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for publication and is not binding precedent of the Board.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. 76

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte GARY F. BLACKBURN, CHARLES DURFOR,
MICHAEL J. POWELL, and RICHARD J. MASSEY

Appeal No. 2003-0480
Application No. 08/090,245

ON BRIEF

Before WINTERS, ADAMS, and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 83-90, which are all the claims pending in the application.

Claims 83, 85, 86 and 88 are illustrative of the subject matter on appeal and are reproduced below:

83. A method for detecting physical or chemical changes in an environment wherein said changes are the result of a chemical reaction taking place therein in which at least one reactant is converted to at least one product, which method comprises:

    (a) contacting said reactant with a catalytically active antibody or fragment thereof which is capable of catalyzing a chemical reaction, whereby said chemical reaction occurs in said environment, said antibody or fragment thereof being immobilized on a surface of, or on a surface associated with, a

sensing means, and thereby forming an antibody-reactant complex, catalytically converting said complexed reactant to said product and releasing said product from said complex, thereby regenerating said antibody or fragment; and

(b) collecting from the sensing means information relating to said changes and thereby detecting physical or chemical changes in the environment.

85. A method as recited in claim 83, wherein said catalytically active antibody or fragment is contained in or on a cell, a component of a cell, or a tissue.

86. A method for detecting physical or chemical changes in an environment wherein said changes are the result of a chemical reaction taking place therein in which at least one reactant is converted to at least one product, which method comprises:

(a) contacting said reactant with a catalytic monoclonal antibody or fragment thereof which is capable of catalyzing said chemical reaction, whereby said chemical reaction occurs in said environment, said catalytic monoclonal antibody or fragment thereof being immobilized on a surface of, or on a surface associated with, a transducer, and thereby forming an antibody-reactant complex, catalytically converting said complexed reactant to said product and releasing said product from said complex, thereby regenerating said antibody or fragment;

(b) transducing the physical or chemical changes in the environment as a result of said chemical reaction into information related to said changes; and

(c) processing the information generated by the transducer in response to the physical or chemical changes resulting from said chemical reaction and thereby detecting physical or chemical changes in the environment.

88. A method for detecting an analyte of interest in an environment wherein the analyte is consumed or generated during the course of a chemical reaction, which method comprises

(a) contacting said analyte of interest to bind a catalytic monoclonal antibody or a fragment thereof immobilized on a surface, or on a surface associated with sensing means, thereby forming an antibody-analyte complex

said catalytic monoclonal antibody or fragment thereof being capable of catalyzing a chemical reaction, wherein at least one reactant is converted to at least one product by forming an antibody reactant complex, catalytically converting said complexed reactant to said product and releasing said product from said complex thereby regenerating said antibody or fragment, wherein said chemical reaction occurs in said environment.

(b) detecting by the sensing means the binding of the analyte to the catalytic monoclonal antibody and transducing information related to said binding by a transducer;

(c) processing the information generated by the transducer; and

(d) releasing the analyte from the antibody or antibody fragment by catalyzing said chemical reaction of said analyte and thereby detecting the analyte of interest in the environment.

The references relied upon by the examiner are:

Schenck	4,238,757	Dec. 9, 1980
Conover et al. (Conover)	4,713,165	Dec. 15, 1987
Schochetman et al. (Schochetman)	4,888,281	Dec. 19, 1989

GROUND OF REJECTION

Claims 83-90 stand rejected under 35 U.S.C. § 103 as being unpatentable over Schochetman in view of Schenck and Conover, further in view of appellants statements as to the state of the art at pages 3-6 of the specification.

We affirm the rejection of claims 83-87, and reverse the rejection of claims 88-90.

CLAIM GROUPING

Appellants set forth the following four groupings of claims: I. claims 83 and 84; II. claim 85; III. claims 86 and 87; and IV. claims 88-90. Brief, page 6. In response to appellants' claim groupings we limit our discussion to representative claims 83, 85, 86 and 88. Claim 84 will stand or fall together with claim 83.

Claim 87 will stand or fall together with claim 86. Claims 89 and 90 will stand or fall together with claim 88. 37 CFR § 1.192(c)(7).

DISCUSSION

"The test for obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." In re Rosselet, 347 F.2d 847, 851, 146 USPQ 183, 186 (CCPA 1965).

