

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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 JAN McDONAGH,
MYOUNG H. LEE AND MARCIN J. MANKOWSKI

Appeal No. 1997-3600
Application No. 08/300,447

ON BRIEF

Before WINTERS, SCHEINER, and ADAMS, 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 22-35, 41 and 42, which are all the claims pending in the application.

Claims 22, 25 and 41 are illustrative of the subject matter on appeal and are reproduced below:

41. A method for obtaining an initial activity of plasminogen activator inhibitor-1, an initial activity of tissue plasminogen activator, or a half-life of tissue plasminogen activity in a sample comprising the steps of:
 - (a) measuring activity of tissue plasminogen activator in the sample as a function of time; and
 - (b) obtaining a value of $(PAI)_0$, $(t-PA)_0$ or $\frac{1}{2} (t-PA)_0$ from formula:

Appeal No. 1997-3600
Application No. 08/300,447

$$kt = -1/((PAI)_0 - (tPA)_0) \ln\{(tPA)_0 [(PAI)_0 - (tPA)_0 + (tPA)]\} / (PAI)_0 (tPA)$$

wherein $(PAI)_0$ is the initial activity of plasminogen activator inhibitor-1 in the sample;

$(tPA)_0$ is the initial activity of tissue plasminogen activator in the sample;

(tPA) is an activity of tissue plasminogen activator at time t ; and

the half-life of tissue plasminogen activator in the sample is the value for t wherein (tPA) is $\frac{1}{2} (tPA)_0$;

k is a second order rate constant for a reaction:



22. The method of [c]laim 41 wherein the sample is a body fluid.

25. The method of [c]laim 22 further comprising acidifying the sample, thereby obtaining an acidified sample.

The references relied upon by the examiner are:

Zeffren et al. (Zeffren), The Study of Enzyme Mechanisms, 54-61 (John Wiley & Sons 1973)

Chmielewska et al. (Chmielewska), "Determination of Tissue Plasminogen Activator and Its 'Fast' Inhibitor in Plasma," Clinical Chemistry, Vol. 32, No. 3, pp. 482-485 (1986)

Wun et al. (Wun), "An Inhibitor of Plasminogen Activation from Human Placenta," J. Biol. Chem., Vol. 262, No. 8, pp. 3646-3653 (1987)

GROUND OF REJECTION¹

Claims 22-24, 29-35, 41 and 42² stand rejected under 35 U.S.C. § 103 as being unpatentable over Wun in view of Zeffren.

¹ We acknowledge the examiner's withdrawal (Supplemental Answer, page 2) Paper No. 24, mailed March 20, 1997) of the rejection under 35 U.S.C. § 112, second paragraph. In addition, we note the examiner's statement (Supplemental Answer, page 2) that "[c]laims 22-35, [and] 41-42 are currently pending in this application." Claims 37-40 were canceled, accordingly the examiner's Final Rejection (Paper No. 10, mailed November 8, 1995) of these claims under 35 U.S.C. § 103 is moot.

Appeal No. 1997-3600
Application No. 08/300,447

Claims 25-28 stand rejected under 35 U.S.C. § 103 as being unpatentable over Wun in view of Zeffren as applied to claims 22-24, 29-35, 41 and 42³ and further in view of Chmielewska.

We reverse.

DISCUSSION

The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). In meeting this initial burden, 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. Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

According to the examiner (Answer⁴, page 5) Wun teach “[o]n page 3649 Fig. 12 depicts plots of tPA with inhibitor where the activity of tPA is measured as function of time and is plotted as a first order reaction.” The examiner finds (Answer, page 5) that Wun differs from the claimed invention, in that the claims “include a determination of half-life and calculate activity based on a second order rate constant.” To make up for this deficiency, the examiner applies Zeffren (Answer, page 5) to teach “second order rate reactions depend upon the

² We note appellants’ statement (Paper No. 17, received August 15, 1996) that as a result of the amendments “[c]laim 21 [is] ... now [c]laim 41...” (page 6) and “[c]laim 36 has been cancelled and replaced with [c]laim 44 [sic, 42]...” (page 7).

³ Id.

Appeal No. 1997-3600
Application No. 08/300,447

concentration of two reactants[,] ... methods of determining the rate order of a given reaction[,] ... curves of concentration vs time[, and that] reaction half-time is defined and discussed.”

From this evidence the examiner concludes (Answer, page 6):

It would have been obvious to one of ordinary skill in the art at the time the invention was made to assay for activity by determination of half-life in the method of ... [Wun] because Zeffren shows half life determination is a standard technique in this art and would have the expected result. Further, Zeffren shows second order rate reactions and calculations based upon such calculations are also known for the same function as presently claimed.

In response, appellants argue that Wun teach placental plasminogen activator inhibitor, not PAI-1. Appellants argue (Brief, page 8) that Wun teaches that “there are at least three distinct types of PA inhibitors (page 3646, right column, first full paragraph): 1) protease nexin originally found in human foreskin fibroblast; 2) endothelial cell type PA inhibitor originally found in bovine aortic endothelial cell; and 3) placental type PA inhibitor.⁵” Accordingly, we are not persuaded by the examiner’s argument (Answer, page 10) that “claim 21 [sic 41] is directed to PAI-1 and does not specify any source or group.”

