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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SUNG K. KIM, GREGORY HANNUM, JENNIFER GEIS, and COSMIN DECIU

Appeal 2019-003792[1]
Application 14/311,070
Technology Center 1600

Before RICHARD M. LEBOVITZ, FRANCISCO C. PRATS, and RYAN H. FLAX, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

The claims in this appeal are directed to a computer-implemented, fetal gender-independent, fetal ploidy independent, and fetal polymorphism-independent method for determining a fraction of fetal nucleic acid in a test sample from the blood of a pregnant female. The Examiner rejected the claims under 35 U.S.C. § 101 as reciting patent ineligible subject matter. Pursuant to 35 U.S.C. § 134, Appellants appeal the Examiner's determination that the claims are unpatentable. We have jurisdiction for the appeal under 35 U.S.C. § 6(b). The Examiner's decision is reversed.

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[1] The Appeal Brief ("Appeal Br." entered Dec. 21, 2018) identifies Sequenom, Inc. and Illumina, Inc. as the real-parties-in-interest. Appeal Br. 3.

STATEMENT OF THE CASE

The Examiner finally rejected claims 1–6 and 13–26 under 35 U.S.C. § 101 because the claimed invention is directed to a judicial exception to patent eligibility. Final Act. 3; Ans. 3.

Claim 1, the only independent claim on appeal, is reproduced below:

> 1. A computer-implemented, fetal gender-independent, fetal ploidy independent and fetal polymorphism-independent method for determining a fraction of fetal nucleic acid in a test sample from sequenced test sample nucleic acid, comprising:
>
> (a) receiving onto a memory counts of sequence reads of sequenced test sample nucleic acid that are mapped to corresponding portions of a reference genome, which test sample nucleic acid comprises circulating cell-free (CCF) nucleic acid from blood of a pregnant female bearing a fetus;
>
> (b) receiving onto a memory a set of weighting factors that have been calculated for each portion of the reference genome from a fitted relation between (i) a fraction of fetal nucleic acid for each of multiple training samples, and (ii) counts of sequence reads mapped to each portion of the multiple training samples, wherein at least one weighting factor corresponds to the each portion and is indicative of the fraction of fetal nucleic acid of the each portion;
>
> (c) assigning, using a microprocessor, the set of weighting factors to the portions of the reference genome, wherein each of the portions is independently associated with a corresponding weighting factor;
>
> (d) generating, using a microprocessor, portion-specific fetal fraction calculations for the portions according to (i) the count of the sequence reads of the sequenced test sample nucleic acid mapped to the portion of the reference genome for the each portion of the sequenced test sample, and (ii) the assigned weighting

> factors for the each portion of the sequenced test sample; and
>
> (e) determining, using a microprocessor, a fraction of fetal nucleic acid for the test sample based on the portion-specific fetal fraction calculations.

SECTION 101 REJECTION

The Examiner rejected claims 1–6 and 13–26 under 35 U.S.C. § 101 as directed to a judicial exception to patent eligibility. Final Act. 3; Ans. 3. The Examiner found that the claims are directed to an abstract idea and law of nature. Final Act. 7; Ans. 3, 8.

Under 35 U.S.C. § 101, an invention is patent-eligible if it claims a "new and useful process, machine, manufacture, or composition of matter." However, not every discovery is eligible for patent protection. *Diamond v. Diehr*, 450 U.S. 175, 185 (1981). "Excluded from such patent protection are laws of nature, natural phenomena, and abstract ideas." *Id.* The Supreme Court articulated a two-step analysis to determine whether a claim falls within an excluded category of invention. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 216 (2014); *Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 566 U.S. 66, 75–77 (2012).

In the first step, it is determined "whether the claims at issue are directed to one of those patent-ineligible concepts." *Alice*, 573 U.S. at 217. If it is determined that the claims are directed to an ineligible concept, then the second step of the two-part analysis is applied in which it is asked "'[w]hat else is there in the claims before us?'" *Id.* The Court explained that this step involves

> 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."

