

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

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MARK NORMAN BOBROW, and KARL EDWIN ADLER

Appeal No. 2006-3006
Application No. 10/123,713

HEARD: December 13, 2006

Before SCHEINER, ADAMS, and LEBOVITZ, Administrative Patent Judges.

LEBOVITZ, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to an analytical system comprising an array of different first members of a specific binding pair. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 134. We affirm.

Claims

Claims 1-13 are pending and subject of this appeal. They stand rejected under 35 U.S.C. § 103(a). Br. 1. Claim 5 stands or falls apart from claims 1-4 and 6-13 because Appellants have provided separate arguments for its patentability. Br. 7. We select claims 1 and 5 as representative of each claim grouping. *See* 37 C.F.R. § 41.37(c)(1)(vii).

1. An analytical system comprising:

a support member having a plurality of chemically active, phenolic or proteinaceous receptor sites thereupon;

an array of different first members of a specific binding pair immobilized on an uppermost surface of said support and separated spatially from one another on the uppermost surface, said first members being selected from the group consisting of: protein, peptide, polysaccharide, cell fragments, cells, tissue, organometallics, metal ion chelating organic ligands, and combinations thereof, said first members each being capable of binding to a complementary second member of said specific binding pair, whereby when said array is contacted with a plurality of analyte complementary second members, a plurality of specific binding pairs will be formed on said support;

a peroxidase enzyme;

a coupling agent operative to couple said enzyme to said specific binding pairs; and

a conjugate of a labeling agent and a substituted phenol substrate for said enzyme, said substrate being activatable by said enzyme so as to cause said substrate to bind to one of said chemically active receptor sites whereby said substrate and said labeling agent are immobilized upon said support member.

5. An analytical system as in claim 1, wherein said labeling agent comprises a fluorescent cyanine dye.

Obviousness under 35 U.S.C. § 103

Claims 1-13 stand rejected under 35 U.S.C. § 103(a) as obvious over Bobrow¹ in view of Lizardi.²

Claims 1-4 and 6-13

Claim 1 is drawn to an analytical system having six key limitations: 1) a “support member”; 2) an array of different first members of specific binding pairs which are 3) immobilized “on an uppermost surface” of the support member and separated spatially; 4) a peroxidase enzyme; 5) a “coupling agent”; and 6) a conjugate of a labeling agent and a substituted phenol substrate.

The Examiner asserts that Bobrow describes all elements of the claimed analytical system, but does not “specifically teach [that] the different binding pairs are immobilized on the same support.” Answer 3: 15-16.

However, arrays of different first binding members were well known in the art at the time the claimed invention was made as taught by Lizardi et al. Lizardi et al[.] teach an analysis system similar to that of Bobrow wherein nitrocellulose is a preferred support for immobilization (Column 24, line 9) and wherein the analytical system comprises multiple and different binding members on the support (Column 50, lines 22-56; Example 5, Column 65, line 1-Column 66, line 31; and Fig. 9 and 29).”

Answer 3: 17-22.

Appellants do not challenge the Examiner’s finding that Bobrow describes limitations 1) and 4)-6) of the claimed subject matter, and we find no error in it. However, Appellants assert that the combination of Bobrow in view of Lizardi does not suggest “an array of different first members of a specific binding pair

¹ Bobrow et al. (Bobrow), *J. Immunol. Methods*, 137: 103-112 (1991).

² Lizardi, U.S. Pat. 6,143,495, Nov. 7, 2000.

immobilized on an uppermost surface of said support and separated spatially from one another on the uppermost surface.” Br. 4. For the purposes of this appeal, we need focus our attention only on these disputed limitations (*see supra*. elements 2) and 3) of the claimed analytical system).

Appellants assert that the properly construed claim 1 requires that the array members are immobilized on the “uppermost surface” of the claimed support which “precludes an interpretation that the arrays . . . encompass wells within a well plate.” Br. 6-7. As we understand it, Appellants interpret “uppermost surface” to mean the top and highest point of the support. A well (or microwell) is a depression in the support’s top surface and therefore, in Appellants’ construction, does not satisfy the claim limitation. They argue that each of Bobrow and Lizardi teach microwell supports in which the array members are present in the wells, not on the support’s uppermost surface, which is “inconsistent” with the claimed subject matter. *Id.* at 4.

We do not find that Appellants have correctly characterized the disclosure in Bobrow. As pointed out by the Examiner (Answer 7:17-19), Bobrow, in fact, describes arrays in which the array members are immobilized on the uppermost surface of a support, not in “microwell strips” as Appellants contend (Br. 4: 10-11).

Serial four-fold dilutions of rabbit IgG . . . or mouse IgG . . . were spotted (1 μ l) on nitrocellulose strips.

Bobrow, p. 105. A strip of nitrocellulose paper is a flat surface. Consequently, applying the antibody to it would result in an array on its top and “uppermost surface” as required by claim 1. Figs. 2-5 of Bobrow illustrate this configuration, showing also that the arrays of antibodies are separated from each other on the nitrocellulose paper which meets the limitation in claim 1 that the array members

are “separated spatially from one another on the uppermost surface” of the array support. In sum, we find no merit in Appellants’ factually incorrect argument.³

Lizardi is relied upon by the Examiner for its teaching of an array with different array members immobilized on it. Answer 3: 17-23. Appellants assert that “the term ‘array’ in Lizardi . . . is logically consistent only with a well plate.” Reply Br. 2.

We also do not find any merit in Appellants’ argument regarding Lizardi. As noted by the Examiner (Answer 7: 20-25), Lizardi very clearly describes support surfaces which are not well plates. “Solid-state substrates . . . include . . . nitrocellulose . . . thin films or membranes . . . glass slides.” Lizardi, col. 24, ll. 6-21. Appellants’ argument to the contrary is contradictory to Lizardi’s express disclosure.

