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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte TIMOTHY L. RAMSEY, BHARAT MEHROTRA, and MARK D. BRENNAN[1]

Appeal 2016-000321
Application 13/269,365
Technology Center 1600

Before ERIC B. GRIMES, RICHARD J. SMITH, and JOHN E. SCHNEIDER, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of treating a psychotic disorder, which have been rejected as being directed to patent-ineligible subject matter and as nonenabled. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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[1] Appellants identify the Real Party in Interest as SureGene, LLC. (Appeal Br. 3.)

STATEMENT OF THE CASE

The Specification discloses a method of treating psychotic disorders such as schizophrenia. (Spec. ¶ 2.) The Specification states that "there are individual differences in response to specific drugs based on differences in drug pharmacology and metabolism, combined with genetic differences between patients. There are currently no proven ways to identify which antipsychotic drug is optimal for a given patient." (*Id.* ¶ 4.)

The Specification discloses that "a genetic signature, which the inventors refer to as the Olanzapine Poor Response Predictor (OPRP), is a biomarker" that can be used to select an antipsychotic treatment plan. (*Id.* ¶ 6.) "For example, the inventors have discovered that patients that are OPRP negative respond better than patients that are OPRP positive when treated with olanzapine, clozapine, or quetiapine." (*Id.*)

"Determination of the genotype of SNP [single nucleotide polymorphism] marker rs11960832, which is located within the SV2C gene, comprises one aspect of the OPRP genetic signature test." (*Id.* ¶ 63.) "Determination of the genotype of SNP marker rs7975477, which is located within the MGAT4C gene, comprises one aspect of the OPRP genetic signature test." (*Id.* ¶ 64.)

Claims 1–10 are on appeal. Claim 1 is illustrative and reads as follows:

> 1. A method for treating a human subject having or suspected of having a psychotic disorder, comprising:
>
> a) selecting a subject having or suspected of having a psychotic disorder and who has been determined to have the OPRP genetic signature, wherein the OPRP genetic signature is defined as a genotype comprising a homozygous genotype for the T allele at rs11960832 and

either a homozygous or heterozygous genotype for the T allele at rs7975477; and

b) treating the subject that was determined to have the OPRP signature with an antipsychotic treatment other than clozapine or quetiapine.

The claims stand rejected as follows:

Claims 1–10 under 35 U.S.C. § 101 as being directed to patent-ineligible subject matter (Final Action[2] 3) and

Claims 1–10 under 35 U.S.C. § 112, first paragraph, for lack of enablement (*id.* at 9).

I

The Examiner has rejected claims 1–10 as being directed to patent-ineligible subject matter. The Examiner finds that, under the standard set out in *Mayo Collaborative Services v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012), "the claims inform a relevant audience about certain laws of nature. The additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community. The additional steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately." (Final Action 5.)

Specifically, the Examiner reasons that "[t]he correlation between whether particular OPRP genetic signature is present and response to clozapine or quetiapine treatment is considered a 'law of nature' in accordance with Mayo." (*Id.*) The Examiner concludes that the "selecting" step of claim 1 is not sufficient to transform the nature of the claim and the

[2] Office Action mailed March 4, 2014.

treatment step did not distinguish the claimed process from *Mayo* because the claims in that case were also directed to a method of treatment. (*Id.* at 6, 9.)

We agree with the Examiner that claim 1 is not eligible for patenting. In our view, claim 1 falls squarely into the category of inventions that were held ineligible for patenting by the *Mayo* Court.

Claim 1 at issue in *Mayo* was directed to:

> A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6–thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6–thioguanine in said subject having said immune-mediated gastrointestinal disorder,

wherein levels of 6–thioguanine below or above certain thresholds indicate a need to increase or decrease, respectively, the amount of drug being administered. *Mayo*, 566 U.S. at 74.

Similarly, claim 1 of the present appeal is directed to a method of treating a patient with a psychotic disorder by selecting a patient who has the OPRP genetic signature and avoiding clozapine and quetiapine based on the presence of that genotype. In other words, claim 1 is directed to a method of optimizing therapeutic efficacy for treatment of a psychotic disorder by choosing the antipsychotic medication to administer based on the presence of the OPRP genetic signature.

The *Mayo* Court concluded that "Prometheus' patents set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm." *Mayo*, 566 U.S. at 77. Similarly, claim 1 on

appeal sets forth a law of nature—namely, a relationship between the OPRP genetic signature and the likelihood that particular antipsychotic drugs will prove ineffective.

