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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JOHN CHAMBERLAIN,
HALINA FITZ-CLARENCE, and MARK THOMAS[1]

Appeal 2014-009849
Application 12/293,763
Technology Center 1600

Before FRANCISCO C. PRATS, JEFFREY N. FREDMAN and JOHN E. SCHNEIDER, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134(a) involves claims to methods of treating individuals with bone disorders, such as osteoporosis. The Examiner rejected the claims under 35 U.S.C. § 101 as being directed to non-statutory subject matter.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The Specification discloses that bone disorders, "such as osteoporosis, result in a decrease in bone mass and bone density and/or an increased risk and/or incidence of fracture. Oral bisphosphonates are the commonest first-

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[1] Appellants identify the real party in interest as UCL Business PLC. Br. 2.

choice treatment where a reduction in osteoclasis would be beneficial, for example, for post-menopausal osteoporosis . . . ." Spec. 1. Nonetheless, "around 40% of individuals treated with bisphosphonates do not fully respond to the drug." *Id.*

To address that issue, the "present inventors have shown that polymorphism in and around the coding region of the farnesyl diphosphate synthase (FDPS) gene is predictive of the densitometric response of patients subsequent to commencing treatment with amino-bisphosphonates." *Id.* at 1–2. In particular, Appellants discovered that the "presence of a T residue at SNP rs2297480 in both copies of the FDPS gene (i.e. a TT genotype at rs2297480) is indicative that the individual has a bone disorder which is responsive to treatment with bisphosphonate." *Id.* at 4.

Claims 1, 25, 43, and 44, the independent claims under rejection, illustrate the appealed subject matter and read as follows (Br. 10–12):

> 1. A method of treating a human individual having a bone disorder, the method comprising:
>
> determining in a nucleic acid sample obtained from the individual, the presence of a TT genotype at a single nucleotide polymorphism rs2297480 (SNP rs2297480) in the farnesyl diphosphate synthase (FDPS) gene,
>
> the presence of the TT genotype at SNP rs2297480 being indicative that the individual as is responsive to bisphosphonates; and
>
> administering a bisphosphonate to the individual if the TT genotype is present.
>
> 25. A method of treating a bone disorder in a human individual, the method comprising:
>
> identifying the individual as having a TT genotype at single nucleotide polymorphism rs2297480 (SNP rs2297480) in the farnesyl diphosphate synthase (FDPS) gene, the presence of the TT genotype at SNP rs2297480 being indicative that the individual is responsive to bisphosphonates; and,

administering a bisphosphonate to the individual.

43. A method of treating a bone disorder in a human individual, the method comprising:

administering to the individual a bisphosphonate selected from the group consisting of alendronate, clodronate, ibandronate, pamidronate, risedronate and zoledronate,

wherein the individual has been identified as having a TT genotype at single nucleotide polymorphism rs2297480 (SNP rs2297480) in the farnesyl diphosphate synthase (FDPS) gene.

44. A method of treating osteoporosis in a human individual having a BMD T score of -1 or less, the method comprising:

determining in a nucleic acid sample obtained from the individual, the presence of a TT genotype at single nucleotide polymorphism rs2297480 (SNP rs2297480) in the farnesyl diphosphate synthase (FDPS) gene,

wherein the presence of the TT genotype is determined by hybridizing the nucleic acid sample to a nucleic acid probe which comprises SEQ ID NO: 1 or the complement thereof; wherein the probe or the nucleic acid sample is immobilized in a nucleic acid array, and;

administering intravenous palmadronate [sic, pamidronate[2]] to the individual if the TT genotype is present in the sample.

The sole rejection before us for review is the Examiner's rejection of claims 1, 13–17, 25, 30, 31, and 37–44 under 35 U.S.C. § 101 as being directed to non-statutory subject matter (Final Action 2–4).[3]

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[2] Appellants' Specification exemplifies the "use of regular intravenous Pamidronate" (Spec. 21), not palmadronate.

[3] Final Action entered June 3, 2013.

DISCUSSION

The Examiner's Position

The Examiner determines that the rejected claims "set forth laws of nature and focus on the relationship between a specific genotype TT for rs2297480 in the FDPS gene and responsiveness to bisphosphonates. The instant claims essentially provide steps for a practitioner to gather data from which they may draw an inference (phenotype)." Final Action 3.

Therefore, the Examiner reasons, the claimed process "is taken to recite a law of nature because the claim simply describes that relationship. Mental activities such as forming a judgment, observation, evaluation or opinion are examples of general concepts." *Id.*

As to the actual process steps required by the rejected claims, the Examiner finds as follows:

> The claim features of amplification, sequencing and hybridization are typically taken by those in the field to determine a genotype and do not add anything substantial to the process of claim 1, while the treatment claims essentially set forth the law of nature with the generalized instructions to apply it and covers every substantial practical application of the correlation.

Id. at 4.

