

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 24

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ULRIC WEIDLE, EBERHARD RUSSMANN, KLAUS-PETER HIRTH,
TIBERIU DIAMANTSTEIN and BRIGITTE KALUZA

Appeal No. 1996-1002
Application 07/988,945¹

ON BRIEF

Before WINTERS, ROBINSON and LORIN, Administrative Patent Judges.

ROBINSON, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 18-22 and 25-27, which are all of the claims pending in this application.

¹ Application for patent filed March 10, 1993.

Claim 18 is illustrative of the subject matter on appeal and reads as follows:

18. Antibody composition useful for inhibiting the binding of IL-2 to the high affinity interleukin 2 receptor (IL-2R) comprising, a) a monoclonal antibody which specifically binds to high affinity IL-2R α chain and inhibits binding of IL-2 thereto and b) a monoclonal antibody which specifically binds to high affinity IL-2R β chain and inhibits binding of IL-2 thereto, wherein said monoclonal antibody which specifically binds to said high affinity IL-2R β chain is C68/41 (ECACC 90090704) or A23A41 (DSM ACC2015).

The references relied upon by the examiner are:

Takeshita et al. (Takeshita), "Monoclonal Antibody Defining a Molecule Possibly Identical to the p75 Subunit of Interleukin 2 Receptor," Journal of Experimental Medicine, Vol. 169, pp. 1323-1332, 1989.

Kupiec-Weglinski et al. (Kupiec-Weglinski), "Selective Immunosuppression with Anti-Interleukin 2 Receptor-Targeted Therapy: Helper and Suppressor Cell Activity in Rat Recipients of Cardiac Allografts," European Journal of Immunology, Vol. 17, pp. 313-319, 1987.

Williams, "Novel Antibody Reagents: Production and Potential," TibTech., Vol. 6, pp. 36-42, 1988.

Morrison et al. (Morrison), "Production and Characterization of Genetically Engineered Antibody Molecules," Clinical Chemistry, Vol. 34(9), pp 1668-1675, 1988.

Queen et al. (Queen), "A Humanized Antibody that Binds to the Interleukin 2 Receptor," Proc. Natl. Acad. Sci. USA, Vol. 86, pp. 10029-10033, 1989.

Waldmann, "Monoclonal Antibodies in Diagnosis and Therapy," Science, Vol. 252, pp 1657-1662, 1991.

Hird et al. (Hird), "Immunotherapy with Monoclonal Antibodies," Genes and Cancer, Eds. Carney and Sikora, John Wiley & Sons, Ltd., pp 183-189, 1990.

Harris et al. (Harris), "Therapeutic Antibodies the Coming of Age," TibTech., Vol. 11, pp. 42-44, 1993.

GROUND OF REJECTION

Claim 27 stands rejected under 35 U.S.C. § 112, second paragraph, as failing to particularly point out and distinctly claim the invention.

Claims 18-22 and 25-27 stand rejected under 35 U.S.C. § 112, first paragraph, as being non-enabled by the specification. As evidence, the examiner relies on Waldmann, Hird, and Harris.

Claims 18-22 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Takeshita and Kupiec-Weglinski.

Claims 26-27 stand rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Takeshita, Kupiec-Weglinski, Morrison and Queen.

Claim 25 stands rejected under 35 U.S.C. § 103. As evidence of obviousness, the examiner relies on Takeshita, Kupiec-Weglinski, and Williams.

We reverse the rejection under 35 U.S.C. § 112, second paragraph, and the rejections under 35 U.S.C. § 103 and remand the application to the examiner for further consideration of the rejection under 35 U.S.C. § 112, first paragraph.

BACKGROUND

The invention is described at page 3 of the specification as being directed to an antibody composition which inhibits the binding of interleukin 2 to its high affinity receptor. The composition is described as a combination comprising a monoclonal antibody against the α chain of the interleukin 2 receptor (IK-2R α) and a monoclonal antibody against the interleukin 2 receptor β chain (IK-2R β) of the interleukin 2 receptor. The use, in combination, of monoclonal antibodies against the α -chain and the β -chain of the IL-2 receptor is said to lead to a synergistic effect resulting in a stronger inhibition of the IL-2 induced proliferation of human peripheral blood lymphocytes.

DISCUSSION

The rejection under 35 U.S.C. § 112, second paragraph

The examiner has rejected claim 27 based on the presence, therein, of the term "humanized" which the examiner urges is ambiguous. We point out that it is well established that "definiteness of the language employed must be analyzed, not in a vacuum, but always in light of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971). Here, both the examiner (Answer, page 14) and appellants (Brief, page 10) agree that the term "humanized", used in the context of claim 27, is an art recognized term and that

humanized antibodies are known in the art. In addition, we note page 2 of the specification which explicitly defines this terminology. Thus, we do not agree that the claim is rendered indefinite by the use of this terminology. Therefore, we reverse the rejection of claim 27 under 35 U.S.C. § 112, second paragraph.

