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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/129,999	09/02/2011	Paul Cales	0727-1036-1	3821

466 7590 06/27/2018

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EXAMINER
FRITCHMAN, REBECCA M

ART UNIT	PAPER NUMBER
1797	

NOTIFICATION DATE	DELIVERY MODE
06/27/2018	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte PAUL CALES,
CHRISTOPHE AUBE, and VINCENT ROULLIER

Appeal 2017-007437
Application 13/129,999
Technology Center 1700

Before MICHAEL P. COLAIANNI, GEORGE C. BEST, and
N. WHITNEY WILSON, *Administrative Patent Judges*.

WILSON, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellants[1] appeal under 35 U.S.C. § 134(a) from the Examiner's March 28, 2016 decision finally rejecting claims 1, 4, and 22–24. We have jurisdiction over the appeal under 35 U.S.C. § 6(b).

We affirm.

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[1] Appellants identify the real parties in interest as Université d'Angers and Centre Hospitalier Universitaire d'Angers (Appeal Br. 2).

CLAIMED SUBJECT MATTER

Appellants' invention relates to the field of hepatic diagnosis (Spec. 1:4). According to the Specification, the described *in vitro* non-invasive method facilitates quantifying liver lesions, which are due or related to liver impairment, liver steatosis, non-alcoholic fatty liver disease (NAFLD), or nonalcoholic steatohepatitis (NASH) (*id.* at 1:5–8). Claims 1 and 23 are representative and are reproduced below from the Claims Appendix of the Appeal Brief:

> 1. An *in-vitro* non-invasive method for quantifying lesions of a liver of a patient, comprising:
>
> obtaining a blood sample from the patient;
>
> measuring the following five biomarkers in the blood sample: glycemia, AST (aspartate aminotransferase), ALT (alanine aminotransferase), ferritin, and platelets;
>
> measuring the following two clinical markers in the patient: age and weight;
>
> combining said measures in a logistic function;
>
> obtaining a score value reflecting the stage of liver fibrosis and the quantification of liver lesions.

Appeal Br. 22 (Claims App.).

> 23. A method of quantifying fibrosis of a liver of a patient, comprising:
>
> obtaining a blood sample from the patient;
>
> measuring the following five biomarkers in the blood sample: glycemia, AST (aspartate aminotransferase), ALT (alanine aminotransferase), ferritin, and platelets;
>
> measuring the following two clinical markers in the patient: age and weight;

performing binary logistic regression analysis combining the seven measures of the five biomarkers and the two clinical markers to calculate a score value; and

quantifying the fibrosis of a liver based on the score value reflecting the stage of liver fibrosis.

Id. at 22–23.

REJECTIONS

(1) Claims 1, 4, and 22–24 are rejected under 35 U.S.C. § 101 as directed to patent-ineligible subject matter.

(2) Claims 1, 4, and 22–24 are rejected under 35 U.S.C. § 103(a) as unpatentable over Maor[2] in view of Callewaert,[3] and further in view of Salonen.[4]

The Examiner has withdrawn the rejection of claims 1 and 23 under 35 U.S.C. § 112, ¶ 2, as indefinite (Ans. 5; *see also* Final Act. 2–3).

With respect to the rejections maintained by the Examiner, Appellants do not make separate substantive arguments in support of patentability of any of the claims (*see generally* Appeal Br. 12–21; Reply Br. 1–3). Accordingly, our discussion will focus on the rejections of independent claims 1 and 23. Claims 4, 22, and 24 will stand or fall with each of their respective independent claims. 37 C.F.R. § 41.37(c)(1)(iv).

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[2] Y. Maor et al., "*Improving estimation of liver fibrosis using combination and newer noninvasive biomarker scoring systems in hepatitis C-infected haemophilia patients*," 13 Haemophilia 722–29 (2007).
[3] Callewaert et al., US 2005/0112691 A1, published May 26, 2005.
[4] Salonen et al., US 2007/0072798 A1, published Mar. 29, 2007.

DISCUSSION

Rejection I

The Examiner concludes that claims 1 and 23 are directed to two judicial exceptions: (i) an abstract idea and (ii) a law of nature (Final Act. 4). The Examiner further concludes that the claims are drawn "towards performing statistical analysis, mathematical functions (logistic function, binary logistic regression, etc.), . . . which is [sic] a mental process/abstract idea" (*id.* at 2). According to the Examiner, these claims are also "drawn towards the measurement of naturally occurring 'markers' and correlating these markers to the presence of disease" (*id.* at 3).

