

The Continuing Saga Of Mayo V. Prometheus

Law360, New York (February 25, 2014, 12:47 PM ET) -- For decades, Congress and the U.S. Supreme Court had assured patentees in the biotechnology space that “anything under the sun that is made by man” could be patent-eligible.[1] This understanding was upended in 2012, when the Supreme Court revisited the question of patentability under 35 U.S.C. § 101 in *Mayo Collaborative Services v. Prometheus Laboratories Inc.*[2]



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In *Prometheus*, the court explained that a method of optimizing a therapy was not patentable when that method simply relied upon a law of nature — the relationship between concentrations of metabolites in a patient’s blood and the likelihood that a particular drug dosage would be either harmful or ineffective.[3] While *Prometheus’* claims also recited specific steps to be performed by a physician, the court concluded that the steps were not enough to confer patentability when the claims did not “add enough” to a naturally occurring correlation.[4]

Although practicing the claimed methods required human intervention in the form of administering a manmade drug to a patient and thereafter determining a bloodstream metabolite level, those additional steps were nothing more than “well-understood, routine and conventional activity already engaged in by the scientific community.”[5] *Prometheus* left open the question of what steps, exactly, are sufficient to “transform unpatentable natural correlations into patentable applications.”[6]

Fast forward to 2014. Not surprisingly, federal courts continue to grapple with the “enough” that must be added to a law of nature to confer patent eligibility.

In *SmartGene Inc. v. Advanced Biological Laboratories*, the Federal Circuit upheld a determination that a claim to a method of selecting a therapeutic treatment was patent-ineligible.[7] The claim at issue required patient information to be provided to a “computing device” that included three databases (“knowledge bases”), and the generation in the “computing device” of a ranked set of therapeutic options, as well as advisory information based on the options and the individual patient’s information.[8]

Under § 101, those claims were not patent-eligible because they “embrace[d] a process defined simply as using a computer to perform a series of mental steps,” and those very same steps could be performed just as well in a person’s head.[9] The Federal Circuit limited its ruling to the circumstances presented in the case, “in which every step is a familiar part of the conscious process that doctors can and do perform in their heads.”[10]

The court reasoned that, under *Prometheus*, patentability requires that a “claim involve ‘enough’ else,” which means that a claim to an abstract idea must apply the idea in “realm of tangible physical objects,” or in connection with “physical actions ... beyond ‘well-understood, routine, conventional activity.’”[11] In the case of Advanced Biological Laboratories’ claims, the recited use of a computer required nothing that even arguably advanced “routine mental information comparison and rule-application.”[12]

Up next at the Federal Circuit is the Roslin Institute case, raising the question of whether a cloned animal is patent-eligible.[13]

The University of Edinburgh’s Roslin Institute is perhaps best known to the public in connection with “Dolly the sheep,” the world’s first mammal cloned from an adult somatic cell.[14] One of the questions presented in Roslin Institute is whether a “clone” is patent-eligible because it is distinct from animals found in nature, as nature simply does not make clones of pre-existing donor mammals.[15]

Appealing the Board of Patent Appeals and Interferences decision to uphold the examiner’s rejection of pending claims, Roslin argued that a clone is a “time-delayed genetic copy” of an older animal, the creation of which necessarily requires significant human intervention.[16] Clones of this sort have only a single, parental donor, are subject to environmental stimuli that are by no stretch of the imagination “natural,” and can be created even after the death of their donors.[17]

In response, the board argued that patent eligibility cannot be conferred on subject matter based on unclaimed differences.[18] In the board’s view, what Roslin has invented is a new cloning method, which does not render the clones themselves patentable.[19] The clones are not analogous to the genetically modified bacteria claimed in *Chakrabarty*, or to the manmade cDNA claimed by *Myriad*. [20] *Chakrabarty*’s engineered-bacteria were able to degrade oil, in a manner that their “naturally occurring” kin could not.[21] And *Myriad*’s patent-eligible cDNA lack the introns that are found in genomic DNA in its native context.

The Federal Circuit heard oral argument in the Roslin case on Feb. 5, 2014, and the judges — not surprisingly — focused on the genetic identity between a clone and its donor. Judge Kimberly Moore questioned how, after *Myriad*, a genetically identical copy of a naturally occurring animal could be patentable.[22]

Roslin first argued that there are phenotypic differences inherent between a clone and its donor.[23] The judges pointed out that Roslin’s position on patent eligibility was at odds with its likely position on infringement, and therefore not tenable. For the purposes of patentability, Roslin embraced unclaimed, phenotypic differences that arise inherently as part of the cloning process, arguing that those differences are sufficient to distinguish its clones from nature. In the infringement context, however, Roslin acknowledged that what was actually claimed would be key.