The *Mayo* Court noted that "[w]hile it takes a human action (the administration of a thiopurine drug) to trigger a manifestation of this relation in a particular person, the relation itself exists in principle apart from any human action." *Id.* Similarly here, while it takes a human action (administration of clozapine or quetiapine) to trigger a manifestation of the relationship between these drugs and the OPRP genetic signature, the relationship exists in principle apart from the human action.

The *Mayo* Court concluded that the "administering" step of the method claimed in that case "simply refers to the relevant audience, namely doctors who treat patients with certain diseases with thiopurine drugs." *Id.* at 78. Similarly here, the "selecting" step of claim 1 on appeal simply directs the audience of doctors who treat patients having psychotic disorders to a particular subset of those patients.

The *Mayo* Court concluded that "[a]nyone who wants to make use of these laws must first administer a thiopurine drug and measure the resulting metabolite concentrations, and so the combination amounts to nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients." *Id.* at 79. Similarly here, anyone who wants to make use of the natural law—the relationship between the OPRP genetic signature and the lack of efficacy of clozapine or quetiapine—must first determine whether a given patient has the OPRP genetic signature before determining which antipsychotic medication to treat them with. Thus, claim

1 amounts to nothing significantly more than an instruction to doctors to apply the applicable law when treating their patients.

In summary, we agree with the Examiner that under the standard set out in *Mayo*, claim 1 is directed to patent-ineligible subject matter.

Appellants argue that, under the examination guidelines issued in December 2014, claim 1 is patent-eligible. (Appeal Br. 5.) Appellants argue that "the new guidelines specifically identify a new use for an old drug as an example of patent eligible subject matter." (*Id.*)

This argument is unpersuasive. The Specification states that "'Typical' antipsychotics refer to so called first generation or classical antipsychotics. This class of drug was first developed in the 1950s." (Spec. ¶ 44.) "'Atypical' antipsychotics refer to a newer class of antipsychotic drugs first introduced in the 1990s." (*Id.* ¶ 45.) The Specification lists several atypical antipsychotics with FDA approval dates ranging from 1990 to 2006. (*Id.* ¶¶ 46–52.)

Thus, treatment of schizophrenic patients with antipsychotic drugs other than clozapine or quetiapine does not represent a new use for the known antipsychotic drugs. True, the decisions to treat certain patients with certain drugs was not based on knowing that the patients had the OPRP genetic signature, but in the method of claim 1 the antipsychotic drugs are nonetheless administered for their conventional use of treating schizophrenia.

Appellants point to two claims in an example analysis issued by the USPTO of the patent-eligibility of nature-based products. (Reply Br. 2–3.) Appellants argue that the exemplary claims "are said to be patent eligible on the basis that '[a]lthough the claim recites a nature-based product (amazonic acid), analysis of the claim as a whole indicates that the claim is focused on

a process of practically applying the product ***to treat a particular disease (colon cancer)***, and not on the product per se.[']" (*Id.* at 2.) Appellants argue that claim 1 is directed to treating a disease and therefore should be patent-eligible. (*Id.* at 3.)

This argument is unpersuasive, because the cited exemplary claims address analysis of a different class of inventions that have been held to be patent-ineligible; specifically, products of nature. *See Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013):

> In *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 68 S.Ct. 440, 92 L.Ed. 588 (1948), this Court considered a composition patent that claimed a mixture of naturally occurring strains of bacteria . . . . His patent claim thus fell squarely within the law of nature exception. So do Myriad's. Myriad found the location of the BRCA1 and BRCA2 genes, but that discovery, by itself, does not render the BRCA genes "new . . . composition[s] of matter," § 101, that are patent eligible.

Id. at 2117. In this appeal, by contrast, the issue is whether the method of claim 1 is effectively directed to a law of nature or a natural phenomenon; i.e., the relationship between the OPRP genetic signature and lack of efficacy of clozapine and quetiapine.

Appellants also argue that claim 1

> does not foreclose all uses of the underlying natural principal [sic]. . . . Under the current claims, the only thing foreclosed by the claim is to use this specific genotype as a means of identifying responders or non-responders to specific drugs or classes of drugs. Otherwise, the natural phenomenon is free to use for any other purpose.

(Appeal Br. 5–6.)