The Examiner determines that Appellants do not claim anything, including "the mathematical/statistical analysis," "which is significantly more/not conventional than" correlating naturally occurring markers to the presence of disease (*id.* at 6, 3). Thus, the Examiner concludes that the subject matter of claims 1 and 23 is within the scope of the judicially-created exception that places abstract ideas and natural laws outside of the scope of patent-eligible subject matter.

We agree with the Examiner that, under the two-step test of *Alice Corp. v. CLS Bank International*, 134 S. Ct. 2347 (2014), claims 1 and 23 are not directed to patent-eligible subject matter. The *Alice* Court stated that "[i]n *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. [66] . . . (2012), we set forth a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice Corp.*, 134 S. Ct. at 2355.

The *Alice* Court described the *Mayo* test as follows:

> First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts. If so, we then ask, "[w]hat else is there in the claims before us?" To answer that question, we consider the elements of each claim both individually and "as an ordered combination" to determine whether the additional elements "transform the nature of the claim" into a patent-eligible application. We have described step two of this analysis as a search for an "inventive concept"—*i.e.*, an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself."

Id. (alterations in original, citations omitted).

Appellants make the following arguments urging reversal of the Examiner's § 101 rejection: (1) the claims amount to significantly more than a logistic function because claims 1 and 23 require "the measurement in a blood sample of five specific biomarkers and two specific clinical markers and the combination of the values measured in a logistic function, with the stated aim of obtaining a score value useful for the quantification of a liver lesion," (Appeal Br. 13); (2) because "three biomarkers may each be associated to a number of disorders[,] . . . there is no direct correlation between the . . . seven markers recited in the present invention and the presence of liver lesions" (*id.* at 14); (3) "measuring the five cited biomarkers and the two cited clinical markers and combining them in a specific mathematical function . . . amounts to significantly more than applying a law of nature" (*id.* at 14–15); and (4) the seven measured markers are not "well-understood, routine or conventional in the field" (Reply Br. 2).

We are not persuaded by these arguments.

Appellants' argument (2) is directed to the first step of the *Alice/Mayo* test. In other words, Appellants argue that the Examiner reversibly erred in determining that the claims at issue are directed to the patent-ineligible concept of "applying a law of nature, a natural correlation" (Ans. 3; *see also* Appeal Br. 14).

We note, however, Appellants admit that the claimed method facilitates "quantifying liver lesions, *especially due or related to* liver impairment, liver steatosis, non-alcoholic fatty liver disease (NAFLD), or nonalcoholic steatohepatitis (NASH)" (Spec. 1:5–8 (emphasis added)).[5] Moreover, the Examiner finds that one of the three biomarkers allegedly associated with a number of disorders, i.e., platelet count, is a known biomarker related to liver fibrosis (Ans. 4 (citing Maor 722, col. 1); *see also* Appeal Br. 14).[6] Thus, we agree with the Examiner that detecting the claimed combination of naturally occurring 5 biomarkers and 2 clinical markers informs a relevant audience of certain laws of nature: specifically, that levels of certain biomarkers and clinical markers will differ in diseased patients compared to normal patients based on the natural correlation.

Appellants' arguments (1), (3), and (4) are directed to the Examiner's allegedly erroneous analysis of the claims under step two of the *Alice/Mayo* test. However, we are unpersuaded that the Examiner erred by determining

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[5] Appellants further disclose that "several tests using non-invasive biomarkers have already been developed and proposed for the diagnosis of fibrosis," thereby admitting that the natural correlation between biomarkers and hepatic disease was known (Spec. 2:26–28).

[6] With regard to ferritin and blood glucose, Appellants do not direct our attention to any authority that supports the proposition that the patent-ineligible concept of natural correlation must distinguish between direct and indirect correlations (Appeal Br. 14).

that the additional elements recited in claims 1 and 23 fail to transform the nature of these claims into patent-eligible subject matter.

