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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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte VINCENT AGNELLO

Appeal No. 95-4481
Application 07/911,667¹

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and LORIN, Administrative Patent Judges.

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 7, all the claims in the application.

¹ Application for patent filed July 8, 1992.

Claims 1 through 3 are illustrative of the subject matter on appeal and read as follows:

1. A method of assaying for antibodies to human double-stranded DNA in a liquid, human-serum specimen, said method comprising the steps of:

forming a first incubation mixture of said specimen and a solid phase immunoabsorbent having immobilized thereon animal anti-human IgG antibody including F(ab')₂ fragment specific for IgG Fc;

incubating said first mixture under conditions and for a period of time sufficient for Fc in human IgG in said specimen to become bound by said F(ab')₂ fragment in said animal anti-IgG antibody;

forming a second incubation mixture of said first mixture and digoxigenin-labelled synthetic double-stranded DNA under such conditions and for a period of time sufficient to bind to said immunoabsorbent any anti-DNA antibodies which may be present in the serum so as to form a double-stranded DNA antibody that has substantially no single stranded or denatured components;

detecting the amount of digoxigenin labelled synthetic double-stranded DNA bound to said immunoabsorbent; and

relating the amount of bound labelled synthetic double-stranded DNA detected to a predetermined quantitative relationship between the amount of labelled double-stranded DNA and the amount of animal anti-human IgG antibody to determine the amount of human IgG in said specimen.

2. A method of assaying for antibodies to human double-stranded DNA in a human serum specimen, said method comprising the steps of:

capturing the anti-double-stranded DNA portion of IgG in said human serum specimen by the Fc part of a molecule using solid phase immobilized F(ab')₂ fragment of anti-human IgG specific for Fc;

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incubating the captured IgG with synthetic double-stranded DNA tagged with a moiety from which a signal proportional to the quantity of said synthetic double-stranded DNA can be elicited;

eliciting said signal; and

quantifying the amount of antibody to double-stranded DNA in accordance with the elicited signal.

3. A method as defined in claim 2 wherein said

captured IgG is incubated with synthetic double-stranded DNA tagged with alkaline phosphatase, and said elicited signal is proportional to the quantity of alkaline phosphatase tagging said synthetic double-stranded DNA.

The references relied on by the examiner are:

Litman et al. (Litman)	4,391,904	July 5, 1983
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Denise Pollard-Knight (Pollard-Knight), "Current Methods In Nonradioactive Nucleic Acid Labeling and Detection," 2 Technique-A Journal of Methods in Cell and Molecular Biology, no. 3, 112-132 (June 1990).

Richard M. Pope, et al. (Pope), "IgG Rheumatoid Factor: Analysis of Various Species of IgG for Detection by Radioimmunoassay," 97 Journal of Methods, no.6, 842-853 (1981).

Woodruff Emlen, et al. (Emlen), "A New ELISA for the Detection of Double-Stranded DNA Antibodies," 132 Journal of Immunological Methods, 91-101 (1990).

Claims 1 and 2 stand rejected under 35 U.S.C. § 103 as unpatentable over Litman in view of Pope and Emlen and claims 3 through 7 stand rejected under 35 U.S.C. § 103 as unpatentable over Litman in view of Pope and Emlen and further in view of Pollard-

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Knight. We reverse both rejections. In addition, we raise an issue for the examiner to consider upon return of the application.

DISCUSSION

The claims on appeal are directed to measurement of circulating human antibodies to double stranded DNA (dsDNA). A serum sample is incubated with immobilized antibodies or F(ab')₂ fragments specific for the Fc region of human IgG to capture and immobilize IgG present in the sample; the captured, immobilized IgG is incubated with labeled synthetic dsDNA, forming an immunological complex if antibodies specific for dsDNA are present; and the amount of dsDNA-specific antibody in the sample is determined by measuring the amount of bound labeled dsDNA. Claim 1 recites that the dsDNA label is digoxigenin, while claim 3 recites that the label is alkaline phosphatase.

Litman discloses a generic immunoassay protocol "employing rigid solid surfaces which may or may not be separated from the assay medium for measurement, where the signal may be developed without concern as to the presence of reagents in the solution affecting the observed signal on the solid surface." IgG is listed as one of hundreds of analytes which can be detected by Litman's assay protocol. There is no mention of IgG of any particular specificity. See column 1, lines 41-45 and column 17, line 67.

Pope analyzes various species of IgG to determine “which species of IgG is the most sensitive and specific antigen for the detection of IgG [rheumatoid factor] by radioimmunoassay.” See page 842.