Analysis

As stated in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992):

> [T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. . . .
>
> After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

Appellants do not persuade us that a preponderance of the evidence fails to support the Examiner's conclusion that the rejected claims recite subject matter ineligible for patenting under 35 U.S.C. § 101.

35 U.S.C. § 101 states that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

The Supreme Court has "long held that this provision contains an important implicit exception: Laws of nature, natural phenomena, and abstract ideas are not patentable." *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, 134 S.Ct. 2347, 2354 (2014).

Our reviewing court has summarized the Supreme Court's two-part test for distinguishing between claims to patent-ineligible exceptions, and claims to patent-eligible applications of those exceptions, as follows:

> Step one asks whether the claim is "directed to one of [the] patent-ineligible concepts." [*Alice*, 134 S.Ct. at 2354]. If the answer is no, the inquiry is over: the claim falls within the ambit of § 101. If the answer is yes, the inquiry moves to step two, which asks whether, considered both individually and as an ordered combination, "the additional elements 'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo* [*Collaborative Services v. Prometheus Labs, Inc.*, 132 S.Ct. 1289, 1297 (2012)]).
>
> Step two is described "as a search for an 'inventive concept.'" *Id.* (quoting *Mayo*, 132 S.Ct. at 1294). At step two, more is required than "well-understood, routine, conventional activity already engaged in by the scientific community," which fails to transform the claim into "significantly more than a patent upon the" ineligible concept itself. *Mayo*, 132 S.Ct. at 1298, 1294.

Rapid Litigation Mgmt. Ltd. v. CellzDirect, Inc., 827 F.3d 1042, 1047 (Fed. Cir. 2016) (paragraphing added).

In the present case, claim 1 recites the step of "determining in a nucleic acid sample obtained from the individual, the presence of a TT genotype at a single nucleotide polymorphism rs2297480 (SNP rs2297480) in the farnesyl diphosphate synthase (FDPS) gene, the presence of the TT genotype at SNP rs2297480 being indicative that the individual as is responsive to bisphosphonates." Br. 10 (claim 1).

We, therefore, agree with the Examiner that, as to part one of the Supreme Court's test, Appellants' claim 1 is expressly directed to the law of nature discovered by Appellants--that the presence of the TT genotype at SNP rs2297480 is indicative that an individual having a bone disorder will respond to treatment with bisphosphonates.

As to part two of the Supreme Court's test, the only other step in Appellants' claim 1, administering bisphosphonate to the individual having the bone disorder, is a well understood and routine treatment step for such patients, as explained in Appellants' Specification. *See* Spec. 1 ("Oral bisphosphonates are the commonest first-choice treatment where a reduction in osteoclasis would be beneficial, for example, for post-menopausal osteoporosis . . . .").

We, therefore, agree with the Examiner that, under the Supreme Court's two-part test, claim 1 recites subject matter ineligible for patenting under § 101.

Appellants' arguments do not persuade us to the contrary.

As to Appellants' contentions that claim 1 is distinguishable from the claims of *Mayo* on the basis of the recited treatment step, and recites

additional elements that amount to a practical application of their discovered law of nature (*see* Br. 5–8), we first note that, contrary to Appellants' assertion, the claims in *Mayo* recited a treatment step. *See Mayo*, 132 S.Ct. at 1295 ("[C]laim 1 of the '623 Patent, which describes one of the claimed processes[, recites] as follows: 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 . . . .") (internal quotations omitted).

As noted above, moreover, it is undisputed that the step of administering a bisphosphonate recited in Appellants' claim 1 was a well-known and routine treatment for individuals suffering from bone disorders. Claim 1's treatment step, therefore, does not transform the claim into something significantly more than the discovered law of nature itself. To the contrary, on this record, claim 1's treatment step administers a drug, a bisphosphonate, to a patient population, bone disorder sufferers, that was undisputedly already known to receive the drug routinely.

We are not persuaded, moreover, that claim 1's step of determining the presence of the critical TT genotype at SNP rs2297480 of the FDPS gene is sufficient to render claim 1 eligible for patenting under § 101. Like the determining step in the patent-ineligible process at issue in *Mayo*, 132 S.Ct. at 1297–98, the genotype determining step in claim 1's process is performed using conventional techniques. *See* Spec. 5:

> The presence of a variant allele at the one or more sites of polymorphism may be determined by any convenient technique, including amplification of all or part of the genomic region of the FDPS gene, including the FDPS gene itself,

> sequencing all or part of the genomic region of the FDPS gene, including the FDPS gene itself, and/or hybridisation of a probe which is specific for a variant allele.

See also Spec. 6 ("PCR is well-known in the art . . . ."); *id.* at 7 ("Binding of a probe to target nucleic acid (e.g. DNA) may be measured using any of a variety of techniques at the disposal of those skilled in the art."); *id.* at 10 ("Sequencing may be performed using any one of a range of standard techniques.").