⁴ Paper No. 21, mailed October 29, 1996.

⁵ Consistent with the teachings of the Wun reference, we note that United States Patent No. 5,112,955, issued May 12, 1992 (two years prior to the filing of the instant application) discloses (column 1, lines 29-32) that several plasminogen activator “inhibitors have been recognized: endothelial cell type PA inhibitor (PAI-1), placental type PA inhibitor (PAI-2), urinary PA inhibitor (PAI-3) and protease nexin.” We note that a copy of this patent was present in the administrative file. However, it does not appear that this reference was made of record in the administrative file, or that a copy of this reference was made available to appellants. Accordingly, we attached a copy of this patent to our decision.

Appeal No. 1997-3600
Application No. 08/300,447

Furthermore, we are not persuaded by the examiner's argument (Answer, page 10) that "[o]ne would have a high expectation of success in employing an assay for the same substance derived from placenta as derived from plasma when the same substance is known to be found in both plasma and placenta." Instead, we agree with appellants (Brief, page 9) that "the mere fact that placenta inhibitor and PAI-1 have a common activity (the ability to inhibit t-PA) does not support the [e]xaminer's conclusion that the compounds are the same or behave in the same manner."

In addition, we emphasize that the examiner recognized (Answer, page 5) that in contrast to the claimed invention, Wun teach a first order reaction. In this regard we note appellants' argument (Brief, page 15) that although Zeffren "teach that second order reaction rates depend on the amount of the two reagents, nowhere does Zeffren teach that the reaction between tPA and PAI-1 occurs according to second order kinetics or that it can be used to determine the initial amounts of these two reactants in a sample." On these facts, we agree with appellants (Brief, page 15) that "Zeffren does not provide the motivation to modify the kinetic study disclosed in ... [Wun] to achieve [a]ppellant's [sic] claimed invention."

We re-emphasize, that the initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d at 1445, 24 USPQ2d at 1444. In satisfying this initial burden, "[t]he Patent Office has the initial duty of supplying the factual basis for its rejection. It may not, because it may doubt that the

Appeal No. 1997-3600
Application No. 08/300,447

invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in its factual basis.” In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057 (1968).

On the record before us, we find no reasonable suggestion for combining the teachings of the references relied upon by the examiner in a manner which would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. On these facts the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

Accordingly, we reverse the examiner’s rejection of claims 22-24, 29-35, 41 and 42 under 35 U.S.C. § 103 as being unpatentable over Wun in view of Zeffren.

With regard to the examiner’s rejection of claims 25-28 under 35 U.S.C. § 103 as being unpatentable over Wun in view of Zeffren as applied to claims 22-24, 29-35, 41 and 42 and further in view of Chmielewska. The examiner relies (Answer, page 6) on Chmielewska to teach “determination of tPA where samples were mixed with plasminogen, incubated and the reaction was terminated by adding an acidifying agent....”

However, as explained by appellants (Brief, page 17) that while Chmielewska does teach PAI-1, Chmielewska does not involve a kinetic study, but instead teaches a method in which standard curves are generated. According to

Appeal No. 1997-3600
Application No. 08/300,447

appellants “Chmielewska also does not suggest the many advantages of using kinetics compared with the standard curve methodology to evaluate tPA activity or PAI-1 concentration in a sample.” As set forth in Ecolochem Inc. v. Southern California Edison, 227, F.3d 1361, 1375, 56 USPQ2d 1065, 1075 (CAFC 2000) the:

“[S]uggestion to combine may be found in explicit or implicit teachings within the references themselves, from the ordinary knowledge of those skilled in the art, or from the nature of the problem to be solved.” ... However, there still must be evidence that “a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.” [Citations omitted].

On this record, we are compelled to agree with appellants (Brief, page 17) that “Chmielewska does not cure the deficiencies of ... [Wun] and Zeffren.” We again, find no reasonable suggestion for combining the teachings of the references relied upon by the examiner in a manner which would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. On these facts the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d at 1074, 5 USPQ2d at 1598.

Appeal No. 1997-3600
Application No. 08/300,447

Accordingly, we reverse the examiner's rejection of claims 25-28 under 35 U.S.C. § 103 as being unpatentable over Wun in view of Zeffren as applied to claims 22-24, 29-35, 41 and 42 and further in view of Chmielewska.

REVERSED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
)	
)	BOARD OF PATENT
TONI R. SCHEINER)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
)	
DONALD E. ADAMS)	
Administrative Patent Judge)	

Appeal No. 1997-3600
Application No. 08/300,447

DAVID E. BROOK
HAMILTON BROOK SMITH & REYNOLDS
TWO MILITIA DRIVE
LEXINGTON, MA 02173-4799

DEA/jlb