

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MARC FELDMANN, RAVINDER N. MAINI and RICHARD O. WILLIAMS

Appeal No. 2002-0253
Application No. 09/093,450

ON BRIEF

Before WILLIAM F. SMITH, ELLIS and ADAMS, Administrative Patent Judges.
ELLIS, 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 15 through 17. Claims 18-30 have been withdrawn from consideration pursuant to 37 C.F.R. § 1.142(b). Claims 1-14 and 31-45 have been canceled.

Claims 15-17, the only claims before us, read as follows:

15. A method of treating rheumatoid arthritis in an individual in need thereof comprising administering to the individual cyclosporin in combination with a tumor necrosis factor alpha antagonist, in therapeutically effective amounts.

16. A method of Claim 15 wherein the tumor necrosis factor alpha antagonist is an anti-tumor necrosis factor alpha antibody or antigen-binding fragment thereof.

17. A method of Claim 16 wherein the antibody or fragment is a chimeric antibody or chimeric fragment, wherein said chimeric antibody or chimeric fragment comprises a non-human variable region specific for TNF α or an antigen-binding fragment thereof and a human constant region.

The references relied upon by the examiner are:

Ackerman et al. (Ackerman)	5,204,329	Apr. 20, 1993
Le et al. (Le)	5,656,272	Aug. 12, 1997
Aggarwal et al. (Aggarwal)	5,672,347	Sep. 30, 1997

I. Claims 15 and 16 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Aggarwal.

II. Claims 15-17 stand rejected under 35 U.S.C. § 103 as being unpatentable over Aggarwal in view of the appellants' acknowledgment in the specification (pages 13-15 and 19-25) that the use of chimeric antibodies for therapeutic uses was well known in art at the time the invention was made.

III. Claims 15-17 stand rejected under 35 U.S.C. § 103 as being unpatentable over Le and Ackerman in view of the appellants' acknowledgment in the specification (pages 13-15 and 19-25) that the use of chimeric antibodies for therapeutic uses was well known in art at the time the invention was made.

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The rejection of claim 15 under 35 U.S.C. § 112, first and second paragraphs, has been withdrawn. Answer, p. 2.

Having carefully considered the record before us which includes, inter alia, the specification, the appellants' Brief (Paper No. 16), the examiner's Answer (Paper No. 19) and the declaration of Dr. Marc Feldmann (Paper No. 12), we affirm each of the examiner's rejections.

Background

Tumor necrosis factor α (TNF α) and tumor necrosis factor β (TNF β) are cytokines which are said to be produced by monocytes and macrophages in response to endotoxins or other stimuli. Id., col. 1, lines 28-31. Prior to the present invention, it was known in the art that TNFs cause inflammatory actions which result in tissue injury, and that they are associated with infections, immune disorders and other pathologies. Id., col. 1, lines 46-47 and lines 55-57. TNF-related pathologies were known to include, inter alia, "acute and chronic immune and autoimmune pathologies, such as systemic lupus erythematosus (SLE) rheumatoid arthritis, thyroidosis, graft versus host disease, scleroderma, diabetes mellitus, [and] Graves' disease." Id., col. 34, lines 7-13. It had been the goal of researchers in the field to devise methods of treating or inhibiting such disorders using compounds which inhibit or neutralize the effects of TNF α and TNF β . Id., col. 9, lines 46-50; Aggarwal, the abstract. Such compounds, known as TNF antagonists, include anti-TNF α and anti-TNF β antibodies (i.e., "polyclonal antibodies,

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monoclonal antibodies, chimeric antibodies, anti-idiotypic antibodies ... as well as fragments, regions or derivatives thereof"); anti-TNF peptides; etc. Le, col. 9, line 51-col. 10, line 11; Aggarwal, col. 3, line 53- col 5, line 67.

As indicated by the claims above, the appellants' specification discloses a method of treating rheumatoid arthritis which comprises using therapeutically-effective amounts of a TNF α antagonist and cyclosporin, a known immunosuppressive agent.

Discussion

I. 35 U.S.C. § 102(e)

The examiner argues that Aggarwal discloses a method of treating rheumatoid arthritis using therapeutically-effective amounts of TNF α antibodies in conjunction with cyclosporin. Answer, p. 2. Accordingly, the examiner finds that Aggarwal anticipates the claimed invention.

In response, the appellants contend that Aggarwal does not describe the claimed methods with sufficient specificity to render the claims anticipated. Brief, pp. 8 and 9. According to the appellants, Aggarwal provides too many variables from which it would be necessary to choose in order to arrive at the present invention. Id., p. 9. The appellants rely on In re Petering, 301 F.2d 676, 133 USPQ 275 (CCPA 1962), for support. We find these arguments unpersuasive.

