, 20 USPQ2d at 1445. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation “must not be unduly extensive.” Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

How to Make

It is the examiner’s position that the diverse embodiments embraced by all the claims are not adequately enabled, as sources of starting materials are not set forth or the

means by which they may be prepared for the plethora of functional groups permitted in R^3 , R^4 , R^7 , $R^{7'}$, R^{33-34} which include hetero rings at many locations and cycloalkyl rings interspersed in the basic framework. Answer, page 6. The examiner further argues that the specification is particularly silent with regard to the availability of necessary starting materials such as the amine on page 30, the sulfamoyl halides on page 31, as well as the succinic acid derivatives on page 33. Id.

With respect to the how to make aspect of the rejection, we find the examiner has failed to establish a prima facie case of lack of enablement with proper argument and/or evidence. The examiner's position is the specification is silent as to the availability of all necessary starting materials such as the amino on page 30, the sulfamoyl halides on page 31, as well as the succinic acid derivatives on page 33.

We find the examiner's position to be without basis. First, the examiner argues there is no support in the specification as to how to make the amine mentioned on page 30. The amine is of the formula, R_3NH_2 . The specification, page 30, lines 21-23 indicates that exemplary amines include benzyl amine, isobutyl amine, n-butyl amine, isopentyl amine, isoamylamine, cyclohexanemethyl amine, naphthyl methyl amine. Appellants further indicate that such amines are readily available from Aldrich Chemical Company or Fluka Chemical Company. Reply Brief, page 11. The examiner has failed to rebut this argument of appellants. In addition, the specification page 32, lines 11-24, page 47,

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Example 4, and page 68, lines 26-37, describes the procedure one of ordinary skill in the art can use to prepare sulfamoyl halides. The specification, pages 55, 56, example 8 and pages 58-59, appears to support methods of preparing succinic acid (succinate) derivatives.

The examiner additionally argues that appellants have failed to show how to selectively prepare hetero rings at one ring position versus the many positions possible for ring systems that include mono-, bi- and tri- cyclic rings. Answer, page 6. The specification, page 63, however, states that utilizing the procedures set forth therein, the compounds of Tables 4-14 can be prepared and that utilizing the intermediates of examples 1-13 according to the procedures of example 14, the compounds shown in tables 4-16 could be prepared. The appellants further argue that a person skilled in the art would recognize where and how the heteroatom containing rings could be attached to the backbone structure set forth in the disclosure. Brief, page 10. Appellants reference several patents and general chemistry reference materials to support this position. Brief, pages 10-14. The examiner responds to this argument with the statement (Answer, pages 6-7):

The fact that rings included within the instant scope may be known rings as appellants urge by referring to various organic textbooks, is not the issue but rather if the specification as filed provides sufficient enablement to make hetero-substituted final products of the scope being claimed. ... While the generalized routes in the specification may provide sufficient guidelines for making final products listed in the tables, the

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instant case is similar to Lund, previously cited in which the Court agreed the specific aldehyde reactants mentioned in the specification fell within the claimed range and thus far short of the claim's scope.

The test for enablement is whether one skilled in the art could make and use the claimed invention from the disclosure coupled with information known in the art without undue experimentation. See United States v. Telectronics, Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988), cert. denied, 109 S.Ct. 1954 (1989); In re Stephens, 529 F.2d 1343, 1345, 188 USPQ 659, 661 (CCPA 1976). In the present case, the examiner appears to acknowledge the patent and general reference material provided by appellants, but fails to establish with specific argument why one of ordinary skill in the art, coupling the knowledge in the art provided by appellants and the teachings of the specification, would not be able to make compounds within the claim scope. Nor has the examiner indicated why the examples provided in the specification are not representative of the claimed subject matter, as a whole.

In view of the above, we find the examiner has failed to provide a prima facie case of lack of enablement based on how to make the compounds of the claimed invention.

How to Use

Secondly, the examiner argues the specification fails to teach how to use the invention within the claim scope. The examiner also argues that there is no reasonable

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assurance that the tests presented in the specification for inhibition of HIV proteases, or other undisclosed retroviral proteases are art-accepted predictors of in vivo effectiveness in man or other non-murine hosts. Answer, page 7. It is suggested that, in view of the state of the art of retroviral inhibition and the persistent difficulty in treating viral infections, such as AIDS, that more than screening tests are need to support the method claims directed to in vivo use.

In this regard, the examiner relies on Kayegama for its disclosure that the ability to inhibit HIV protease is only a starting point in developing potential drugs for treating HIV infections and not in itself an indicator of useful drugs. Answer, page 7. The examiner suggests that compound and composition claims are not commensurate in scope with the examples listed in Table 12.

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. In re Marzocchi, 439 F. 2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). It has long been held that "[t]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting from In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir.

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1993)). Further, in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated that:

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman [230 USPQ 546, 547 (Bd. Pat. App. Int. 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. [Footnote omitted.]

These factors are neither mandatory nor cumulative. Enzo Biochem Inc. v. Calgene Inc., 188 F.2d 1362, 1371, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999).