This argument is also unpersuasive, because the claims in *Mayo* could have been characterized as foreclosing only the use of specific metabolite

levels to identify patients who were likely to experience either an ineffective response or harmful effects. The *Mayo* Court stated:

> The laws of nature at issue here are narrow laws that may have limited applications, but the patent claims that embody them nonetheless implicate this concern [i.e., preemption]. . . . [T]hey tie up the doctor's subsequent treatment decision whether that treatment does, or does not, change in light of the inference he has drawn using the correlations. And they threaten to inhibit the development of more refined treatment recommendations (like that embodied in Mayo's test), that combine Prometheus' correlations with later discovered features of metabolites, human physiology or individual patient characteristics.

Mayo, 566 U.S. at 86–87.

Appellants also argue that "the use of this particular genotype indicator for patient responders can in no way be characterized as 'well-understood, routine and conventional' in the field." (Appeal Br. 6.)

This argument seems to be based on a misreading of *Mayo*. The issue in that case was not whether the law of nature itself was well-understood, routine, and conventional, but whether the claimed method steps added to the law of nature anything more than well-understood, routine, and conventional activity. *See Mayo*, 566 U.S. at 73 ("[T]he steps in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity previously engaged in by researchers in the field."); *id.* at 79–80 ("[T]he claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community.").

Finally, Appellants argue that the "discovery of the fact that some patients are more or less sensitive to certain man-made drugs does indeed 'integrate the natural principle' and is a 'meaningful limit on the

performance of the invention'" and that, "under current USPTO examination guidelines, 'method of treatment' claims that identify a subpopulation of patients for treatment with a particular drug, such as those of the present application, are allowable." (Appeal Br. 6–7.)

This argument is also unpersuasive. For the reasons discussed previously, we do not agree that the examples cited by Appellants based on the USPTO's examination guidelines support patentability of claim 1 on appeal. In any event, the Supreme Court's decision in *Mayo* is controlling based on the facts of this appeal.

We therefore affirm the rejection of claim 1 under 35 U.S.C. § 101. Claims 2–10 have not been argued separately and therefore fall with claim 1. 37 C.F.R. § 41.37(c)(1)(iv).

II

The Examiner has rejected claims 1–10 as nonenabled, on the basis that the Specification "does not reasonably provide enablement for determining which subjects should be administered quetiapine." (Final Action 9.) The Examiner finds that Ramsey[3] "claims methods that provide treating subjects with the OPRP signature with quetiapine. This is in contrast to the instant claims." (*Id.* at 11.) The Examiner also finds that, based on the Specification's Tables 4 and 5, "it is unpredictable why the skilled artisan would administer quetiapine to OPRP negative patients and not OPRP [positive] patients." (*Id.* at 12.)

Appellants argue that "Example 6 of the instant application . . . shows that OPRP positive subjects fare worse than OPRP negative subjects on

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[3] Ramsey et al., US 7,932,042 B1, April 26, 2011.

quetiapine (see Tables 11 and 12 of the instant specification)." (Appeal Br. 7.) Appellants argue that

> the data show that OPRP positive subjects respond more poorly than do OPRP negative subjects to quetiapine. Therefore, as taught by the instant specification and would be clear to one skilled in the art, given the choice of quetiapine versus risperidone or ziprasidone for OPRP positive subjects, quetiapine should be avoided.

(*Id.* at 8.)

We agree with Appellants that the Examiner has not pointed to sufficient evidence to show that practicing the claimed method would require undue experimentation. The Specification states that, "[a]s can be seen from Table 11, the OPRP positive group responded worse to clozapine and to quetiapine than did the OPRP negative group." (Spec. ¶ 367.) The Specification also states that "[a]s summarized in Table 12, when Caucasian patients are segmented by OPRP status and treatment arm, clozapine-treated or quetiapine-treated OPRP positive subjects demonstrated greater likelihood of worsening of symptoms . . . than OPRP negative subjects." (*Id.* ¶ 368.)

The Specification expressly states that "patients that are OPRP negative respond better than patients that are OPRP positive when treated with olanzapine, clozapine, or quetiapine." (*Id.* ¶ 6.) The Specification describes numerous typical and atypical antipsychotic medications. (*Id.* ¶¶ 44–59.) Thus, it would seem that the only experimentation that would be required to practice the method of claim 1 would be reading genetic sequence data to identify particular alleles at two SNP positions and choosing an established antipsychotic medication other than clozapine or quetiapine. The Examiner has not shown that this amount of

experimentation would be considered undue. We therefore reverse the rejection of claims 1–10 for lack of enablement.

SUMMARY

We affirm the rejection of claims 1–10 under 35 U.S.C. § 101.

We reverse the rejection of claims 1–10 under 35 U.S.C. § 112, first paragraph.

TIME PERIOD FOR RESPONSE

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

AFFIRMED