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**EXTENDING THE IMPLICATIONS OF *MYRIAD TO AMBRY* –
THE NEW INTERPRETATION OF SECTION 101**

By Micah O’Keefe

INTRODUCTION

An ongoing legal battle has erupted in the Biotech world in a series of cases involving the patent rights to perform certain diagnostic testing. One of these cases, *Association of Molecular Pathology v Myriad Genetics Inc.* (“*Myriad*”) reached the U.S. Supreme Court, resulting in a landmark decision that is having broad-reaching implications within the Biotechnology field.

On June 13, 2013, the Supreme Court issued a unanimous decision holding that “genes and the information they encode are not patent eligible simply because they have been isolated from the surrounding genetic material.”¹ Somewhat surprisingly, the Supreme Court’s decision against the patentability of isolated DNA prompted more—not less—litigation by Myriad regarding its gene patents.²

The recent Supreme Court decision in *Myriad* has left legal analysts and the USPTO scrambling to make sense of the Court’s seemingly new interpretation of patentable subject matter under 35 U.S.C. § 101. One rival company, Ambry Genetics, relied on the *Myriad* decision, marketed services that it believes are no longer patent protected, and has now found itself in a patent infringement lawsuit against Myriad.³ This article analyzes the *Myriad* decision

¹ *Association for Molecular Pathology et al. v. Myriad Genetics Inc., et al.*, 569 U.S. ____ (2013).

² Law Firm of Dayrel Sewell, PLLC, *Myriad Back in Court on Patent Subject Matter Eligibility*, SEWELLYLAW.COM, (Oct. 26, 2014), <http://sewellylaw.com/myriad-back-in-court-on-patent-subject-matter-eligibility/>.

³ John Conley, *District Court Denies Myriad’s Prelim. Injunction Against Ambry*, GENOMICSLAWREPORT.COM (Mar. 18, 2014), <http://www.genomicslawreport.com/index.php/2014/03/18/district-court-denies-myriads-preliminary-injunction-against-ambry/>.

and the recent USPTO Guidance and proposes the best course of action the Court should take in the current case, *Ambry*, applying the facts to the legal rules embodied in the statutes, guidances, and the applicable case law.

Myriad Genetics and Ambry Genetics are companies that provide hereditary cancer testing services which allow patients to understand their risk of cancer. Both companies are currently offering BRCA1 and BRCA2 genetic tests, in addition to their other product lines and services.⁴

BRCA1 and BRCA2 are tumor suppression genes that help repair DNA and play an important role in controlling a cell's life cycle. If a mutation occurs in one of these genes, it can affect the cell's ability to repair DNA. This can lead to an increased risk for developing cancer over one's lifetime.⁵ Hereditary BRCA1 and BRCA2 mutations are a major contributing cause of breast & ovarian cancer in women, as well as prostate and male breast cancer in men.⁶

If a person has a BRCA1 or BRCA2 mutation in his or her DNA, it means that individual has a considerably higher chance of developing cancer. However, understanding one's risk can help a patient to make informed decisions about his or her health, such as increased monitoring, beginning treatment earlier in the cancer process, or taking other precautionary measures, such as lifestyle changes beforehand. So, these diagnostic tests offer an important healthcare option for the American public.⁷

⁴ *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litig.*, No. 2:13-CV-00640-RJS, 2014 WL 931057 (D. Utah Mar. 10, 2014).

⁵ Yilun Liu & Stephen West, *Distinct Functions of BRCA1 and BRCA2 in Double-strand Break Repair*, BREAST-CANCER-RESEARCH.COM, (Nov. 20, 2001), <http://breast-cancer-research.com/content/4/1/9>.

⁶ Myriad Genetics Laboratories, Inc., BRACNOW.COM, <http://www.bracnow.com/faqs/#40>, (last visited Dec. 7, 2014, 8:49 PM).

