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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

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CENTRAL REEXAMINATION UNIT

EX PARTE REEXAMINATION COMMUNICATION TRANSMITTAL FORM

REEXAMINATION CONTROL NO. : 90008305
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ART UNIT : 3900

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above identified ex parte reexamination proceeding (37 CFR 1.550(f)).

Where this copy is supplied after the reply by requester, 37 CFR 1.535, or the time for filing a reply has passed, no submission on behalf of the ex parte reexamination requester will be acknowledged or considered (37 CFR 1.550(g)).

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Reexamination Control Number: 90/008,305
Reexamination Filing Date: 10/23/2006
U.S. Patent No. 4,940,658
U.S. Application Filing Date: 11/20/1986
Appellant(s): Competitive Technologies, Inc. and The Trustees of Columbia University

REQUEST FOR REHEARING BY EXAMINER UNDER MPEP 1214.04

It is respectfully requested that the decision by the Board of Patent Appeals and Interferences (Board) dated 30 July 2009 in the above identified application (Ex parte Competitive Technologies, Inc. and The Trustees of Columbia University, Appeal No. 2009-005519 (BPAI July 30, 2009)) be reheard and reconsidered by an expanded panel on the written record, as supplemented below.

The Board decision of July 30, 2009 reversed the rejection of claims 13, 15-17 and 33 under 35 U.S.C. § 103 as unpatentable over Refsum in view of Kass, Wilcken and Westhuyzen. The Board decision stated disagreement with the Examiner's obviousness determination and thus did not sustain the rejection. The disagreement is based on the alleged failure by the Examiner to provide a factual basis for extrapolating "total homocysteine" from one or more of the forms which comprise it, especially in view of known redistribution between free and bound forms of homocysteine. The Board's rationale and disagreement is based on a failure to appreciate the

material facts in the primary reference and the explicit disclosures in the secondary references as well as the disclosures in the specification of the patent under reexamination. It is believed that the Board would have sustained the rejection, but for this lack of appreciation.

PERIOD FOR REPLY

Appellant may file a reply to this request for rehearing within **two (2) months** of the mailing date of this request for rehearing. This two-month period may **not** be extended under the provisions of 37 CFR 1.136(a). After the expiration of this two-month period (plus an appropriate period for mail processing), the above-identified application will be forwarded to the Board for consideration of this request for rehearing.

REASONS FOR THE BOARD TO RECONSIDER

1. ***Ground of Rejection***

Claims 13, 15-17 and 33 stand rejected under 35 U.S.C. § 103 as unpatentable as shown by Refsum in view of Kass (1977), Wilcken et al. and Westhuyzen.

Refsum teaches a modified radioenzymatic assay to detect levels of total homocysteine in human serum and urine. Refsum indicates that there is a linear relationship between free homocysteine and bound homocysteine in a given sample (pg. 625, right column). In other words, based on the slope of the line in Figure 2 of Refsum, there will always be a proportionally larger amount of bound homocysteine as compared to free homocysteine. Refsum also recognizes that determinations of homocysteine in urine and plasma may provide information on pertubations of homocysteine metabolism in humans during diseases or pharmacological

interventions that affect metabolism of one carbon compounds. (page 627, right column-bridging left column).

The secondary references are relied upon for teaching the correlation between elevated homocysteine levels and deficiencies of folate or vitamin B_{12} (cobalamin).

Kass teaches that elevated levels of homocysteine exist in human bone marrow sample of persons with pernicious anemia or vitamin B_{12} (cobalamin) deficiency conditions (page 55, right column; page 56, right column). Kass states,

> [h]omocysteine plays a critical role in the enzymatic reaction mediated by methylcobalamin-dependent methyltransferase, resulting in formation of methionine from transmethylation of the methyl group of methyltetrahydrofolate to homocysteine. Accordingly, it was decided to investigate the properties of the nickel–bound homocysteine precipitate further, particularly in terms of its potential applicability as a cytochemical test *for the detection of homocysteine conditions where increased amounts of homocysteine might be anticipated, such as vitamin B_{12} deficiency.*

Kass at page 54 (emphasis added). Furthermore, the mechanism and pathway of methionine and homocysteine is well known, as such, Kass indicates that it is well established that an increase in the homocysteine levels corresponds to a decrease in cobalamin, see page 55 of Kass.

Wilcken teaches an association between elevated plasma homocysteine and low serum B_{12} levels (page 368, right column).

Westhuyzen teaches that NO_2 exposed fruit bats with vitamin B_{12} deficiency have increased levels of homocysteine (page 660).

