

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 25

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte KYOUICHI OHSHIRO

Appeal No. 2002-1360
Application No. 09/133,942

ON BRIEF

Before WILLIAM F. SMITH, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, 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 1-10, all of the claims in the application. Claim 1 is representative and reads as follows:

1. A method for measuring in solution the concentration of urinary trypsin inhibitor in a sample comprising:

adding antibodies against urinary trypsin inhibitor that are not adhered to an insoluble support to the sample in a reaction solution;

measuring the degree of the resulting agglutination in the reaction solution; and

correlating the degree of agglutination to the inhibitor concentration.

immunoassay (LAIA), and the like.” Specification, page 2. Each of these assays has various drawbacks. See id.

The specification discloses that “with respect to UTI, it was found that agglutination reaction can be measured even if free anti-UTI antibodies that are not adhered to an insoluble support such as latex particles etc. are used.” Page 3. Thus, the disclosed method “compris[es] preparing antibodies against UTI that are not adhered to an insoluble support (free anti-UTI antibodies), adding the antibodies to said sample, and measuring the degree of the resulting agglutination. Examples of the insoluble support include latex particles, gold colloid particles, and the like.” Id. According to the specification, this method “is excellent in precision and reproducibility, . . . [and] can be carried out easily without the need of special operations such as immobilization of antibodies, or use of special equipment. Furthermore, compared to LAIA, it has an advantage of causing less contamination in an automatic analyzer.” Id.

Discussion

Claim 1, the only independent claim, is directed to a method of measuring the concentration of UTI in solution by adding, to a sample, anti-UTI antibodies “that are not adhered to an insoluble support,” measuring the degree of agglutination that results, and correlating the degree of agglutination to UTI concentration. The examiner rejected most of the claims as anticipated by Maehara, and rejected all of the claims as obvious in view of Craig and Maehara.

1. Claim construction

“[N]ot unlike a determination of infringement, a determination of anticipation, as well as obviousness, involves two steps. First is construing the claim, . . . followed by, in the case of anticipation or obviousness, a comparison of the construed claim to the prior art.” Key Pharms. Inc. v. Hercon Labs. Corp., 161 F.3d 709, 714, 48 USPQ2d 1911, 1915 (Fed. Cir. 1998).

“It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art.” In re Sneed, 710 F.2d 1544,1548, 218 USPQ 385, 388 (Fed. Cir. 1983) (citation omitted). “Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history.” Vitronics Corp. v. Conceptor, Inc., 90 F.3d 1576, 1582, 39 USPQ2d 1573, 1576 (Fed. Cir. 1996).

In this case, the claims are directed to a method of measuring UTI concentration comprising adding to the sample anti-UTI antibodies “that are not adhered to an insoluble support,” and “measuring the degree of the resulting agglutination.” Claim 1. The specification discloses that “it was found that agglutination reaction can be measured even if free anti-UTI antibodies that are not adhered to an insoluble support such as latex particles etc. are used.” Page

3. In the first working example (pages 8-11), solutions containing varying concentrations of UTI were prepared and mixed with buffer. The absorbance of the mixture was measured, then anti-UTI antibody solution was added and the absorbance was measured again. The change in absorbance indicated the UTI concentration.

As used in immunology, “agglutination” means “[c]lumping of particulate antigens, e.g. red cells, bacteria, etc. by reaction with specific antibody which forms bridges between antigenic determinants on contiguous particles.” See Herbert,¹ page 6. Precipitation, by contrast, means “the formation of a visible complex on the addition of soluble antibody to soluble antigen.” Id., page 179. See also Leffell,² page 120: “Precipitation and agglutination were the first methods employed for demonstrating autoantibodies in human sera. Precipitation of cardiolipin has long served as a method for supporting the diagnosis of syphilis. . . . Agglutination reactions are highly sensitive methods for demonstrating antibody. Indirect, or conditioned, hemagglutination requires that a soluble antigen be attached to a particle, such as a red blood cell or latex.”

The difference between an assay based on precipitation and one based on agglutination is discussed in detail by Tizard.³ Tizard states that the difference between precipitation and agglutination is “determined by the physical state of the reactants. If antibodies combine with soluble antigens in solution

¹ Herbert et al. (eds.), “Dictionary of Immunology,” 3rd edition, Blackwell Scientific Publications (1985), copy attached.