At page 14 of the Answer, the examiner appears to indicate that the real concern addressed by this rejection is that claim 26 claims a "humanized" antibody and therefore, it is not clear how the antibody of claim 27 is different from the antibody of claim 26. Should further prosecution occur, we would encourage the examiner to review both claims 26 and 27 and determine whether claim 27 fails to further limit claim 26, on which it depends. Should the examiner determine that claim 27 is improperly dependent, the examiner should take whatever action is appropriate. (See 35 U.S.C. § 112, fourth paragraph; 37 CFR 1.75(c); MPEP § 608.01(n), 6th ed. Rev. 3, 1997; Ex parte Porter, 25 USPQ2d 1144, 1147 (Bd. Pat. App. & Int. 1992)).

The rejection under 35 U.S.C. § 112, first paragraph

Claims 18-22 and 25-27 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on a non-enabling disclosure. The issue, as framed by the examiner, is whether the specification describes how to use the claimed composition either in vivo or in vitro. (Answer, page 4). We are mindful that the Patent and Trademark Office (PTO) bears the initial burden of providing reasons for doubting the objective truth of the statements made by the applicants as to the scope of enablement. Only when the PTO

meets this prima facie burden, does the burden shift to applicants to provide suitable evidence indicating that the specification is enabling in a manner commensurate in scope with the protection sought by the claims. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) .

Factors appropriate for determining whether undue experimentation is required to practice the claimed invention throughout its full scope are listed in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors 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.

The examiner's rejection, reasoning, and evidence presented in support thereof focus on these factors as they relate to the use of the claimed compositions for immunosuppressive therapy. (Answer, page 5-7). The examiner begins the analysis by noting that the specification (Answer , page 5):

provides no exemplification of how to use the claimed compositions for successful immunosuppression therapy of the various disorders listed in the specification page 2, and further fails to describe how (sic, to) use the claimed composition in vitro.

The examiner also discusses the predictability of the use of such materials in immunosuppression citing confusion in the art as to mechanism of activity as well as

variation of activity from antibody to antibody. (Id.) The examiner cites Waldmann, Hird and Harris in support of the position that murine and other animal testing has not proven readily predictive of effective therapy, in humans, using such monoclonal antibodies. (Answer, page 6). The examiner concludes that (Answer, paragraph bridging pages 6-7):

[i]n view of the contemporary knowledge in the art and the general lack of successful application of monoclonal antibody-based therapy methods for the treatment of human disease and of the limited predictive value of *in vitro* results for efficacy in humans, one of ordinary skill would be forced into undue experimentation in order to use the claimed invention.

Similarly, the examiner urges that, for essentially the same reasons, (Answer, page 7):

the specification has failed to writtenly describe how one of ordinary skill in the art would be enabled for the use of these compositions in *in vitro* applications.

We agree that the specification lacks adequate support to enable those skilled in this art to practice the invention as to the *in vivo* use or application of the claimed monoclonal antibody composition in the absence of undue experimentation. Overall we find that the examiner provides both evidence and sound scientific reasoning in support of his position.

Appellants do not dispute the examiner's position as to the use of the claimed composition *in vivo*. In rebuttal, appellants urge that Table 1 at page 9 of the

specification demonstrates that all of the antibodies of the pending claims have binding properties and therefore can be used in assays as diagnostic tools. The examiner does not explicitly address these arguments. (Answer, page 15). Thus, on this record, we have no indication whether the examiner would regard the specification, as filed, to adequately support the use of the claimed compositions as diagnostic tools as alleged by appellants. We are cognizant of the lack of any specific written description in the specification of such a use. However, a patent application need not teach, and preferably omits, what is well known in the art. In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). Compare In re Malachowski, 530 F.2d 1402, 1405, 189 USPQ 432, 435 (CCPA 1976) ("Having found that the claimed composition has utility as contemplated in the specification, §101 is satisfied and it becomes unnecessary to decide whether it is in fact useful for the other purposes indicated in the specification as possibilities."), citing In re Gottlieb, 328 F.2d 1016, 1019, 140 USPQ 665, 668 (CCPA 1964). We leave to the examiner, in the first instance, to evaluate the present disclosure to determine whether it is sufficient to enable those skilled in this art to practice the use of the claimed composition as a diagnostic tool without undue experimentation. On the record before us, neither the

Appeal No. 1996-1002
Application 07/988,945

appellants nor the examiner have made the factual findings necessary to determine whether the present disclosure would permit one skilled in this art to use the claimed composition in vitro as a diagnostic tool without undue experimentation.

We therefore remand the application to the examiner for the purposes of evaluating the arguments of appellants as to the alleged use of the claimed compositions as diagnostic tools.