According to the examiner (Answer, page 4), Schochetman discloses "a method for the preparation and use of [catalytic] monoclonal antibodies as convenient, readily obtainable and inexpensive catalysts having a degree of specificity and efficiency of action not previously achievable in the catalytic arts…." While Schochetman does not disclose a catalytic antibody immobilized on a surface of, or on a surface associated with, a sensing means, the examiner emphasizes (Answer, page 5), Schochetman discloses "[i]n addition to solution phase and emulsion reaction systems, suitable conditions also include the use of support materials to which the monoclonal antibody is attached. Such support materials are well-known to those of ordinary skill in the art as are methods for attaching monoclonal antibodies to them…."

The examiner relies on Schenck and Conover (id.), as "representative of the state of the art of enzyme sensors and antibody sensors at the time of the invention." According to the examiner (Answer, bridging paragraph, pages 5-6),

> Schenck discloses a field effect transistor which senses and measures the binding of a substrate to an antibody which is

> immobilized in the gate region of the transistor. The changes in the electrochemical potential of the immobilized antibody is measured by the transistor in the absence and presence of the appropriate substrate or antigen for that antibody. The transistors of Schenck then connect to transducers which display or modify the signal of the transistor into comparable data.

In addition, the examiner finds (Answer, page 6), Conover

> disclose ion selective electrodes which can use either immobilized antibodies … or immobilized enzymes … depending on the reactant to be measured. The immobilized enzymes "act on the substrate and produce a pH change proportional to the concentration of the analyte in the sample"…. This change in the pH is what is measured by the electrometer which is connected to the sensor (a transfucer)…. Conover also teaches that it is known in the art to immoblize cells and layers of tissue….

The examiner also finds (id.) that appellants' specification (pages 3-6) admits "that sensors using enzymes or antibodies were well known in the art, and that the macromolecular interactions were highly specific."

Based on this evidence, the examiner concludes (Answer, page 7), "[i]t would have been prima facie obvious to one of skill in the art at the time the invention was have [sic] made to have used immobilized catalytic monoclonal antibodies, in combination with a sensing and transducing means, for the detection of changes in a particular environment." Against this backdrop, we consider representative claims 83, 85, 86 and 88.

Claim 83:

The examiner finds (Answer, page 8), "Schochetman clearly teaches the desirability to produce catalytic antibodies directed against reactants for which enzymes are either unknown or not readily available … and suggests that they would have utility when immobilized…." In addition, the examiner finds (id.):

> In view of the extensive use of immobilized enzymes and antibodies in the prior art [e.g., Schenck and Conover] it would have been obvious to one of ordinary skill in the art to have immobilized such catalytic monoclonal antibodies on known sensors so as to permit monitoring of changes in an environment containing a reactant for which there was no previously known or readily available enzyme.

In response, appellants argue (Brief, page 9), "Schochetman does not disclose the immobilization of catalytic antibodies on a sensor or methods of using such sensors having immobilized catalytic antibodies as claimed." In addition, appellants argue (Brief, page 9), Schenck does not make up for the deficiency in Schochetman because Schenck is limited to "conventional antibodies (i.e., non-catalytic antibodies)." According to appellants (Brief, page 10), in Schenck "[a]s the antigen saturates the antibody, a specific antigen-antibody complex is formed which can then be measured. However, this binding reaction is not readily reversible. The antibody-based sensor thus becomes saturated and the presence of or excess analytes in a subsequent sample cannot be detected." In addition, appellants argue (Brief, page 10), Conover fails to make up for the deficiency in Schochetman. According to appellants (Brief, page 11), "Conover merely relates to a conventional enzyme biosensor coupled to an ion-selective electrode detection means. As a conventional enzyme biosensor,

Conover detects analytes via detection of a product of an enzyme-catalyzed reaction."

In conclusion, appellants argue (Brief, page 13), "the combination of Schochetman and Schenck would yield a device for measuring the rate of catalysis and not analyte concentration." We note, however, that claim 83 does not require the measurement of analyte concentration. Claim 83 requires only that the catalytically active antibody or fragment catalyze a chemical reaction (e.g., a physical or chemical change in an environment) that is detected by the sensing means. In our opinion, measuring the rate of catalysis, as appellants admit is taught by Schochetman and Schenck, is just such a physical or chemical change in an environment as is required by claim 83.

Accordingly, we affirm the rejection of claim 83 under 35 U.S.C. § 103 as being unpatentable over Schochetman in view of Schenck and Conover, further in view of appellants statements as to the state of the art at pages 3-6 of the specification. As set forth above, claim 84 falls together with claim 83.

Claim 85:

According to the examiner (id.), claim 85 "requires that the catalytic antibody be 'contained in or on a cell, a component of a cell, or a tissue.' A component of a cell is literally any … molecular fragment or molecule found therein. Thus immobilization on a cellulose acetate membrane, both cellulose and acetate are components of cells, would suffice to meet the required limitation."