Roslin’s other argument for patent eligibility was based on the time delay that is also inherent in the cloning process. A clone is necessarily younger than its genetically identical donor. No answer, however, was forthcoming, when a hypothetical was posed involving genetically identical twins arising from in vitro fertilization, where one twin was brought to term only after a time delay.

Although Judges Moore, Timothy Dyk and Evan Wallach did not appear to be persuaded by either of Roslin’s arguments, it will be interesting to see whether the panel identifies any inventive activity in the several years of work necessary to create a cloned organism that is identical to a naturally occurring one (apart from potentially patent-eligible methods).

The Federal Circuit will also consider the patentability of certain diagnostic claims in a case between Ariosa Diagnostics and Sequenom.[24] Sequenom alleged that Ariosa's noninvasive, prenatal testing infringed U.S. Pat. No. 6,258,540.[25] The '540 patent claims methods of prenatal diagnostics that require the detection and analysis of cell-free, fetal DNA.[26] On cross-motions for summary judgment, the district court determined that Sequenom's claims were not drawn to patent-eligible subject matter.[27]

Ariosa argued that cell-free, fetal DNA ("cffDNA") is a naturally occurring phenomenon, and that the only additional claim limitations reflect well understood, routine and conventional activities in the field.[28] Sequenom disagreed, arguing that its claims were really directed to novel uses of a natural phenomenon.[29]

The district court agreed with Ariosa because, in addition to fetal DNA that can naturally be found in a pregnant woman's bloodstream, the '540 patent claims added only "amplifying" DNA from a sample and detecting the presence of paternally-inherited DNA in the sample.[30] The intrinsic evidence — and admissions from Sequenom's expert — made it abundantly clear that sample preparation and DNA amplification are standard techniques that are well known in the industry and that predate the claimed invention.[31] The district court drew a distinction between the addition of "conventional" steps to natural phenomena, and "innovative or inventive" uses of the same.[32]

On appeal, Sequenom argues to the Federal Circuit that its claims are patent eligible because they do not claim a naturally occurring phenomenon, cffDNA in maternal blood, but instead claim a specific use of compositions of matter that do not exist in nature.[33] According to Sequenom, the '540 patent's methods transform cffDNA in several ways.[34]

First, the cffDNA is separated from whole blood. Second, it is amplified, or copied, which never occurs in nature, because — in nature — cffDNA is extracellular and removed from the cellular machinery required for DNA replication. Third, the amplified products are distinct from cffDNA because they are of fixed length, and lack the methylation that is normally found on fetal DNA. Fourth, the step of detecting the amplified products requires human intervention in the form of laboratory manipulation.[35]

Based on these observations, Sequenom therefore argues that its claims do not run afoul of the core principle to judicially created exceptions to 35 U.S.C. § 101, which is to bar patentability of claims that preclude all future uses of a naturally occurring phenomenon.[36] The '540 patent claims do not prevent all uses of cffDNA, just specific uses, involving specific steps.[37]

Sequenom argues that, unlike the Prometheus case, the claimed steps are not steps that physicians performed before the patent. While, in Prometheus, physicians had long been administering drugs, measuring metabolites, and adjusting dosages accordingly, Sequenom argues that no one had practiced its claims before they invention of the '540 patent.[38] The "conventional" activities of the prior art involved actually discarding plasma and serum, which is precisely where the cffDNA is located.

Consequently, in Sequenom's view, the claimed steps are an entirely new method, and the district court erred when it considered whether each, individual step — in isolation — was novel .[39] Under the patent statutes, an invention may exist when ordinary elements are combined in an extraordinary way.[40] Ariosa will undoubtedly have a different view.

The Ariosa v. Sequenom case will be far from the last case to make its way to the Federal Circuit on Section 101 grounds. For example, in a case in the District of Delaware, Bristol-Myers has moved to dismiss Genetic Technologies Limited's case on the grounds that the asserted patent claims are simply

directed to naturally occurring correlations between regions of DNA.[41]

Genetic Technologies' theory of infringement is that Bristol-Myers Squibb Co.'s pharmacogenomic activities infringe U.S. Pat. Nos. 5,612,179 and 5,851,762.[42] Each patent claims methods of analysis that rely upon an association of polymorphisms in noncoding genomic sequences with phenotypic traits. The accused activities involve at least Bristol-Myers's studies on single nucleotide polymorphisms (SNPs) associated with variation in patient response to anticoagulants, HIV therapies, or cholesterol lowering drugs, as well as SNPs associated with variation in drug metabolism, generally, or with diabetes progression.[43]