Alice, 573 U.S. at 217–18 (citing from *Mayo*, 566 U.S. at 75–77).

Alice, relying on the analysis in *Mayo* of a claim directed to a law of nature, stated that in the second part of the analysis "the elements of each claim both individually and 'as an ordered combination'" must be considered "to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *Alice*, 573 U.S. at 217.

The PTO recently published revised guidance on the application of 35 U.S.C. § 101. USPTO's January 7, 2019 Memorandum, *2019 Revised Patent Subject Matter Eligibility Guidance*, 84 Fed. Reg. 50, 51–57 (2019) ("2019 Eligibility Guidance"). This guidance provides direction on how to implement the two-part analysis of *Mayo* and *Alice*.

Step 2A, Prong One, of the 2019 Guidelines, looks at the specific limitations in the claim to determine whether the claim recites a judicial exception to patent eligibility. In Step 2A, Prong Two, the claims are examined to identify whether there are additional elements in the claims that integrate the exception in a practical application, namely, is there a "meaningful limit on the judicial exception, such that the claim is more than a drafting effort designed to monopolize the judicial exception." 84 Fed. Reg. 54 (2. Prong Two).

If the exception is not integrated into a practical application, then as in the *Mayo/Alice* framework, Step 2B of the 2019 Guidelines asks whether there is an inventive concept to ensure that the patent is significantly more than a patent on the ineligible concept, itself. 84 Fed. Reg. 56. In making this determination, it must be considered whether there are specific

limitations or elements recited in the claim "that are not well-understood, routine, conventional activity in the field, which is indicative that an inventive concept may be present" or whether the claim "simply appends well-understood, routine, conventional activities previously known to the industry, specified at a high level of generality, to the judicial exception, indicative that an inventive concept may not be present." 84 Fed. Reg. 56 (footnote omitted).

With these guiding principles, we proceed to determine whether the claimed subject matter in this appeal is eligible for patent protection under 35 U.S.C. § 101. As explained in more detail below, we conclude that the claims are directed to patent-eligible subject matter.

Step 2A, Prong One

In Step 2A, Prong One, of the 2019 Guidelines, the specific limitations in the claim are examined to determine whether the claim recites a judicial exception to patent eligibility, namely whether the claim recites an abstract idea, law of nature, or natural phenomenon. The 2019 Guidelines lists three groupings of abstract ideas:

> (a) Mathematical concepts—mathematical relationships, mathematical formulas or equations, mathematical calculations[]
>
> (b) Certain methods of organizing human activity . . .
>
> (c) Mental processes--concepts performed in the human mind (including an observation, evaluation, judgment, opinion).

84 Fed. Reg. 52.

The Examiner found that the claims recite a judicial exception. Final Act. 3. The Examiner described the judicial exception as being a law of nature. *Id.* The Examiner also found that the judicial exception recited in

the claims is an "abstract idea of" the "analysis of abstract data." *Id.* at 4. The Examiner also referred to the claims as reciting the abstract idea of a mental process and mathematical concept. Ans. 3.

We begin the analysis with determining whether the claims recite a judicial exception to patent eligibility under 35 U.S.C. § 101.

The preamble of claim 1 recites that the method is a "method for determining a fraction of fetal nucleic acid in a test sample from sequenced test sample nucleic acid." The test sample "comprises circulating cell-free (CCF) nucleic acid from blood of a pregnant female bearing a fetus."

The Specification defines "fraction of fetal nucleic acid."

> In certain embodiments, the amount of fetal nucleic acid in a sample is referred to as "fetal fraction[.]" In some embodiments "fetal fraction" refers to the fraction of fetal nucleic acid in circulating cell-free nucleic acid in a sample (e.g., a blood sample, a serum sample, a plasma sample) obtained from a pregnant female.

Spec. 118:4–8.

Appellants explain that "[d]etermining the fetal fraction is important because this information allows the provider of the test to understand the extent to which a given sample is representative of the fetus's DNA, which in turn reduces the likelihood that the test will generate a false positive." Appeal Br. 3–4. Consistently, the last step of claim 1 recites "(e) determining, using a microprocessor, a fraction of fetal nucleic acid for the test sample based on the portion-specific fetal fraction calculations."