The rejections under 35 U.S.C. § 103

In rejecting claims 18-22 under 35 U.S.C. § 103, the examiner has relied on the disclosure of Takeshita and Kupiec-Weglinski. The examiner states that Takeshita teaches (Answer, page 8):

the near complete inhibition of IL-2 dependent cell growth resulting from blocking of binding of IL-2 to its receptor, by the combination of TU-27 (anti-IL-2R β) and H31 (anti-IL-2R α) (see figure 5 and see the paragraph at the bottom of page 1328). This reference shows the antiproliferative effects of a combination of IL-2R antibodies.

However, the examiner acknowledges that Takeshita does not (Answer, page 8):

specifically use the antibodies represented by the cell lines in claims 18 and 22, nor do they specifically state the exact concentrations of the antibodies recited in claims 19-20.

The examiner concludes (Answer, page 9):

The person of ordinary skill would have been motivated to produce monoclonal antibodies specific for both IL-2R α and IL-2R β and would have had a reasonable expectation of obtaining such antibodies, in view

of the teaching of Takeshita et. al., that a combination of these antibodies was useful in inhibiting IL-2 dependant cell proliferation and further in view of the teaching of Kupiec Weglinski et. al. that IL-2 targeted immunotherapy would be useful in treating acute allograft rejections (see abstract). One skill in the art would have expected to isolate hybridomas producing anti-IL-2R β and anti-IL-2R α antibodies having similar or identical characteristics to those of of (sic) antibodies recited in the claims. (Emphasis added).

It is the initial burden of the patent examiner to establish that claims presented in an application for patent are unpatentable. In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). We have carefully considered the evidence and discussion in support of the rejection presented by the examiner. However, a fair evaluation of the references, applicants' specification and consideration of the claimed subject matter as a whole, dictates a conclusion that the examiner has failed to provide the factual basis which would reasonably support a prima facie case of unpatentability of the subject matter of claims 18-22. Claims 18-22 are directed to compositions which, in addition to a monoclonal antibody which specifically binds to the high affinity IL-2R α chain, must include one of two deposited monoclonal antibodies, designated as C68/41 and A23A41, which specifically bind to the high affinity IL-2R β chain. While, the prior art, relied upon by the examiner, could reasonably be read to suggest combining a monoclonal antibody which would bind to the IL-2R α chain with a monoclonal antibody

which would bind to the IL-2R β chain, the examiner acknowledges that neither reference discloses either of the monoclonal antibodies explicitly required by the claims. Further, the examiner offers no other evidence which would indicate that either of these two monoclonal antibodies were known at the time of the invention. Instead, the examiner urges that one skilled in this art, given the disclosures of Takeshita and Kupiec-Weglinski, would have been able to isolate similar or identical antibodies to those required by the claims. While it may be true that those skilled in the art could derive monoclonals which would function in a manner similar to those required by the claims, functional equivalence is not the test. Here the claims require the presence of one of two specified monoclonal antibodies. The burden is on the examiner to provide a reason, based on the prior art or knowledge generally available in the art, as to why it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 297, n.24, 227 USPQ 657, 667, n.24 (Fed. Cir. 1985). On this record, the examiner has offered no evidence which would reasonably suggest that either of the two claim designated monoclonal antibodies were known at the time of the invention and which would have suggested that one substitute the specific claim designated monoclonal antibodies for those monoclonal antibodies of either Takeshita or Kupiec-Weglinski. Thus, we find no reasonable suggestion for modifying either Takeshita or Kupiec-

Appeal No. 1996-1002
Application 07/988,945

Weglinski in a manner which would lead one of ordinary skill to arrive at the claimed invention. Where, as here, the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.1988). Therefore, the rejection of claims 18-22 under 35 U.S.C. § 103 is reversed.

We have noted the deficiencies of the combination of Takeshita and Kupiec-Weglinski as those disclosures relate to the claimed invention.

On consideration of the remaining rejections under 35 U.S.C. § 103, we need only determine whether Morrison or Queen, relied on in the rejections of claims 26-27, or Williams, relied on in the rejection of claim 25, provide that which is lacking in the Takeshita and Kupiec-Weglinski.

They do not. As we have previously determined, all of the claims require the presence, in the antibody composition, of one of two specified monoclonal antibodies which would bind to the IL-2R β chain. Neither of these monoclonal antibodies have been demonstrated to be known at the time of the invention. The additional references provide no facts or evidence which would have reasonably suggested the substitution of the specific claim recited monoclonal antibodies, which bind to the IL-2R β chain, into compositions of either Takeshita and Kupiec-Weglinski and therefore do not provide that which is missing from the previously considered references. Therefore, the

Appeal No. 1996-1002
Application 07/988,945

rejections of claim 25 and 26-27 under 35 U.S.C. § 103 are reversed.

CONCLUSION

The examiner's rejection of claim 27 under 35 U.S.C. § 112, second paragraph, is reversed.

The examiner's rejections of claims 18-22, 25, and 26-27 under 35 U.S.C. § 103 are reversed.

The application is remanded to the examiner for further consideration of the rejection of claims 18-22 and 25-27 under 35 U.S.C. § 112, first paragraph.

REVERSED and REMANDED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
)	
)	
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