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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte MAY TOM-MOY and
CARL A. MYERHOLTZ

_____

Appeal No. 1996-1618
Application No. 07/876,804[1]

_____

ON BRIEF

_____

Before WINTERS, SPIEGEL, and SCHEINER, Administrative Patent Judges.

SPIEGEL, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner finally rejecting claims 18 and 24 through 28 and refusing to allow claims 17, 22, 23 and 29 as

[1] Application for patent filed April 29, 1992. According to appellants, this application is a continuation of application 07/404,721 filed September 8, 1989, now abandoned, which is a continuation-in-part of application 07/251,149 filed September 29, 1988, now US Patent 5,130,257, issued July 14, 1992.

amended subsequent to the final rejection, which are all of the claims pending in this application.[2] Claims 23, 24 and 29 are illustrative and read as follows.

> 23. A device for binding a specific chemical in a liquid which device comprises:
>
> a piezoelectric crystal substrate having a surface layer of silicon dioxide containing hydroxyl groups;
>
> a layer of coupling agent bound to said substrate, said agent having a functional group wherein said coupling agent is a silyl compound of the formula:
>
> $$R_nSiX_{(4-n)}$$
>
> wherein R is a nonhydrolyzable organic radical containing a primary alcohol group, X is a hydrolyzable moiety selected from the group consisting of chloro, amino, alkoxy, and acyloxy, and n is an integer from 1 to 3;
>
> a single ligand-binding layer attached to said coupling agent by means of said functional group on said coupling agent, said ligand-binding layer having binding sites thereon for binding a ligand-bearing substance thereto;
>
> a single ligand-bearing layer bound to said ligand-binding layer, said ligand-bearing layer being capable of selectively binding said specific chemical.
>
> 24. A device as in Claim 23 wherein said ligand-binding substance is selected from the group consisting of avidin, streptavidin, acetylated avidin, acetylated streptavidin, succinylated avidin, succinylated streptavidin, genetically engineered avidin with intact biotin binding sites [sic] genetically engineered streptavidin with intact biotin binding sites, modified avidin with intact biotin binding sites, and modified streptavidin with intact biotin binding sites; and said ligand-bearing substance is a biotinylated compound.
>
> 29. A device as in Claim 23 wherein said ligand-bearing substance is a lectin, said lectin having binding affinity for selected sugars.

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[2] The amendment filed March 14, 1994 (Paper No. 16) amending claims 17, 22 and 23 and cancelling claims 19-21 was entered by the examiner in the advisory action mailed April 7, 1994 (Paper No. 18). The amendment filed April 17, 1995 (Paper No. 26) amending claim 29 was entered by the examiner in the supplemental examiner's answer mailed July 10, 1995 (Paper No. 28, page 2).

The references relied on by the examiner are:

Katz et al. (Katz)	4,496,654	Jan. 29, 1985
Bastiaans	4,735,906	Apr. 5, 1988
Richards et al. (Richards)	4,847,193	Jul. 11, 1989
Baer et al. (Baer)[3]	5,130,527	Jul. 14, 1992
European Patent Application (Hansen)	139 489	May 2, 1985

Wilchek et al. (Wilchek), "REVIEW: The Avidin-Biotin Complex in Bioanalytical Applications," 171 Analytical Biochemistry, pp. 1-32 (1988).

Yanagita et al. (Yanagita), "Solubilization and purification of membrane proteins" in TECHNIQUES FOR THE ANALYSIS OF MEMBRANE PROTEINS, Chapter 2, pp. 61-76 (Ragan et al., eds., Chapman and Hall, London, 1986).

ISSUES[4]

Claim 29 stands rejected under 35 U.S.C. § 112, ¶¶ 1 and 2 as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Claims 17, 18, 22-25, 27 and 28 stand rejected under 35 U.S.C. § 103 as being unpatentable over Bastiaans, Wilchek and Katz. Claims 17, 18, 23 and 26 stand rejected under 35

[3] Baer was relied upon in the alternative to Bastiaans in finally rejecting claims 17-29 under 35 U.S.C. § 103 (see Office action mailed November 29, 1993 (Paper No. 14), page 3). However, as indicated infra, Baer was withdrawn as a reference when all prior rejections were withdrawn in the answer. See also reply brief, page 2.

[4] According to the examiner's answer (Paper No. 25), "[a]ll previous rejections have been withdrawn in view of the new grounds of rejection set forth below" (page 3).

U.S.C. § 103 as being unpatentable over Bastiaans, Wilchek and Katz as applied to claims 17, 18, 22-25, 27 and 28 above, and further in view of Hansen and Richards.

We REVERSE.

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's answer (Paper No. 25, mailed February 7, 1995), to the supplemental examiner's answer ("SEA," Paper No. 28, mailed July 10, 1995) and to the second supplemental examiner's answer ("SSEA," Paper No. 30, mailed August 29, 1995) for the examiner's reasoning in support of the rejections and to the appellants' brief (Paper No. 21, filed June 6, 1994), to the appellants' reply brief ("RB," Paper No. 27, filed April 17, 1995) and to the appellants' reply to supplemental examiner's answer ("SRB," Paper No. 29, filed July 31, 1995) for the appellants' arguments thereagainst.