The preamble and last step of the claimed method recite a law of nature or natural phenomenon because the amount of fetal nucleic acid which occurs *naturally* in the blood of a pregnant female bearing a fetus is determined and the detected fetal nucleic acid is, itself, a *natural* product.

As explained in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.* 788 F.3d 1371, 1376 (Fed. Cir. 2015), if "[t]he method . . . begins and ends with a natural phenomenon," as it does here, it recites "matter that is naturally occurring."

We next proceed to the other steps in the claim to determine whether other judicial exceptions to patent eligibility are recited in the claims.

Step (a) of the claim recites a step of receiving data, where the data comprises nucleic "sequence reads of sequenced test sample nucleic acid." Step (a) is therefore a data collection step and does not recite a judicial exception to patent eligibility.

Step (b) of the claim recites "receiving onto a memory a set of weighting factors." The claim recites how the weighting factors have been calculated, but the claim does recite a step in which the calculation is performed. Step (b), like step (a), is therefore also a data collection step and does not recite a judicial exception.

In step (c) of claim 1, the weighting factors are assigned "using a microprocessor" to "portions of the reference." The Examiner found that this step is a mental process. Ans. 3. Appellants identify specific disclosure in the Specification where the assigning function is described. Appeal Br. 5. We have reviewed these disclosures at 4:4–29, 87:13–30, 129:10–29, and 190:25–28 of the Specification, and none of the descriptions provide any detail that would exclude the assignment from being performed in the human mind. Thus, we agree with the Examiner that step (c) of claim 1 recites a mental process.

Step (d) of the claim is "generating . . . portion-specific fetal fraction calculations for the portions [of the reference genome]. The claim recites that the calculations are generated "according to" (i) sequence reads and (ii)

the assigned weighting factors, but does not disclose a formula for how the calculation is performed. Appellants identify sections of the Specification as written description support for this step (Appeal Br. 5) which disclose generally how the calculation is performed, although no specific formula is used (Spec. 128:13–27, 129:10–29, 134:17–135:2, and 140:6–23). For example, the Specification discloses:

> In some embodiments portion-specific fetal fraction estimates are determined *based in part on portion-specific parameters* and their relation to fetal fraction. Portion-specific parameters can be any suitable parameter that is reflective of (e.g., correlates with) the amount or proportion of reads from CCF fragment lengths of a particular size (e.g., size range) in a portion. *A portion-specific parameter can be an average, mean or median of portion-specific parameters determined for multiple samples*. Any suitable portion-specific parameter can be used.

Spec. 128: 13–18 (emphasis added).

Thus, one of ordinary skill in the art reading these disclosure in the Specification would understand the recited "generating" and "calculations" are *defined* in the Specification as mathematical concepts.

Step (d) of the claim comprises "generating . . . portion-specific fetal calculations" according to (i) sequence reads and (ii) the weighting factors. While no specific formula for performing the calculation is recited in the claim, the step is an abstract idea because the claim recites a mathematical relationship between the portion-specific fetal calculations and (i) the sequence read counts and (ii) assigned weighting factors. 84 Fed. Reg. 52 ("[M]athematical concepts" are "mathematical relationships" and "mathematical calculations."). Appellants' contention that the recited step is not an abstract idea does not address the step in the claim of "generating . . .

calculations" or the express recited mathematical relationship. Appeal Br. 22–23; Reply Br. 6.

In sum, we agree with the Examiner's determination that claim recites judicial exceptions to patent eligibility. We thus proceed to the next step of the analysis to determine whether these exceptions are integrated into a practical application, and if not, whether there is an inventive concept to ensure that the patent is significantly more than a patent on the ineligible concepts.