² Leffell et al. (eds.), “Handbook of Human Immunology,” CRC Press (1997), copy attached.

³ Tizard, “Immunology: An Introduction,” Saunders College Publishing (1988), copy attached.

under appropriate conditions, the resulting complexes may precipitate. If, however, the antigens are particulate (for example, bacteria or red blood cells), they will agglutinate (clump).” Page 122.

Tizard describes a precipitation reaction as follows: “If a suitable amount of a clear solution of soluble antigen is mixed with its antisera and incubated at 37°C, the mixture becomes cloudy within a few minutes, then flocculent, and within an hour or so a precipitate settles to the bottom of the tube.” Id. Agglutination is similar, but results from “mixing a suspension of antigenic particles, such as bacteria, with antiserum. Antibody combines rapidly with the particles, the primary interaction, but agglutination is a much slower process, since adherence between particles occurs only when they touch each other.” Page 131.

The instant specification describes assays in which “UTI solutions having various concentrations of” UTI (page 8) were mixed with “Antibody Solution” (page 9). After addition of antibody, the mixtures were allowed to react only five minutes before the change in absorbance was measured. See page 10. Thus, in the assays described in the specification, the reaction takes place between soluble antigen and soluble antibody, and results can be measured in a few minutes. Based on these characteristics, the assays described in the specification appear to be what would normally be called “precipitation”, rather than “agglutination”. However, an applicant is allowed to be his own lexicographer. Since the meaning of the claim is reasonably definite when read in light of the specification, we do not consider the claims indefinite. We will

construe the claim term “agglutination” as being equivalent to the art-accepted term “precipitation”.

2. Anticipation

The examiner rejected claims 1-8 as anticipated by Maehara. The examiner characterized Maehara as “teach[ing] an agglutination assay using polyethylene glycol for immunodiffusion of urinary trypsin inhibitor.” Examiner’s Answer, page 3. According to the examiner, “[t]he samples used in the assay were human serum from males and females (page 119 para. 3). Antibody was added to the reaction solution and distributed onto the plate (page 119 para. 2).” Id., page 4. The examiner concluded that “Maehara et al., teaches a method for measuring the concentration of UTI [i]n a serum sample containing antibodies directed against UTI which are not attached to an insoluble support . . . and measured [sic] the degree of agglutination on immunodiffusion plates.” Id.

Appellant argues that “Maehara, which uses a single radial diffusion detection, does not anticipate claim 1. In the Maehara single radial diffusion, the antibodies are fixed in the gel plate and thus are adhered to an insoluble support.” Appeal Brief, page 5. Appellant notes that Maehara cites a reference by Mancini⁴ for a detailed disclosure of the immunodiffusion method. Appellant argues that Mancini makes clear that the antibody used in the immunodiffusion assay is added to an agar solution that is then allowed to solidify before being used in the assay. See the Appeal Brief, page 5.

⁴ Mancini et al., “Immunochemical quantitation of antigens by single radial immunodiffusion,” Immunohistochemistry, Vol. 2, pp. 235-254 (1965).

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). “[E]very limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim.” Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997).

We agree that Maehara does not anticipate claim 1. As Appellant points out, in the immunodiffusion assay used by Maehara, the anti-UTI antibodies are incorporated into a solidified agar matrix. See Mancini, page 235: “By definition the single-diffusion type of precipitin reaction is performed by incorporating one of the two partners of the reaction, usually the antibody, into the agar gel, at a uniform concentration, whereas the other reactant, usually the antigen, is introduced into a well from which it is allowed to diffuse into the gel.” Maehara’s disclosure confirms that the anti-UTI antibodies used were incorporated into the agar gel. See page 119, first full paragraph: “The concentration of agar in the gel plate was adjusted to 0.9% in 7 ml of veronal buffer . . . containing . . . various amounts of anti-UTlyG.” Anti-UTlyG is short for anti-UTI rabbit γ -globulin. See page 118.

Thus, in the assay disclosed by Maehara, the anti-UTI antibodies are attached to the insoluble agar gel support. Maehara therefore does not anticipate claim 1.