Bristol-Myers' arguments are very similar to those made by Ariosa — that what is claimed is no more than a naturally occurring phenomenon. In this case, the claims relate to the correlation between genetic variation in noncoding sequences, and variations in sequences (typically coding) that are themselves associated with observable phenotypes in patients.[44] In Bristol-Myers' view, any additional limitations in the claim add nothing to the patentability equation, because all of the steps are "well-understood, routine, conventional activity" previously known in the field.[45]

For example, Bristol-Myers argues that the recitation of a "primer pair" — where the pair must amplify a DNA sequence that is linked to a genetic locus associated with a phenotypic trait — requires that someone has previously identified the (1) existence of the gene; (2) the fact that the gene is polymorphic; (3) the sequence of linked, noncoding genomic DNA; and (4) the fact that a polymorphism in the non-coding sequence is a surrogate marker for a physical characteristic created by the linked coding DNA.[46]

Bristol-Myers further argues that no inventive concept is found in the claimed "primer pair," which is "inherently required" to implement the law of nature in the context of the claims,[47] and, in fact, reflects work in the field that has already been performed.[48]

According to Bristol-Myers, "amplifying" DNA adds nothing novel, because amplification of DNA using primers was well known at the time of the invention.[49] Similarly, Bristol-Myers argues that the additional, claimed steps of "obtaining ... genomic DNA samples," "analyzing ... amplified DNA sequences," and "comparing" the degree of heterogeneity in the samples cannot confer patent eligibility. Each of those steps is either a routine and conventional physical step, or a mental step, and, in either case, not patentable under § 101.

Essentially, in Bristol-Myers' view, the only remotely "inventive" concept is the application of conventional techniques to allegedly new locations in the genome, but the DNA sequences that exist at those locations have always existed in nature.[50]

Stay tuned. Genetic Technologies, Ariosa and other litigants will undoubtedly have their own views of whether various, biotech patent claims reflect natural phenomena or an inventive combination, or, in other words, whether under Prometheus, "enough" has been added to Mother Nature.

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information purposes and is not intended to be and should not be taken as legal advice.

[1] *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (internal citations omitted).

[2] *Mayo Collaborative Services Inc. v. Prometheus Laboratories Inc.*, 566 U.S. ___, 132 S. Ct. 1289 (2012).

[3] *Mayo Collaborative Services Inc. v. Prometheus Laboratories Inc.*, 132 S. Ct. at 1297.

[4] *Mayo Collaborative Services Inc. v. Prometheus Laboratories Inc.*, 132 S. Ct. at 1297-1298.

[5] *Mayo Collaborative Services Inc. v. Prometheus Laboratories Inc.*, 132 S. Ct. at 1298.

[6] *Mayo Collaborative Services Inc. v. Prometheus Laboratories Inc.*, 132 S. Ct. at 1298.

[7] *SmartGene Inc. v. Advanced Biological Laboratories SA*, No. 2013-1186, (Fed. Cir. Jan. 24, 2014).

[8] Claim 1 of U.S. Pat. No. 6,081,786.

[9] *SmartGene Inc. v. Advanced Biological Laboratories SA*, No. 2013-1186, (Fed. Cir. Jan. 24, 2014) (slip opinion at 7-8).

[10] *SmartGene Inc. v. Advanced Biological Laboratories SA*, No. 2013-1186, (Fed. Cir. Jan. 24, 2014) (slip opinion at 9).

[11] *SmartGene Inc. v. Advanced Biological Laboratories SA*, No. 2013-1186, (Fed. Cir. Jan. 24, 2014) (slip opinion at 9).

[12] *SmartGene Inc. v. Advanced Biological Laboratories SA*, No. 2013-1186, (Fed. Cir. Jan. 24, 2014) (slip opinion at 9). The Supreme Court granted certiorari in *Alice Corp. v. CLS Bank Int'l.*, 134 S. Ct. 734 (Dec. 6, 2013), on the question of whether claims to computer-implemented inventions are patent-eligible subject matter within the meaning of 35 U.S.C. § 101.

[13] *In re Roslin Institute*, No. 2013-1407, Appellant's Brief from the United States Patent and Trademark Office, Patent Trial and Appeal Board (July 15, 2013) at 1.

[14] The University of Edinburgh, Roslin Institute, Dolly the Sheep, <http://www.roslin.ed.ac.uk/public-interest/dolly-the-sheep/> (last accessed Feb. 5, 2014).

[15] *In re Roslin Institute*, No. 2013-1407, Appellant's Brief from the United States Patent and Trademark Office, Patent Trial and Appeal Board (July 15, 2013) at 17.

[16] Or a TARDIS.

[17] *In re Roslin Institute*, No. 2013-1407, Appellant's Brief from the United States Patent and Trademark Office, Patent Trial and Appeal Board (July 15, 2013) at 21.