Step 2A, Prong Two

Prong Two of Step 2A under the 2019 Guidance asks whether there are additional elements that integrate the exception into a practical application. As in the *Mayo*/*Alice* framework, we must look at the claim elements individually and "as an ordered combination" to determine whether the additional elements integrate the recited abstract idea into a practical application.

Appellants contend that, even if the claims are found to recite patent-ineligible steps, their use "as part of an overall method for determining how much of the nucleic acid in a physical blood sample comes from a fetus instead of the pregnant female herself is absolutely a practical application." Reply Br. 9. Appellants argue that the claimed method is technological improvement to determining the fetal fraction in "a real, physical blood sample" and "is a real-world, practical application of any mathematical concept or mental step that may be recited in the claims." *Id.* at 10. Appellants also argue "the claims are a practical application because they sufficiently limit the use of the alleged abstract idea to determining the fetal fraction as specifically claimed." *Id.* at 12.

We find Appellants' arguments to be persuasive.

As discussed in the 2019 Guidance, "[a] claim that integrates a judicial exception in a practical application will apply, rely on, or use the judicial exception in a manner that places a meaningful limit on the judicial exception, such that the claim is more than a drafting effort designed to monopolize the judicial exception. 84 Fed. Reg. 54. Integration into a practical application is evaluated by identifying whether there are additional element individually, and in combination, which go beyond the judicial exception. *Id.* at 54–55.

In this case, the additional steps of claim 1 place a meaningful limit on the claimed method of determining a fraction of nucleic acid in the test sample. Specifically, the recited "set of weighting factors" received into memory in step (b) of the claim is an integral part of the claim and improves the method of detecting the fetal fraction "beyond generally linking the use of the judicial exception to a particular technological environment." 84 Fed. Reg. 55.

The Specification explains that a weighting factor is "a coefficient or constant that, in part, describes and/or defines a relation between a fetal fraction (e.g., a fetal fraction determined from multiple samples) and a portion-specific parameter for multiple samples (e.g., a training set)." Spec. 129:17–19. In step (b), the weighting factors are received into a memory, in step (c) they are assigned to portions of a reference genome, and in step (d) they are used to generate portion-specific fetal calculations. In the last step of the claim, step (e), "a fraction of fetal nucleic acid for the test sample based on the portion-specific fetal fraction calculations" is determined.

Therefore, the weighting factors recited in step (b) of claim 1 are used in a specific way to improve detecting the fetal nucleic acid fraction. Unlike in *Ariosa*, 788 F.3d at 1374, where the claims recited a *general* steps of amplifying a paternally inherited nucleic acid and detecting it or subjecting it to a test, the rejected claims in this appeal recite a specific and detailed method in which a series of steps are accomplished that results in "determining, using a microprocessor, a fraction of fetal nucleic acid for the test sample based on the portion-specific fetal fraction calculations. The appealed claims are also distinguishable from the claims in *Mayo*, where the uniqueness of the claimed method was not the drug administration or the determination of the levels of the drug in the subject, but instead the discovery of the *relationship* between the drugs levels and the need to adjust the amount of drug administered to the subject. *Mayo*, 566 U.S. at 74–75. Thus, the natural relationship or law of nature was the bulwark of the *Mayo* claim. Here, in contrast, the core of rejected claim 1 is the method steps which enable the detection of the fraction of nucleic acid in the sample which is fetal.

The improvement embodied in claim 1 is to the process of detecting the fraction of fetal nucleic acid and not solely to the mathematical concepts utilized to accomplish the detection. As held in *Flook*, 437 U.S. at 591, "[t]he process itself, not merely the mathematical algorithm, must be new and useful." *Id.* at 591.