With respect to argument (1) that the claims' additional elements transform the nature of the claim from merely an abstract idea, "the 'prohibition against patenting abstract ideas cannot be circumvented by attempting to limit the use of the formula to a particular technological environment.'" *Mayo*, 566 U.S. at 78 (citations omitted). Furthermore, the Examiner correctly determined that "it would be obvious to one of ordinary skill in the art to analyze data mathematically," e.g., through Appellant's claimed statistical analysis (Ans. 7).[7] Thus, we are not persuaded that the Examiner erred in concluding that claims 1 and 23 lack a sufficient inventive concept to transform the abstract idea into patent-eligible subject matter.

With regards to arguments (3) and (4) that the claims' additional elements transform the nature of the claim from simply applying a law of nature, the Examiner correctly determined that Appellants have "not transformed these markers from their natural state in the instant measuring" steps (*id.*). As the Examiner concluded, by "detecting the combination of the 7 markers (5 biomarkers, 2 clinical) . . . [Appellants] ha[ve] merely recognized a natural law[] . . . and applied it" (*id.*). Furthermore, Appellants have not provided any persuasive technical reasoning or evidence to rebut the Examiner's conclusion that "correlating these markers to the presence of disease" is conventional and does not amount to anything "significantly more" than the claiming of the natural correlation (*see id.* at 2–3; *see also in re Mayo*, 566 U.S. at 73).

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[7] There is no dispute that Callewaert explicitly discloses logistic regression analysis (Ans. 4 (citing Callewaert Figs. 3, 6; ¶¶ 11, 14); Appeal Br. 17).

In sum, claims 1 and 23 encompass the use of known mathematical algorithms to the measured amounts of seven known naturally occurring markers to determine the amount of hepatic lesions, which are due or related to liver disease. Such claims are not directed to patent-eligible subject matter.

Accordingly, we affirm the rejection of claims 1, 4, and 22–24 as not directed to patentable subject matter for the reasons set forth above. 37 C.F.R. § 41.37(c)(1)(iv).

Rejection II

Appellants do not dispute the Examiner's finding that Salonen discloses two of the seven claimed markers, namely weight and ferritin (Appeal Br. 19; Ans. 5). Rather, Appellants dispute the Examiner's rationale for modifying Maor's non-invasive biomarker test for liver fibrosis estimation by including Salonen's disclosed markers (Appeal Br. 19). In particular, Appellants argue that because Salonen discloses other markers for diagnosing cardiovascular or metabolic conditions, "a person skilled in the art would have had no reason to combine [Salonen's] ferritin and weight with the other markers of the invention in a logistic regression with the aim to quantify a liver lesion" (*id.* at 19; *see also id.* at 18).

Appellants' arguments are persuasive.

It is well understood that "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). The fact that a reference may be modified to reflect features of the claimed

invention does not make the modification, and hence the claimed invention, obvious unless the prior art suggested the desirability of such modification. *In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990).

The Examiner determines that "[i]t would have been obvious to one of ordinary skill in the art to use the measurements and techniques of S[alonen] with the methods of M[aor] and C[allewaert] due to the benefits these methods offer with determining disease outcome" (Ans. 5 (citing Salonen ¶ 238)). However, the Examiner's relied upon disclosure does not mention the benefits of including weight as a marker for hepatic disease diagnosis. Furthermore, the Examiner has not provided adequate reasoning to explain why a person of skill in the art would have modified Maor's non-invasive biomarker test for estimating liver fibrosis in view of Salonen's body weight marker, which is disclosed as related to cardiovascular and metabolic risk (*see* Ans. 5, 9). Without such reasoning, the Examiner has not established a prima facie case of obviousness.

Thus, Appellants' arguments have identified reversible error in the Examiner's determination that Maor in view of Callewaert, and further in view of Salonen, renders claims 1 and 23 obvious.

Accordingly, we reverse the obviousness rejection of claims 1, 4, and 22–24 for the reasons set forth above. 37 C.F.R. § 41.37(c)(1)(iv).

We express no opinion with respect to Appellants' other arguments urging reversal of the Examiner's § 103(a) rejection.

CONCLUSION

We AFFIRM the rejection of claims 1, 4, and 22–24 under 35 U.S.C. § 101 as directed to patent-ineligible subject matter.

We REVERSE the rejection of claims 1, 4, and 22–24 under 35 U.S.C. § 103(a) as obvious over Maor in view of Callewaert, and further in view of Salonen.

AFFIRMED