In the present case, the examiner has provided evidence that the nature of the invention, and state of the prior art (Kayegama) is such that the relevant art is unpredictable.¹ In addition, the scope of the claims is very broad, encompassing a vast number of compounds and varied substituents. The amount of guidance presented in the specification as to compounds within the scope of the claims having the necessary protease inhibitory activity is minimal. In particular, the examples in the specification

¹ The Federal Circuit acknowledged in In re Wright, that “in February 1993, the physiological activity of RNA viruses was sufficiently unpredictable...”. In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

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appear to be prophetic, i.e, “the compounds set forth in the examples herein would be expected to inhibit the HIV enzyme”. Specification, page 92.

In view of the above, we find that the examiner has provided a reasonable evidentiary basis to question enablement of the use of the claimed compounds and compositions. Once the examiner has established a reasonable basis to question the enablement provided for the claimed invention, the burden falls on the appellants to present persuasive arguments, supported by suitable proofs where necessary, that one skilled in the art would be able to make and use the claimed invention using the disclosure as a guide. See In re Brandstadter, 484 F.2d 1395, 1406, 179 USPQ 286, 294 (CCPA 1973).

In response to the examiner's prima facie case, appellants argue that they need not exemplify every species encompassed by the claims. Reply Brief, page 13. Appellants argue that the specification provides numerous representative examples, which together with the general knowledge in the art provide those of skill in the art with the requisite detail necessary to make and use appellant's invention. Id.

It is well settled from Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991), that a patent applicant is entitled to claim an invention generically if the invention is described sufficiently to meet the requirements of 35 U.S.C. § 112. In Amgen, the applicant claimed erythropoietin (EPO),

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and every possible analog of the gene (containing about 4000 nucleotides), but only provided the details for preparing only a few EPO analogs and did not provide sufficient disclosure to support the claims. Our appellate reviewing court found in Amgen that in view of the structural complexity of the EPO gene, there were manifold possibilities for changes in its structure, and there was uncertainty as to what utility would be possessed by each of the analogs. It was determined that additional disclosure was needed to identify various analogs within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity.

Similarly, in the present case, we find that appellants have failed to rebut the examiner's prima facie case of lack of enablement based on how to use the claimed compounds with appropriate evidence as to the utility possessed by each of the various compounds within the claim scope. "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.... Genentech, Inc. v. Novo Nordisk, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997). Tossing out the mere germ of an idea does not constitute enabling disclosure. See, Brenner v. Manson, 383 U.S. 519, 536 ; 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that `a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.')"). Appellants' disclosure appears to provide an invitation to those of skill in the art to determine how to

use the claimed compounds using the assays of examples 13 and 14, and fails to clearly show that the claimed compounds possess the claimed retroviral protease inhibitory activity. The specification fails to show that the claimed compounds are useful as inhibitors of any retroviral proteases, including HIV protease or other of the varied and multiple retroviral proteases, and thus, fails to show that the claimed compounds can be used in a method for treating retroviral infections, generally. The specification and the record, also fail to establish with any evidence that the claimed compounds can be successfully used in a method of treating AIDS, as claimed. The examiner has provided sufficient evidence of the unpredictability in the art of retroviral protease inhibitors.

Appellants argue that, contrary to the examiner's reading of Kayegama, Kayegama supports their position that protease inhibitors are known in the art to be useful as antiviral drugs, supporting enablement of the claimed compounds. Reply Brief, page 15.

Appellants have failed, however, to establish that the compounds of Kayegama are structurally and functionally similar to the claimed compounds in a manner which would support enablement of the claimed compounds.

Similarly, although appellants suggest that several companies have protease inhibitor compounds in clinical trials (Brief, page 16), we agree with the examiner that appellants have failed to show that the compounds used in the clinical trials are related and

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of a similar class to the claimed compounds in a manner which would support enablement of the full scope of the pending claims (Answer, page 5).

After evidence or arguments are submitted by the appellants in response to a rejection based on lack of enablement, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of the argument. We have carefully studied the arguments and evidence of record. On balance, we believe that the totality of the evidence presented by the examiner and appellants weighs in favor of finding the claimed invention lacks enablement and would require undue experimentation to practice the claimed invention within the full scope of the claims. The rejection of the claims under 35 U.S.C. § 112, first paragraph is affirmed.

Improper Markush Group

Claims 1, 5, 7-11, and 17-25 stand rejected under the judicial doctrine of being drawn to an improper Markush group. As the rejection of all the claims under 35 U.S.C. § 112, first paragraph has been affirmed and disposes of all the claims on appeal, it is not necessary for us to reach, and we have not considered and do not reach the rejection based on an improper Markush group.

Other Issue

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Although not before us on appeal, claim 38 has been indicated by the examiner to be allowable. Answer, page 2. While the Advisory Action dated November 21, 1996 indicated that claim 31 (now claim 38) contained allowable subject matter, we find that the record does not reflect "reasons for allowance" of the subject matter of claim 38. Upon return of the application to the examiner, the examiner is requested to reevaluate the allowability of claim 38 in view of the significant issues of lack of enablement on the record before us. If the examiner maintains allowability of claim 38 upon reevaluation of the record, the examiner should provide reasons for allowance therefor.

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CONCLUSION

The rejection of claims 1, 5, 7-11, 17-25, 27-30 and 32 to 37 under 35 U.S.C.

§ 112, first paragraph is affirmed.

AFFIRMED

SHERMAN D. WINTERS
Administrative Patent Judge

DONALD E. ADAMS
Administrative Patent Judge

DEMETRA J. MILLS
Administrative Patent Judge

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