It is well established that anticipation requires that each and every limitation set forth in a claim be present, either expressly or inherently, in a single prior art reference.

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In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed. Cir. 1999); Celeritas Techs. Ltd v. Rockwell Int'l Corp., 150 F.3d 1354, 1360, 47 USPQ2d 1516, 1522 (Fed. Cir. 1998); Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co., 730 F.2d 1452, 1458, 221 USPQ 481, 485 (Fed. Cir. 1984). In addition, the reference must describe the invention in a manner that would sufficiently place one of ordinary skill in the art in possession of it. In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990); Akzo N.V. v. United States Int'l Trade Comm'n, 808 F.2d 1471, 1479, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986), cert. denied, 482 U.S. 909 (1987).

Turning first to claim 15, we point out that said claim is directed to the treatment of rheumatoid arthritis which comprises the use of any TNF α antagonist and cyclosporin. Here, we agree with the examiner that Aggarwal discloses such a method in column 7. With respect to the choice of variables concerning the disease state, we find Aggarwal discloses that its method of treating transplantation immunity is equally applicable to “arthritis, systemic lupus, Crohn’s disease, and other autoimmune disorders known to those skilled in the art.” Id., col. 7, lines 9-14; see also lines 38-39. In our view, the pointing out of three diseases from the class of autoimmune diseases sets forth a definite and limited class.¹ In re Petering, 301 F.2d at 681-682, 133 USPQ

¹ We need not address the teachings of the class of autoimmune disorders as a whole since Aggarwal has specifically pointed out that its method is applicable to the treatment of arthritis.

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at 279-280. Therefore, as we understand the appellants' argument the only issue is whether one skilled in the art would envision the treatment of rheumatoid arthritis from the disclosure of arthritis? To that end, we find that since the teaching of a method of treating "arthritis" is in conjunction with "other autoimmune disorders" one skilled in the art would have understood the teachings to be directed to rheumatoid arthritis, an autoimmune disorder. Moreover, we note that the prior art of record shows that other investigators in the field were treating rheumatoid arthritis using TNF antagonists. See, e.g., the Le patent. Thus, contrary to the appellants' argument we find that one of ordinary skill in the art would have read the teachings of Aggarwal as being directed to a method of treating rheumatoid arthritis.

As to the appellants' contention that Aggarwal's disclosure requires a selection from a number of TNF antagonists, we point out that the patent only discloses the use of two (2) types of TNF antagonists; i.e., TNF α and TNF β antagonists. Claim 15 is directed to a method of treating rheumatoid arthritis which comprises the administration of therapeutically-effective amounts of any TNF α antagonist. To that end, we direct attention to column 7, lines 24-39, which discloses the treatment of [rheumatoid] arthritis using therapeutically-effective amounts of a TNF α antagonist. We find this teaching sufficient to anticipate the claimed invention. Nevertheless, we point out that the claim is open to the administration of both the TNF α and the TNF β antagonist

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taught by Aggarwal.² Thus, even if we were to assume, arguendo, that one skilled in the art would have understood the teachings of Aggarwal to be directed to the administration of both TNF α and TNF β antagonists for treating rheumatoid arthritis, we would still find that the patent discloses the invention set forth in claim 15. That is, the teachings in column 7 of Aggarwal read directly on the method of treating rheumatoid arthritis comprising the administration of therapeutically-effective amounts of a TNF α antagonist. In view of the foregoing, we find that one of ordinary skill in the art would not need to choose between the two types of TNF antagonists taught by Aggarwal in order to be in possession of the claimed invention.

As to the alleged need to make a selection of the co-therapy; i.e., cyclosporin, we find that the teachings of Aggarwal are directed to a limited selection of anti-inflammatory agents, each one of which would be effective with the TNF antagonist. To that end, we point not only to the teachings in column 7, lines 60-63, but we also direct attention to claim 6, which indicates a preference for cyclosporin as the anti-inflammatory agent. Thus, we find that one of ordinary skill in the art would have understood the teachings of the patent as describing a method of treating rheumatoid arthritis which comprises the co-administration of cyclosporin. We make this finding

² The claims are directed to a method of treatment which “comprises” the administration of a TNF α antagonist and cyclosporin. We point out that it is well established that the term “comprising” is a term of art which opens the claim to the inclusion of other elements. Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 1271, 229 USPQ 805, 812 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981).