Appellants contend that claim 1's step of determining the presence of the critical TT genotype at SNP rs2297480 does not preempt others from detecting and using variant alleles other than rs2297480, or detecting genotypes other than the claimed TT genotype. Br. 6, 8.

That alleles other than the claimed allele might also be linked to responsiveness to bisphosphonates does not persuade us that Appellants' claim 1 fails to effectively preempt the application of the specific law of nature recited in claim 1--that the presence of the TT genotype at SNP rs2297480 is indicative that an individual having a bone disorder will respond to treatment with bisphosphonates.

Indeed, our reviewing court has expressly rejected similar contentions regarding preemption, stating that a patentee's "attempt to limit the breadth of the claims by showing alternative uses . . . outside of the scope of the claims does not change the conclusion that the claims are directed to patent ineligible subject matter." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1379 (Fed. Cir. 2015). The court explained that, "[w]hile preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility. . . . Where a

patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework . . . preemption concerns are fully addressed and made moot." *Id.*

In the present case, as discussed above, Appellants' claim 1 is limited to patented ineligible subject matter under the *Mayo* framework. Thus, that alternatives outside the claims are not preempted does not demonstrate patent eligibility.

In sum, for the reasons discussed, Appellants do not persuade us that a preponderance of the evidence fails to support the Examiner's conclusion that Appellants' claim 1 is patent-ineligible under § 101. Accordingly, we affirm the Examiner's rejection of claim 1 on that ground. Because they were not argued separately, claims 13–17, 25, 30, and 31 fall with claim 1. *See* 37 C.F.R. § 41.37(c)(1)(iv).

Turning to Appellants' arguments separately directed to claims 37–44, we first note that Appellants do not present their arguments under the separate subheadings required by § 41.37(c)(1)(iv). In any event, we do not find Appellants' arguments persuasive.

Claim 37 recites "[a] method according to claim 1 wherein the individual has a bone mineral density (BMD) T score of -1 or less" and claim 38 recites "[a] method according to claim 37 wherein the bone disorder is osteoporosis." Br. 11.

As noted above, however, administering bisphosphonates to osteoporosis sufferers was routine in the art (Spec. 1), and the Specification discloses that a BMD T score of -1 or less was known to be the clinical definition of osteoporosis (*see id.* at 10–11). Appellants do not persuade us, therefore, that claims 37 and 38 add anything to the discovered law of nature

beyond routine, conventional activity. We, therefore, affirm the Examiner's rejection of claims 37 and 38 as well.

Claims 39 and 40 both depend ultimately from claim 1, and require the TT genotype to be determined by hybridization to a nucleic acid having SEQ ID NO: 1. Br. 11–12. Claims 41 and 42 both depend from claim 40, and recite the use of a nucleic acid array in the hybridization. *Id.* at 12.

As noted above, however, the use of hybridization as a technique for determining the presence of a particular nucleic acid sequence was routine and conventional in the art. *See* Spec. 7 ("Binding of a probe to target nucleic acid (e.g. DNA) may be measured using any of a variety of techniques at the disposal of those skilled in the art."). The Specification also discloses that nucleic acid arrays were conventionally used in hybridization assays. *Id.* at 8. ("Nucleic acid arrays are well known in the art and may be produced in a number of ways.").

Appellants do not persuade us, therefore, that claims 39–42 add anything to the discovered law of nature beyond routine, conventional activity. We, therefore, affirm the Examiner's rejection of claims 39–42 as well.

Claim 43 is similar to claim 1, discussed above, except that claim 43 limits the bisphosphonate administered to the bone disease sufferer to specific compounds. Br. 12.

The Specification discloses, however, that the claimed compounds were conventionally used to treat bone disorders. *See* Spec. 11 ("Examples of bisphosphonates currently in use as pharmaceuticals include alendronate, clodronate, ibandronate, pamidronate, risedronate and zoledronate."). Appellants do not persuade us, therefore, that claim 43 adds anything to the

discovered law of nature beyond routine, conventional activity. We, therefore, affirm the Examiner's rejection of claim 43 as well.

Claim 44 is similar to claim 1, discussed above, except that claim 44 requires the determination of the TT genotype to be made by hybridization, and also requires the bisphosphonate specifically to be pamidronate, and specifically requires the compound to be administered intravenously. Br. 12.

As discussed above, however, hybridization was a conventional technique known to be used for detecting nucleic acids of interest, and pamidronate was among conventionally used bisphosphonates. As to intravenous administration of the drug, Appellants' Specification discloses that "[m]ethods of determining the most effective means and dosage of administration are well known to those of skill in the art . . . ." Spec. 18. Appellants do not persuade us, therefore, that claim 44 adds anything to the discovered law of nature beyond routine, conventional activity. We, therefore, affirm the Examiner's rejection of claim 44 as well.

SUMMARY

For the reasons discussed, we affirm the Examiner's rejection of claims 1, 13–17, 25, 30, 31, and 37–44 under 35 U.S.C. § 101 as being directed to non-statutory subject matter.

TIME PERIOD

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