In *Flook*, 437 U.S. at 594–95, claims to updating alarm limits were found to be ineligible for patent, despite providing "a new and presumably better method for calculating alarm limit values." The claim at issue in *Flook* was directed to a "method for updating the value of at least one alarm

limit on at least one process variable involved in a process comprising the catalytic chemical conversion of hydrocarbons." *Flook*, 437 U.S. at 596–97 (Appendix to Opinion of the Court). The steps comprised determining a new alarm base using a mathematical algorithm, using the alarm base to update an alarm limit, and then adjusting the alarm limit to the updated value. *Id.* The Court found the claim to be a judicial exception to subject matter eligibility

In contrast, the claims in *Diamond v. Diehr*, 450 U.S. 175 (1981) were found to be patent-eligible, although a mathematical equation was recited in the claim. In *Diehr*, the claims were directed to a method of operating a rubber-molding press to mold a compound by curing it in a mold cavity. *Application of Diehr*, 602 F.2d 982, 983–84 (CCPA 1979). The temperature in the mold during the rubber-molding process was constantly determined and provided to a digital computer. *Id.* The computer calculated the Arrhenius equation for the reaction time during the cure to determine when the compound was cured and to then automatically open the press. *Id.* Although the claim recited a mathematical formula, the Arrhenius equation, the Court held that the claim was eligible for a patent.

> [W]hen a claim containing a mathematical formula implements or applies that formula in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect (e.g., transforming or reducing an article to a different state or thing), then the claim satisfies the requirements of § 101.

Diehr, 450 U.S. at 192–93.

In this case, the weighting factors recited in claim 1, step (b), are used to determine the fraction of fetal nucleic acid in the blood of pregnant female. The claimed method, using such factors in steps (c) through (e),

reduces the probability of false positives, require fewer steps (Kim Decl.[2] ¶ 3), improves accuracy of the detection (Reply Br. 9), and is less expensive and faster than the prior art (Reply Br. 10; Kim Decl. ¶ 7). The Examiner found the improvement is to an "abstract idea" (Ans. 7), but the determination of a fraction of fetal nucleic acid in a test sample is not "abstract," but rather is an improvement to a process in which fetal nucleic acid is detected.

Our conclusion is consistent with *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 837 F.3d 1299, 1313 (Fed. Cir. 2016). The *McRO* claims involved the manipulation of data, e.g., generating morph weight sets to animate lip and facial expressions of three dimensional characters similar to the weighting factors recited in the claims. The court in *McRO* found that the "claimed process uses a combined order of specific rules that renders information into a specific format that is then used and applied to create desired results: a sequence of synchronized, animated characters." *McRO*, 837 F.3d at 1313. Here, the order of the specific rules in the claim utilizing weighting factors is used to create the desired result of determining the fetal nucleic fraction which improves the corresponding technological process. The claim as a whole, unlike the claims in *Flook* and in *Ariosa*, is an "application of the principle." *Flook*, 437 U.S. at 594.

Rapid Litigation Management Ltd. v. CellzDirect, Inc., 827 F.3d 1042 (Fed. Cir. 2016) is also consistent with the conclusion reached here. In *CellzDirect*, 827 F.2d at 1048, the court found that claims comprising steps of isolating and freezing naturally-occurring hepatocytes were patent-

[2] Sung Kyun Kim, Ph.D. (filed February 12, 2018, hereinafter "Kim Decl.").

eligible, despite being based on the discovery that cells could survive freeze-thaw cycles, because the end result was "not simply an observation or detection of the ability of hepatocytes to survive multiple freeze-thaw cycles." Rather, the court found "the claims are directed to a new and useful method of preserving hepatocyte cells." *Id.* The court observed that the inventors did not stop at "their discovery," but employed it "to create a new and improved way of preserving hepatocyte cells for later use." *Id.* Here, the inventors did not simply perform mathematical operations and make an observation about the relationship of weighting factors and nucleic acid in a sample, but instead employed the recited abstract ideas in a useful way to determine the fraction of nucleic acid in a sample. Accordingly, we find that claim as a whole integrates the abstract ideas into a practical application. Thus, the claim is eligible for a patent under 35 U.S.C. § 101 because it is not directed to a judicial exception, and it is unnecessary for us to proceed to Step 2B.

Summary

For the foregoing reasons, we conclude that the Examiner erred in rejecting claim 1, and dependent claim 2–6 and 13–26, as ineligible for a patent under 35 U.S.C. § 101.

REVERSED