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based on the teachings of Aggarwal, but we nevertheless point out that the use of cyclosporin for the treatment of rheumatoid arthritis was known in the art at the time the appellants' invention was made. See, the Ackerman patent. Thus, with respect to a method of treating rheumatoid arthritis, the record indicates that those of ordinary skill in the art would not have considered Aggarwal as describing a generic class of compounds; rather, such persons would have had a specific preference for cyclosporin. In re Petering, 301 F.2d at 681, 133 USPQ at 279.

As to claim 16, it differs from claim 15 only in that it comprises the use of an anti-TNF α antibody as the antagonist. We find from a fair reading of the Aggarwal patent that one skilled in the art would have reasonably read the TNF antagonists taught therein for the treatment of rheumatoid arthritis to include anti-TNF α antibodies. See, e.g., the abstract, col. 4, lines 34-63; Example 1, cols. 8-9. Moreover, we point that the prior art of record demonstrates that anti-TNF α antibodies were known to be useful for the treatment of rheumatoid arthritis at the time the present invention was made. See, Le, col. 37, line 45- col. 38, line 21. Thus, our finding that one skilled in the art would

have understood the teaching of the patent to include the treatment of rheumatoid arthritis using an anti-TNF α antibody is consistent with the prior art of record.

Accordingly, in view of the foregoing, Rejection I is affirmed.

II. 35 U.S.C. § 103

A. The examiner has predicated his conclusion of obviousness on the teachings of Aggarwal and the appellants' admission on pages 13-15 and 19-25 of the specification that the use of chimeric antibodies for therapeutic purposes was well known in the art. Answer, p. 3.

In response, we find that the appellants do not contest the examiner's position, but rather they contend that they have obtained unexpected results. The appellants rely on the teachings of the specification (Examples 4-6, pp. 49-55; Table 10, p. 51; Table 11, p. 53; Table 13, p. 55; and Figures 4-7) which are said to demonstrate that it was unexpected that "a combination of sub-optimal doses of cyclosporin A and anti-TNF α antibody produced a highly significant reduction in the clinical severity of arthritis (Example 4)." Brief, p. 10. The appellants further rely on the declaration of co-inventor, Dr. Marc Feldman, which is said to provide additional evidence that the administration of sub-optimal doses of cyclosporin and anti-TNF α antibody had an unexpected synergistic ameliorative effect in the treatment of arthritis. Id. We find these arguments unpersuasive.

As indicated above, the appellants have not challenged the examiner's conclusion that the claimed invention would have been obvious to one of ordinary skill over the teachings of Aggarwal and knowledge generally available in the art. Rather, the appellants have limited their response to a showing of unexpected results.

We agree that in response to a prima facie case of obviousness, the appellants

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can submit objective evidence of nonobviousness, such as evidence of unexpected results. In re Soni, 54 F.3d 746, 749, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995); In re Piasecki, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984). However, the showing of unexpected results must be commensurate in scope with the claimed invention. In re Self, 671 F.2d 1344, 1348, 213 USPQ 1, 5 (CCPA 1982). This the appellants have not done. We point out that none of the claims is directed to a method of treating rheumatoid arthritis using “sub-optimal dosages of cyclosporin.” Thus, in the case before us, the prior art need only to teach or suggest a method of treating rheumatoid arthritis which comprises the use of a therapeutically-effective amount of cyclosporin to render the claimed invention obvious.

Accordingly, Rejection II is affirmed.

B. The examiner has rejected claims 15-17 as being unpatentable under 35 U.S.C. § 103 over Le, Ackerman and the appellants’ admission on pp. 13-15 and 19-25

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of the specification that the use of chimeric antibodies for therapeutic purposes was well known in the art. Answer, p. 3.

The examiner argues that Le and Ackerman disclose methods of treating rheumatoid arthritis which comprise the use of anti-TNF α antibodies and cyclosporin A, respectively. Answer, p. 3. The examiner concludes that since it was well known in the art to use chimeric antibodies for human therapy to reduce the immunogenicity of the therapeutic antibody, it would have been obvious to one of ordinary skill in the art to employ chimeric TNF α antibodies in combination with cyclosporin to treat rheumatoid arthritis. Id., p. 4.

The appellant has not contested the examiner's position. Since it reasonably appears that the appellants are using compounds which were known in the art to treat rheumatoid arthritis, for that very purpose, we agree with the examiner that it would have been obvious to one of ordinary skill in the art to arrive at the claimed method of treating rheumatoid arthritis using therapeutically effective amounts of anti-TNF α antibodies and cyclosporin. That is, it would have been obvious to employ known compounds for their known and expected results. Cf., In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Accordingly, Rejection III is affirmed.

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

AFFIRMED

WILLIAM F. SMITH
Administrative Patent Judge

JOAN ELLIS
Administrative Patent Judge

DONALD E. ADAMS
Administrative Patent Judge

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