In response, appellants argue (Brief, page 13), "Schochetman does not teach or suggest using a catalytic antibody contained in or on the cell, a component of a cell, or a tissue." Therefore, appellants opine (id.), "[i]t would not have been obvious to one of ordinary skill in the art, at the time the invention was made, that the catalytic antibody would remain accessible to the analyte of interest when it was contained within a larger complex." While appellants appreciate "that Conover discloses that whole cells or tissues maybe immobilized on sensors … [appellants argue that] neither Schochetman nor Conover teach or suggest that catalytic antibodies in cells or tissues would produce measurable and transducible signals." Reply Brief, page 15. Accordingly appellants conclude (Brief, page 13), "Schenck and Conover, alone or in combination, fail to compensate for the deficiencies of Schochetman."

As we understand appellants' argument, it is not that the prior art fails to recognize that catalytic antibodies can be immobilized on a cell, component of a cell or a tissue, instead, appellants' argument is that the analyte would not be accessible to a catalytic antibody contained in cells/tissues or a "larger complex." Claim 85, however, is not so limited. Instead, claim 85 is drafted broadly to include a catalytically active antibody or fragment on a cell, component of a cell or a tissue. In our opinion, in contrast to appellants' argument, a catalytically active antibody on a cell/tissue or component of a cell would be accessible to an analyte. See also, Answer, page 11 ("The claim is not limited to those embodiments wherein the antibody is necessarily inside the cell."). Therefore, we are not persuaded by appellants' argument.

We also recognize appellants' argument (Reply Brief, bridging paragraph, pages 14-15), "the [e]xaminer assigns a meaning to the term 'component' contrary to the meaning accepted in the art…. References to … cellulose acetate membranes are irrelevant in view of the disclosure in the specification." Appellants, however, fail to direct our attention to a particular section of their specification that supports their argument. Nevertheless, upon review of appellants' specification we find (page 15), the catalytic antibodies "may be contained in or on cells, components of cells or tissue, and may be in purified or unpurified form." We believe it would be fair to state that a component of a cell or tissue is a biological molecule. In this regard we note that appellants' specification (page 17) broadly defines "biological molecule … as a molecule which has been constructed from the compounds from which organisms are formed. Such compounds can be amino acids, nucleic acids, saccharides, membrane lipids, or biological cofactors." In our opinion, a cellulose acetate membrane falls within the scope of this definition. Accordingly, we do not find, and appellants have not identified, any portion of the specification which supports appellants' position that the examiner's interpretation of the term "component" is contrary to the art accepted meaning. Therefore, we are not persuaded by appellants' argument. Compare In re Morris, 127 F.3d 1048, 1056, 44 USPQ2d 1023, 1029 (Fed. Cir. 1997):

> The appellants urge us to consult the specification and some of the cited prior art, … and interpret the disputed language more narrowly in view thereof. When read in light of this material, according to applicants, the "true" meaning of the phrase emerges. We decline to attempt to harmonize the applicants' interpretation with the application and prior art. Such an approach puts the

> burden in the wrong place. It is the applicants' burden to precisely define the invention, not the PTO's.

Here, as in Morris[1], appellants fail to make the intended meaning of their claim explicitly clear. Accordingly, we find no error in the examiner's rejection. Therefore, we affirm the rejection of claim 85 under 35 U.S.C. § 103 as being unpatentable over Schochetman in view of Schenck and Conover, further in view of appellants statements as to the state of the art at pages 3-6 of the specification.

Claim 86:

Appellants do not dispute the examiner's finding (Answer, page 8) that transducers are known in the art. See Reply Brief, page 15, "transducers are known in the art, as discussed on pages 3-6 of the specification…." Instead, appellants argue (Brief, page 14):

> One of ordinary skill in the art would not have had a reasonable expectation of success that the catalytic antibodies of Schochetman would be able to change the environment in response to an analyte in a way that a transducer … can measure without the hindsight afforded by the present invention.

Claim 86 requires, inter alia, the catalytic monoclonal antibody be immobilized on a surface of, or on a surface associated with a transducer. To aid our interpretation of this limitation we note that appellants' specification discloses (bridging paragraph, pages 41-42), "catalytic antibodies … may be immobilized on a surface of the transducer or on a separate surface which is

[1] In re Morris, 127 F.3d at 1056, 44 USPQ2d at 1029.

associated with the transducer." Appellants' specification also discloses (page 29), "transducers used in prior art biosensors generally fall into three basic categories: electrochemical; optical; and physical." At page 33 of appellants' specification, appellants disclose that "[s]ensors for pH … are examples of optical fiber-based sensors."