Appellants also assert that

[f]urther support of Applicant’s position that Lizardi et al. requires physical isolation of specific binding pair first members in separate wells is found in Example 5 (column 65, line 1 - column 66, line 31). It is respectfully submitted that one of ordinary skill in the art would appreciate that without isolating the solutions of target molecules to individual wells, per Example 5, step 3 (column 65, lines 29-36), fluorescent development would result in a completely uniform test result, which would be devoid of information.

Br. 6. *See also* Reply Br. 2.

The section in Example 5 referred to by Appellants describes the preparation of fluorescently labeled probes. When the entire example is read, it is apparent that the labeled probes are then applied to an array of different oligonucleotides immobilized on the uppermost and top surface of a glass slide.

³ In the Reply Brief, Appellants concede they erred in their statement that Bobrow teaches “microwell strips.” Reply Br. 2.

Hybridization is performed by contacting the mixture of amplified RNAs [prepared by the method at col. 65, l. 5 to col. 66, l. 10], under a cover slip, with *the surface of a glass slide containing three separate dots of 2x10¹¹ molecules of three different covalently bound 31-mer oligonucleotides (A, B, C)* The last 16 bases of each oligonucleotide are complementary to a specific segment (4 bases+8 bases+4 bases), centered on the 8-base gap sequence, of each of the possible amplified RNAs generated from tag sequences A, B, or C. Hybridization is carried out for 90 minutes at 37°C. The glass slide is washed once with 2xSSPE . . . , then washed twice with 2xSSC . . . , and then incubated with fluoresceinated avidin (5 µg/ml) in 2xSSC for 20 minutes at 30°C. The slide is washed 3 times with 2xSSC and *the surface-bound fluorescence is imaged* at 530 nm using a Molecular Dynamics Fluorimager to determine if any of tag sequences A or B or C was amplified.

Col. 66, ll. 14-31 (emphasis added).

Thus, contrary to Appellants' argument, Lizardi utilizes a flat top surface array to fluorescently label and detected fluorescently labeled array members. Example 5 is therefore not "logically consistent only with a well plate" as they allege. Reply Br. 2: 7. Moreover, as indicated at col. 66, ll. 14-31 (quoted above), the assay does not "result in a completely uniform test result . . . devoid of information" as Appellants assert. Br. 6: 8-9.

We also find Appellants' argument deficient because the Examiner has not relied on Lizardi for its teaching of an assay method, but for its description of arrays with different members. Answer 3: 17-23.

Appellants' challenge the Examiner's finding that both Bobrow and Lizardi describe arrays of spatially separated array members as required by claim 1. Br. 6: 10-13. Appellants rely on Fig. 29A to refute the Examiner's findings, asserting that it depicts an antigen, "not an array." Br. 5. We find this argument disingenuous. Fig. 29A is a depiction of a *single* spot in an *array* of spatially

separated spots. *See Lizardi*, Example 11 at col. 80, l. 61; col. 81, ll. 8-12; and col. 82, ll. 27-34.

The Examiner bears the initial burden of showing unpatentability. *See, e.g.*, *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness requires evidence that the prior art disclosed or suggested all of the elements of the claimed invention, and that those skilled in the art would have been motivated to combine those elements with a reasonable expectation of success. *See In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970); *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1443 (Fed. Cir. 1991). All the elements of the claimed subject matter have been identified in the prior art by the Examiner, and motivation with a reasonable expectation of success has been provided for combining them. *See Answer 3:24 to 4:8*. Consequently, we find sufficient evidence of prima facie obviousness. Appellants have not provided persuasive evidence or arguments to rebut it. For the foregoing reasons, the rejection of claim 1 is affirmed. Because separate reasons for patentability were not provided, claim 2-4 and 6-13 fall with claim 1.

In affirming this rejection, we have adopted Appellants' construction that the claim limitation "uppermost surface of said support" as recited in claim 1 excludes the array members from being immobilized in microwells. However, because we concur with the Examiner that the prior art describes arrays on top surfaces that satisfy the claim limitation as construed by Appellants, we have not found it necessary to perform our own independent claim construction nor determine whether this is the exclusive construction of claim 1.

Claim 5

Claim 5, which is dependent on claim 1, recites that the “labeling agent comprises a fluorescent cyanine dye.” The Examiner asserts that Lizardi teaches that cyanine dyes are “known in the art.” Answer 4. She argues that “[i]t would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the fluorescent dyes suggested by Lizardi et al to the fluorescent labeling of Bobrow et al because one of ordinary skill in the art would have expected the cyanine dye to function as desired.” *Id.*

Appellants argue that Lizardi “mentions cyanine dyes in the context of incorporating cyanine dye-labeled UTP analogs into a nucleotide sequence during rolling circle replication in RCA, or during transcription in RCT Thus, the theoretical reference combination of Bobrow et al. with the cyanine dye labeled UTP fails to afford a ‘labeling agent that comprises cyanine dye’ that is ‘immobilized upon said support member.’” Br. 7.

We do not find Appellants’ argument persuasive. An obviousness determination under 35 U.S.C. § 103 requires consideration of “the scope and contents of the prior art” in the context of the level of the person of ordinary skill in the art. *Graham v. John Deere Co.*, 383 U.S. 1, 13-14 (1966). Lizardi describes a number of well-known detectable labels which can be used as labeling agents, leaving the choice of the particular labeling reagent up to the person of ordinary skill in the art. Based on this disclosure, we conclude that selection of the particular labeling agent to utilize in Bobrow’s method is the type of choice a skilled worker would have routinely made at the time the invention was made. The rejection of claim 5 is affirmed.

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

AFFIRMED

Toni R. Scheiner)
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