OPINION

A. Rejections under 35 U.S.C. § 112, ¶¶ 1 and 2

The examiner rejected claim 29 under 35 U.S.C. § 112, ¶¶ 1 and 2, because the metes and bounds of "glycosylated receptor protein with said selected sugars attached" was indefinite (answer, page 3) and because the specification failed to enable the skilled

artisan to prepare such glycoprotein receptors in soluble, active form (answer, page 4).

Appellants subsequently amended claim 29 as follows

> 29. A device as in Claim 23 wherein said ligand-bearing substance is a lectin, said lectin having binding affinity for selected sugars[, and said ligand-bearing substance is a glycosylated receptor protein with said selected sugars attached].[5]

In response, the examiner stated that this deletion

> renders the claim indefinite in that the claim no longer recites a ligand-bearing substance. Moreover, the deletion of the phrase adds to the problem of what the metes and bounds of the claimed invention are in as much as it is unclear whether or not glycosylated receptor proteins are still envisioned as falling within the scope of the claim. [SSEA, paragraph bridging pages 3-4.]

First, a specification of a patent application is presumed to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. An examiner may reject claims in a patent application on the basis of an alleged failure of the applicants to comply with the enablement requirement if the examiner can establish by a preponderance of the evidence that there is reason to doubt the objective truth of the statements contained in the specification. In re Marzocchi, 439 F.2d 220, 223-24,
169 USPQ 367, 369-70 (CCPA 1971). Here, both lectin:glycoconjugate (i.e., sugar containing molecules, e.g., glycosylated membrane proteins) and avidin:biotin binding

[5] The double recitation of "said ligand-bearing substance" in claim 29 as set forth in the appendix of claims attached to the brief appears to be an obvious typographical error which requires appellants to clarify whether the lectin recited in the subsequently amended claim 29 refers to the "ligand-binding layer" or the "ligand-bearing layer" of claim 23.

pairs are known in the art (See e.g., TABLE 2 in Wilchek, page 3). The examiner has not challenged either the extrapolation of the avidin:biotin techniques exemplified in the specification to lectin:glycoconjugate binding pairs or the ability of the skilled artisan to select proper combinations of lectin and glycoconjugates. Rather, the examiner relies on Yanagita to show that purification of some glycoconjugates, e.g., some glycosylated membrane receptors, may present possible problems, problems which Yanagita not only explicitly identifies but also suggests means of dealing with. For example, Yanagita identifies "(1) Contaminants in detergents (3.3.1.a)" (page 73) as a possible problem and discloses in § 3.3.1.a that some detergents, e.g., nonionic detergents, must be purified before use, as well as two methods for purifying nonionic detergents (page 66). A specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). Moreover, it is not a function of the claims to specifically exclude possible inoperative combinations. Atlas Powder Co. v. E.I. DuPont De Nemours & Co., 750 F.2d at 1576, 224 USPQ at 414 citing In re Dinh-Nguyen, 492 F.2d 856, 858-59, 181 USPQ 46, 48 (CCPA 1974).

Second, the legal standard for indefiniteness under 35 U.S.C. § 112, second paragraph, is whether a claim reasonably apprises those of skill in the art of its scope. See, Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030

(Fed. Cir.), cert. denied sub nom., Genetics Inst., Inc. v. Amgen, Inc., 112 S.Ct. 169 (1991). The definiteness of claim language is analyzed, not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing an ordinary level of skill in the pertinent art. There has been no showing on this record by the examiner that one skilled in the art would have any particular difficulty in determining the meaning of these terms or of being reasonably apprised of their scope.

Finally, claim 23, from which claim 29 depends, recites a "ligand-bearing substance."

For the above reasons, we find the examiner has not carried his burden of establishing a prima facie case of lack of an enabling disclosure or of indefiniteness.

B. Rejections under 35 U.S.C. § 103

All of the claims on appeal require the presence of or preparation of a specific three layer structure on a piezoelectric crystal substrate having a surface layer of silicon dioxide containing hydroxyl groups; i.e., (1) a layer of a specifically defined organosilane coupling agent, e.g., 3-glycidoxypropyltrimethoxysilane (GOPS), bound to said substrate; (2) a single ligand-binding layer attached to said coupling agent by means of said functional group on said coupling agent, said ligand-binding layer having binding sites thereon for binding a ligand-bearing substance thereto, e.g., a single layer of avidin; and (3) a single

ligand-bearing layer bound to said ligand-binding layer, said ligand-bearing layer being capable of selectively binding a specific chemical, e.g., a single layer of biotinylated antibody which antibody selectively binds said specific chemical.