To highlight the disclosure of Conover we note that claim 1 of Conover is directed to a sensor for the potentiometric determination of the activity of an ion or other concentration of a component in a sample comprising inter alia, ion selective electrodes comprised of an ion selective membrane. According to claim 5, which depends from claim 1 of Conover, the ion selective membrane is additionally comprised of an enzyme immobilized on the membrane which catalyzes a reaction which produces a change in pH … or a substance which is a substrate of an enzymatic reaction which produces a change in pH. Accordingly, as appellants recognize (Brief, page 11), "Conover detects analytes via detection of a product of an enzyme-catalyzed reaction."

Based on this evidence, we arrive at the same conclusion as the examiner (Answer, page 12), "it is unclear why it is unreasonable [as appellants argue] to conclude that catalytic antibodies would also produce transducible signals." In the regard, we note appellants' argument (Brief, page 9), "[c]atalytic antibodies are not simply substitutes for enzymes. One of ordinary skill in the art would not have been provided with the motivation or suggestion to replace enzymes with catalytic antibodies and that catalytic antibodies can replace enzymes as molecular recognition elements." According to appellants (Brief, page 12), "[o]ne

of ordinary skill in the art, at the time the invention was made, would have easily concluded that the catalytic properties of a catalytic antibody would be easily disrupted via the chemical or physical immobilization process." In support of this argument, appellants argue (id.):

> It is generally accepted in the art that specific binding (e.g., antigen-antibody binding) allows a certain level of flexibility while chemical catalysis requires sub-angstom precision in the position of the key amino acid residues in the catalytic site. The change in the antibody structure on immobilization can make functional groups inaccessible, modified, or improperly positioned for the catalysis. Thus, one of ordinary skill in the art would not have had a reasonable expectation of success with respect to the use of immobilized catalytic antibodies as sensors.

We note that in their Reply Brief, appellants' rely on Stryer[2] to shore these arguments. Notwithstanding appellants' reliance on Stryer and their argument that it could in theory be possible to disrupt the catalytically active portion of a catalytic antibody by immobilization, we are compelled to agree with the examiner (Answer, page 11) that Schochetman, which issued after the Stryer publication, discloses that catalytic antibodies can be immobilized on support materials. As the examiner points out (Answer, page 11), "[a]ppellant's [sic] assertion is unaccompanied by evidence…." We remind appellants that obviousness does not require absolute predictability of success. For obviousness under §103, all that is required is a reasonable expectation of success. In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). In our opinion, the evidence relied upon by the examiner provides a person of ordinary skill in the art with a reasonable expectation of success.

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[2] (Stryer) Biochemistry pp. 893-895 (L. Stryer, ed., W.H. Freeman and Company, New York, 1988).

For the foregoing, we affirm the rejection of claim 86 under 35 U.S.C. § 103 as being unpatentable over Schochetman in view of Schenck and Conover, further in view of appellants statements as to the state of the art at pages 3-6 of the specification. As set forth above, claim 87 falls together with claim 86.

Claim 88:

According to step (b) of claim 88, the sensing means detects the binding of the analyte to the catalytic monoclonal antibody. As appellants point out (Brief, page 15), "catalysis is utilized not as the basis of the signal generation, but as a means to regenerate the antibody or antibody fragment on the surface after the measurement is completed."

We recognize the examiner's theory (Answer, page 9), "[g]iven that one could make a catalytic antibody against an antigen of interest, which antibody was not terribly efficient as a catalyst … one could measure the amount [of analyte] bound and then allow the sensor to regenerate over time." However, in our opinion, while one could imagine this possibility after reading appellants' specification, we find no suggestion in the combination of references provided by the examiner to support such a theory. In re Gordon, 733 F.2d 900, 902, 211 USPQ 1125, 1127 (Fed. Cir. 1984).

Accordingly, we reverse the rejection of claims 88-90 under 35 U.S.C. § 103 as being unpatentable over Schochetman in view of Schenck and Conover, further in view of appellants statements as to the state of the art at pages 3-6 of the specification.

SUMMARY

We affirm the rejection of claims 83-87 under 35 U.S.C. § 103 as being unpatentable over Schochetman in view of Schenck and Conover, further in view of appellants statements as to the state of the art at pages 3-6 of the specification.

We reverse the rejection of claims 88-90 under 35 U.S.C. § 103 as being unpatentable over Schochetman in view of Schenck and Conover, further in view of appellants statements as to the state of the art at pages 3-6 of the specification.

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

AFFIRMED-IN-PART

Sherman D. Winters	)
Administrative Patent Judge	)
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	)
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	)
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