3. Obviousness

The examiner also rejected all of the claims as obvious in view of the disclosures of Craig and Maehara. According to the examiner, Craig discloses an immunoassay that meets all of the limitations of claim 1 except that Craig does not disclose the use of anti-UTI antibodies in the assay. See the Examiner's Answer, pages 4-6. Maehara teaches anti-UTI antibodies. The examiner concluded that "it would have been obvious at the time of applicant[']s invention to use the method of agglutination where antibodies are not adhered to an insoluble support as taught by Craig et al., with the antibodies of Maehara et al., because Maehara et al., teach that it is well known i[n] the art to use UTI antibodies to detect urinary trypsin inhibitor in agglutination assays." Id., page 7.

Appellant argues that "Craig specifically teaches that the reactant (i.e. antibody in the context of the present detection reaction) be bonded to the polymer particles. Thus, Craig merely is teaching an insoluble support that is considered to possess certain useful properties. As such, Craig also teaches directly away from claim 1, which requires addition of antibody that is not adhered to an insoluble support." Appeal Brief, page 6. Appellant also argues that "[e]ven if this combination is made . . . at best the combination would suggest that an antibody against UTI could be bonded to the Craig shell-core polymer particle. This still fails to suggest the addition of antibody not adhered to an insoluble . . . support as required by claim 1." Id.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness." In re Rijckaert, 9 F.3d

1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). “The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art.” In re Young, 927 F.2d 588, 591, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991). “The Patent and Trademark Office (PTO) must consider all claim limitations when determining patentability of an invention over the prior art.” In re Lowry, 32 F.3d 1579, 1582, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994).

Here again, we agree with Appellant that the cited references do not support the examiner’s rejection. The examiner characterizes Craig as teaching a “method of agglutination where antibodies are not adhered to an insoluble support.” See the Examiner’s Answer, page 7. The examiner, however, cites nothing in the reference to support that interpretation.

We agree with Appellant’s interpretation of the reference: in Craig’s assay, the antibodies are attached to an insoluble support, because the polymer particles disclosed by Craig are insoluble. For example, in discussing the process of binding antibody to the disclosed polymer particles, Craig teaches that

[a]fter sufficient time has elapsed to allow covalent attachment, a separation of particle reagent from the suspending buffered medium is effected, usually by centrifugation, although filtration, gravitational settling, etc. would suffice to allow the removal of unbound protein.

Column 10, lines 47-52.

Since Craig teaches that the particle-bound antibodies can be separated from the medium by centrifugation, filtration or gravitational settling, it necessarily follows that the particles are insoluble; soluble reagents cannot be taken out of solution by centrifugation, filtration, or settling. Thus, neither Maehara nor Craig

teach a method in which antibodies “are not adhered to an insoluble support,” as required by claim 1. The rejection under 35 U.S.C. § 103 is reversed.

Other Issues

As discussed above (pages 3-6), the art-accepted meaning of the term “agglutination” is an assay based on clumping of antibodies or antigens attached to particulate antigens. “Precipitation”, on the other hand, means formation of visible complex between soluble antigen and soluble antibody. Thus, the claimed assay would conventionally be described as based on precipitation, rather than agglutination. If the examiner’s initial search of the claimed assay was directed toward art disclosing an “agglutination” assay involving only soluble components, it probably did not produce the most relevant prior art.

Upon return of this case, the examiner should review the search that was performed and, if necessary, re-search the relevant sources for assays based on precipitation rather than agglutination. If a new search turns up prior art that anticipates or renders obvious the instant claims, entry of new rejections under 35 U.S.C. § 102 and/or 35 U.S.C. § 103 would be appropriate.

We also note that Appellant has submitted two Information Disclosure Statements since the Examiner’s Answer was filed. The examiner should act on those IDSs as appropriate under 37 CFR § 1.97.

Summary

The references cited by the examiner do not anticipate or render obvious the claimed method. We therefore reverse the rejections on appeal.

REVERSED

William F. Smith)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
Toni R. Scheiner)	
Administrative Patent Judge)	APPEALS AND
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)	INTERFERENCES
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Eric Grimes)	
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