[18] *In re Roslin Institute*, No. 2013-1407, Appellee's Brief from the United States Patent and Trademark Office, Patent Trial and Appeal Board (Sept. 11, 2013) at 22-28.

[19] *In re Roslin Institute*, No. 2013-1407, Appellee's Brief from the United States Patent and Trademark

Office, Patent Trial and Appeal Board (Sept. 11, 2013) at 29.

[20] In re Roslin Institute, No. 2013-1407, Appellee's Brief from the United States Patent and Trademark Office, Patent Trial and Appeal Board (Sept. 11, 2013) at 30, citing Chakrabarty, 447 U.S. at 305; Ass'n for Molecular Pathology v. Myriad Genetics Inc., 133 S. Ct. ___, 2119 (2012).

[21] After Prometheus and Myriad, Chakrabarty's engineered bacteria are still patent-eligible, and there are guidelines regarding the genes they were engineered to carry. Under Myriad, genes are not patent-eligible if they are claimed simply in a form that focuses on the genetic information that exists in nature, 133 S. Ct. 2107, 2118-2119 (2013), but a nonnaturally occurring molecule, for example, a cDNA, is patent-eligible. Under Myriad, it would appear that Chakrabarty's recombinant DNA constructs pass muster under 35 U.S.C. § 101.

[22] In re Roslin Institute, No. 2013-1407, Oral Argument (Feb. 5, 2014), Tr. at 14:45-14:50.

[23] Counsel for Roslin acknowledged that phenotypic differences also exist between genetically identical twins, for example, who will have unique fingerprints and irises, based on environmental differences during development.

[24] Ariosa Diagnostics Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144.

[25] See Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 33 at 9 (Mar. 8, 2012).

[26] U.S. Pat. No. 6,258,540.

[27] Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 244 (Oct. 30, 2013).

[28] Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 244 (Oct. 30, 2013) at 12.

[29] Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 244 (Oct. 30, 2013) at 12.

[30] Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 244 (Oct. 30, 2013) at 13.

[31] Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 244 (Oct. 30, 2013) at 13-14.

[32] Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 244 (Oct. 30, 2013) at 15.

[33] Ariosa Diagnostics Inc. v. Sequenom Inc., N.D. Cal. Case No. 3:11-cv-06391-SI, D.I. 244 (Oct. 30, 2013) at 31-32.

[34] Ariosa Diagnostics Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144, Consolidated Opening Brief of Appellant Sequenome (Jan. 21, 2014) at 5-9, 31-36.

[35] Ariosa Diagnostics Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144, Consolidated Opening

Brief of Appellant Sequenome (Jan. 21, 2014) at 5-9.

[36] Ariosa Diagnostics, Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144, Consolidated Opening Brief of Appellant Sequenome (Jan. 21, 2014) at 25.

[37] Ariosa Diagnostics Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144, Consolidated Opening Brief of Appellant Sequenome (Jan. 21, 2014) at 32, 36-38.

[38] Ariosa Diagnostics Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144, Consolidated Opening Brief of Appellant Sequenome (Jan. 21, 2014) at 49.

[39] Ariosa Diagnostics Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144, Consolidated Opening Brief of Appellant Sequenome (Jan. 21, 2014) at 49, 51.

[40] Ariosa Diagnostics Inc. v. Sequenom Inc., Nos. 14-1139, 14-1142, 14-1144, Consolidated Opening Brief of Appellant Sequenome (Jan. 21, 2014) at 52, citing *Diamond v. Diehr*, 450 U.S. 175, 193 n.15.

[41] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014).

[42] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 31 (Dec. 16, 2013) at 18-25.

[43] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 31 (Dec. 16, 2013) at 18-23.

[44] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014) at 3.

[45] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014) at 3.

[46] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014) at 12-13.

[47] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014) at 13, citing *Ultramercial Inc. v. Hulu LLC*, 722 F.3d 1335, 1348 (Fed. Cir. 2013). In *Ultramercial*, the Federal Circuit explained that the Supreme Court's reference to "inventiveness" in *Prometheus* could be read as "shorthand" for whether implementing an abstract idea inherently requires the recited steps of the claim. 722 F.3d at 1348. "If, to implement the abstract concept, one must perform the additional step, or the step is a routine and conventional aspect of the abstract idea, then the step merely restates and element of the abstract idea, and thus does not further limit the abstract concept to a practical application." *Id.*

[48] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014) at 13-14.

[49] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014) at 13.

[50] Genetic Technologies Limited v. Bristol-Myers Squibb Co., D. Del. Case No. 1:12-cv-00394-LPS, D.I. 36 (Feb. 3, 2014) at 13.

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