Emlen discloses an ELISA for the detection of circulating antibodies specific for dsDNA in which biotinylated dsDNA is immobilized in streptavidin-coated wells, the immobilized dsDNA is used to capture antibodies specific for dsDNA, and the captured antibodies are detected with peroxidase-labeled anti-human IgG antibodies. The reference focuses on avoiding the problems of a number of conventional assays for detection of anti-dsDNA antibodies, most of which rely on immobilized DNA to capture circulating antibodies, and all of which are “plagued with the problem of purity of dsDNA, as well as problems unique to each assay.” See the Introduction section, especially the sentence bridging pages 91 and 92. Emlen overcomes the problems associated with the other assays by controlling the purity and antigenicity of the immobilized dsDNA.

Pollard-Knight discloses a number of non-radioactive substances used to label nucleic acids in hybridization assays. The labeling substances include digoxigenin, biotin and alkaline phosphatase.

The examiner believes that it would have been obvious for one of ordinary skill in the art “to combine the solid phase immunoabsorbent for use in a reversible sandwich immunoassay as disclosed by Litman et al., combined with a method of purifying IgG via

the Fc regions as taught by Pope et al. to bind to the immunoabsorbent solid support and immunoassays for the detection of dsDNA antibodies as taught by Emlen.” With regard to claims 3 through 7, the examiner believes that it would have been obvious “to develop a range of dsDNA labels used for quantitative detection.” According to the examiner, the reason, suggestion or motivation to combine these references is “to achieve methods of assaying for antibodies to human double-stranded DNA in a human-serum specimen as a whole . . . for the expected advantage of diagnosis and management of patients with . . . diseases associated with antibodies to double-stranded DNA.” See the Answer, pages 5 and 7.² We disagree.

We have no doubt that the prior art could be modified in a manner consistent with appellant’s specification and claims. The mere fact that the prior art could be so modified, however, would not have made the modification obvious unless the prior art suggested the desirability of the modification. In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Here, we find no cogent reason stemming from the prior art which would have led a person having ordinary skill to the claimed invention. In our judgment, the

² As stated in Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996) (citation omitted), “It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion or motivation to lead an inventor to combine those references.”

examiner's proposed reason for combining references amounts to a restatement of the objectives of appellant's invention and does not stem from the cited prior art.

Even assuming *arguendo* that the combination of references were proper, nevertheless, the combined disclosures of these references are insufficient to support the examiner's conclusion that the claimed method of detecting double-stranded DNA-specific IgG would have been obvious to one of ordinary skill in the art.

Suffice it to say that Litman and Pope have little or nothing in common with the claimed invention. At best, Litman teaches that IgG, as a class, can be detected by solid phase immunoassay. Pope was cited to show immobilization of IgG on an anti-Fc column, but actually shows immobilization of only the Fc portion of the antibody (which does not exhibit antigen specificity).³

Emlen, which discloses a solid phase assay for detection of antibodies specific for dsDNA, would appear to be the most relevant of the references relied upon. In the last paragraph of the Answer, after addressing appellant's arguments, the examiner contends that the claimed invention is simply the Emlen assay with the order of binding reversed. In our view, this is the strongest argument presented in support of the examiner's conclusion

³ Pope's starting material was papain-digested IgG. Papain digestion cleaves IgG into Fc and Fab fragments; only the Fc fragments would be retained on Pope's anti-Fc column. See Methods, lines 9 through 11. Also see Illustrated Dictionary of Immunology, R.E. Lewis, CRC Press, Inc., Boca Raton, FL, 1995, "papain hydrolysis," page 227. (Copy enclosed).

of obviousness. However, it is factually inaccurate. Merely reversing the order of binding in Emlen's assay would leave a number of differences between the two assays unaddressed, e.g., differences in specific reagents. Even if Emlen did describe the present assay in reverse order, on this record, the examiner has provided no reason, suggestion or motivation stemming from the prior art to disassemble Emlen's assay and reassemble it in reverse order.

In conclusion, we agree with appellant that the examiner did not meet the initial burden of establishing a prima facie case of obviousness of claims 1 through 7. Accordingly, the rejection of claims 1 through 7 under 35 U.S.C. § 103 is reversed.

OTHER ISSUE

Claims 1 through 7 are now free of rejection. However, we note that the claims are confusing in a number of respects. Merely by way of example, the third step of claim 1 recites that the first mixture (i.e., captured human IgG, immobilized on the immunoabsorbent of the first step) is incubated with dsDNA "for a period of time sufficient to bind to said immunoabsorbent any anti-DNA antibodies which may be present in the serum." This is confusing because the anti-dsDNA antibodies are already on the immunoabsorbent at this point in the assay; it is the dsDNA that is captured in the third step. Also, the last step of claim 1 is inconsistent with the preamble; the method does not determine the amount of IgG in the sample, it determines only that portion of the population

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specific for dsDNA. On return of this application to the Examining Corps, we recommend that both appellant and the examiner take steps to clarify the language of the claims.

The decision of the examiner is reversed.

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

REVERSED

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SHERMAN D. WINTERS)
Administrative Patent Judge)
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) BOARD OF PATENT
WILLIAM F. SMITH)
Administrative Patent Judge) APPEALS AND
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) INTERFERENCES
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