1. Rejection of claims 17, 18, 22-25, 27 and 28 over Bastiaans, Wilchek and Katz

Bastiaans discloses a piezoelectric crystal substrate having a GOPS coupling layer and antigen or antibody attached directly to the coupling layer (col. 2, lines 45-59). Wilchek is a review article which describes avidin-biotin complex as a general mediator in a variety of bioanalytical applications,

> mainly for isolation (affinity chromatography), localization (affinity cytochemistry, cell cytometry, and blotting technology), and diagnostics (for immunoassay and histopathology and as gene probes). More recently, current usage of the system has been extended to include various other areas, such as hybridoma technology, bioaffinity sensors, affinity targeting, and drug delivery, as well as crosslinking, immobilization, and fusogenic studies. [Page 1, col. 1.]

Katz describes a solid phase support, coated in whole or in part with avidin, and upon which biotinylated antibody is coated in selected areas (Fig. 1; col. 2, lines 19-24) useful in an enzyme immunoassay. For example, biotinylated anti-HCG antibody is reacted with an avidin-coated support, followed by contact with a sample suspected of containing HCG and then by contact with a labeled anti-HCG antibody to determine HCG based upon the amount of detectable label bound to the support (col. 1, line 59 - col. 2, line 9).

According to the examiner,

> [i]n view of the teachings of Katz et al. and Wilchek et al. one of ordinary skill in the art at the time the invention was made would have been motivated to and would have found it obvious to have replaced the direct coupling of binding agents, e.g., antibodies, to surfaces utilized in immunoassays taught by Bastiaans et al. by replacing the direct coupling of immunoglobulin with coupling of avidin. [Answer, page 8.]

The examiner relies on "the relatedness of the teachings of the prior art to the immobilization of reagents on solid-phases, including piezoelectric crystals" (SEA, page 2), a "[g]iven ... interest in exploiting piezoelectric crystals in analyte assays, an interest clearly apparent from Bastiaans, and in commercializing such assays" (SEA, page 3), and the "general teachings present" in the prior art (SSEA, page 2).

According to appellants,

> *Nowhere in the prior art, including the Katz and Bastiaans patents and the Wilchek reference, is there disclosed or suggested the use of avidin-biotin technology on a piezoelectric crystal substrate let alone in conjunction with a coupling layer.* [RB, page 11.]

It is insufficient that the prior art discloses the components of the claimed invention, either separately or in other combinations; there must be some teaching, suggestion, or incentive to make the combination made by appellants. Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1988) (insufficient to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor); W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d

1540, 1551, 220 USPQ 303, 312 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984) (individual references can not be "employed as a mosaic to recreate a facsimile of the claimed invention.")

Here, the only place we find the suggested combination of the three required layers on the specified piezoelectric crystal surface is in appellants' specification. Based on this record, we find that the examiner has relied on impermissible hindsight in making his determination of obviousness. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) ("It is impermissible to engage in hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps.")

Accordingly, the rejection of claims 17, 18, 22-25, 27 and 28 under 35 U.S.C. § 103 over Bastiaans, Wilchek and Katz is reversed.

2. Rejection of claims 17, 18, 23 and 26 over Bastiaans, Wilchek and Katz as applied to claims 17, 18, 22-25, 27 and 28 above, and further in view of Hansen and Richards

Hansen describes a sandwich hybridization which uses a labeled nucleic acid probe specific for a given portion of a desired sequence of interest and a biotinylated nucleic acid probe specific for a different portion of the desired sequence bonded to an avidin coated microparticle to "sandwich" the desired sequence therebetween, wherein determination of label to the microparticle after separation of unbound label thereform

indicates the presence of the desired sequence (page 2, lines 14-33). Richards discloses a member of a specific binding pair, e.g., a nucleic acid probe, antigen or antibody, immobilized on the surface of a piezoelectric oscillator (col. 2, lines 8-68). Immobilization includes coating the surface of the oscillator with a polymer, applying the specific binding pair member onto the polymer coated surface, and grafting the specific binding pair member to the polymer by UV irradiation (col. 3, lines 7-11).

We find nothing in Hansen or Richards which makes up for the deficiencies in Bastiaans, Wilchek and Katz. Accordingly, based on this record, the rejection of claims 17, 18, 23 and 26 over Bastiaans, Wilchek and Katz as applied to claims 17, 18, 22-25, 27 and 28 above, and further in view of Hansen and Richards is reversed.

CONCLUSION

To summarize, the decisions of the examiner to (I) reject claim 29 under 35 U.S.C. § 112, ¶¶ 1 and 2 for indefinitenss and lack of enablement; (II) to reject claims 17, 18, 22-25, 27 and 28 under 35 U.S.C. § 103 as being unpatentable over Bastiaans, Wilchek and Katz; and (III) to reject claims 17, 18, 23 and 26 under

35 U.S.C. § 103 as being unpatentable over Bastiaans, Wilchek and Katz as applied to claims 17, 18, 22-25, 27 and 28 above, and further in view of Hansen and Richards are reversed.

REVERSED

SHERMAN D. WINTERS Administrative Patent Judge	)
CAROL A. SPIEGEL Administrative Patent Judge	) BOARD OF PATENT) APPEALS) AND) INTERFERENCES
TONI R. SCHEINER Administrative Patent Judge	)

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