In this case, Refsum teaches the first step of the claimed method. Appellant's own specification discloses that elevated homocysteine levels in serum and urine were present in a few children with life-threatening cobalamin deficiency (col. 4, lines 64-66). The content of the prior art, Kass, Wilcken and Westhuyzen, provides additional support for the proposition that deficiencies of cobalamin or folate correlate with elevated homocysteine, which is detected as part of the forms which constitute the "total" homocysteine. Therefore, it would have been obvious to use the test of Refsum for determining total homocystein and correlate the elevated homocysteine levels with a deficiency characterized by elevated homocysteine. Specifically, correlating the elevated homocysteine with folate or cobalamin deficiencies since Kass, Wilcken and Westhuyzen teach such correlations.

2. The Board decision failed to fully consider the teachings of Refsum.

The decision (page 4) made a single finding of fact with respect to Refsum and provided no further discussion of the primary reference. Specifically, the Board stated:

> Refsum determines total homocysteine by treating the plasma with dithierthyitol to reduce the various homocysteine forms to free homocysteine, converting the free homocysteine to S-[14C]adenosylhomocysteine with [14C]adenosine and S-adenosylhomocysteine hydrolase, and quantifying the s-[14C]adenosylhomocysteine by HPLC. (FF4)

However, Refsum, as noted above, clearly indicates that there is a linear correlation between the free homocysteine and the bound homocysteine as shown in Figure 2. Furthermore, Refsum, taken as a whole, indicates releasing homocysteine from plasma proteins as free homocysteine is required to determine the "total" homocysteine. Refsum at 626, right column. Lastly, Refsum teaches that the detection of total homocysteine levels is a useful tool for providing "information on pertubations of homocysteine metabolism . . . . " (see Refsum page

627). Thus, Refsum provides explicit motivation to gather data on total homocysteine levels and correlate such findings to a particular disease. However, Refsum does not explicitly teach which such disease states could be identified by increased homocysteine levels. These teachings are provided by the secondary references as informed by the specification of the patent, as explained *supra*.

3. The Board decision overanalyzed the homocysteine taught by the secondary references Kass, Wilcken and Westhuyzen.

The secondary references are relied upon solely for the proposition that detection of elevated homocysteine correlates with a deficiency of cobalamin or folate. The Federal Circuit recognized this same feature of the claims and stated the scope of this limitation as: "[t]he claim only requires association of homocysteine levels with vitamin deficiencies." *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 304 F.3d 1354, 1362 (Fed. Cir. 2004). Therefore, it is irrelevant if Kass, Wilcken or Westhuyzen are detecting "less than total" homocysteine. Furthermore, the secondary references teach that increased homocysteine (free and/or bound) levels correlates with vitamin deficiencies. If the secondary references were directed to detecting "total" homocysteine and correlating that detected "total" homocysteine level with cobalamin or folate deficiency, then the secondary references would themselves anticipate the claimed subject matter. However, as noted in the obviousness rejection, the secondary references teach the missing element from Refsum, *i.e.*, that an elevated homocysteine level correlates with cobalamin or folate deficiency. Based on the established nature of the linear relationship between free homocysteine and bound homocysteine as evidenced by Refsum, clearly, where an increase in free homocysteine correlates with a deficiency in cobalamin or folate, then an increase in total homocysteine would similarly correlate with a deficiency of cobalamin or folate.

This is especially true since total homocysteine is made up of free and bound homocysteine and a person having ordinary skill in the art would recognize that there is a similar linear relationship between free and total homocysteine as there is with bound and total homocysteine. Since elevated homocysteine levels are known to correlate to deficiencies of cobalamin or folate, one skilled in the art would find it predictable that elevated total homocysteine levels would correlate with a deficiency of the cobalamin or folate. Furthermore, such elevated homocysteine levels and the correlation to the deficiencies is a well-established physiological phenomena which was known prior to the present invention (Kass, Wilcken & Westhuyzen and the patent specification at column 4, lines 64-66 and column 5, lines 32-36).

Accordingly, the examiner requests a rehearing where the Board considers the rejection of claims 13, 15-17 and 33 as unpatentable under 35 U.S.C. § 103 over Refsum in view of Kass, Wilcken and Westhuyzen.

Conclusion

For the foregoing reasons, it is submitted that the examiner has set forth a proper *prima facie* case establishing the unpatentability of claims 13, 15-17, and 33 under 35 U.S.C. § 103 as unpatentable over Refsum in view of Kass, Wilcken and Westhuyzen. Therefore, it is respectfully requested that the Board decision of July, 30, 2009, in the above-identified application be reconsidered and that the rejection of claims 13, 15-17 and 33 under 35 U.S.C. § 103 as unpatentable over Refsum in view of Kass, Wilcken and Westhuyzen be sustained.

Respectfully submitted,

Padmashri Ponnaluri
Primary Examiner

Approved:

Gregory A. Morse
Director-Central Reexamination Unit

Andrew H. Hirshfeld
Deputy Commissioner for
Patent Examination Policy