⁷ *See id.*

The current case began when Ambry Genetics announced that it would offer BRCA1 and BRCA2 genetic testing, following the Supreme Court decision in *Myriad*. Plaintiffs, including Myriad Genetics, filed for a preliminary injunction in *University of Utah Research Foundation v. Ambry Genetics Corporation* to stop Ambry Genetics from selling genetic tests that Plaintiffs claimed were infringing upon their patents that were still valid, according to their interpretation of the Supreme Court decision.⁸ Myriad Genetics views the holding in *Myriad* as an affirmation of the validity of its remaining claims, while Ambry Genetics is shocked, believing that the decision in *Myriad* meant that the marketplace is now open to offer competition for BRCA1 and BRCA2 testing.⁹

As a look into Myriad's 2013 second quarter fiscal results show, BRCAAnalysis[®] is big BRCABusiness for Myriad. Diagnostic testing revenue in that quarter came to \$140.7 million. Revenue generated from Myriad's Oncology line equaled \$90.9 million. Women's Health revenue was \$49.8 million, which was a 27% increase over the prior year. Revenue from the BRCAAnalysis[®] Test came in at \$110.3 million, representing 74% of total revenue.¹⁰ In the Fourth Quarter, revenue increased by 31%. Full-year revenues totaled \$613 million in 2013, with the BRCAAnalysis[®] Test again representing 74% of revenues in the 4th quarter.

Myriad's revenue from the BRCAAnalysis[®] Test totaled more than \$2 billion from 1997 to 2013.¹¹

⁸ *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litig.*, No. 2:13-CV-00640-RJS, 2014 WL 931057 (D. Utah Mar. 10, 2014).

⁹ See Ambry Genetics Corp., *Ambry Genetics Sues Myriad Genetics for Violating Federal Antitrust Laws*, AMBRYGEN.COM, (last visited Dec. 7, 2014, 7:20 PM), <http://www.ambrygen.com/press-releases/ambry-genetics-sues-myriad-genetics-violating-federal-antitrust-laws>.

¹⁰ Myriad Genetics, Inc., *Myriad Genetics Reports Second Quarter Fiscal Year 2013 Results*, INVESTOR.MYRIAD.COM, (Feb. 5, 2013), <http://investor.myriad.com/releasedetail.cfm?releaseid=738080>.

¹¹ See Law Firm of Dayrel Sewell, *supra* note 2.

Due to the dollar value at stake, Myriad clearly wants to maintain their control of the BRCA1/2 testing market. Myriad Genetics had been the sole provider of BRCA1/2 Testing from 1997 until the Supreme Court invalidated the patent in 2013.¹² So, when the Association of Molecular Pathology began using diagnostic testing based upon technology covered under its patent, it fought to safeguard against the proclaimed infringement the same way it had against others over the years.

Other companies and research institutes were excited about the possibility of using this technology to advance research, uninhibited.¹³ But, Myriad has sought to fend-off would-be competitors through a strategy of aggressive legal action, starting with Ambry.

On the sidelines of this genetic testing arena are those interested parties – the patients and their friends & family – some of whom believe that this testing should be more widely available and affordable. The American Civil Liberties Union (ACLU) and The American College of Medical Genetics and Genomics are two groups that support such a view.¹⁴

SCIENCE & TECHNOLOGY OVERVIEW

Genetics, DNA, and Cellular Biology

Genes form the basis for hereditary traits in living organisms.¹⁵ They are made up of sections of DNA and give cells instructions to make amino acids, which are the building blocks

¹² In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litig., No. 2:13-CV-00640-RJS, 2014 WL 931057 (D. Utah Mar. 10, 2014).

¹³ See Thomas J. Engellenner, *United States: Myriad – One Year Later*, MONDAQ.COM, (June 23, 2014), <http://www.mondaq.com/unitedstates/x/322282/Patent/Myriad+One+Year+Later>.

¹⁴ But see Donald Zuhn, *Reaction to Supreme Court's Decision in AMP v. Myriad*, BIOTECH & PHARMA PATENT LAW & NEWS BLOG, PATENTDOCS.ORG, (July 1, 2014) <http://www.patentdocs.org/2013/07/reaction-to-supreme-courts-decision-in-amp-v-myrriad.html>.

¹⁵ National Institutes of Health, U.S. National Library of Medicine, *What is a Gene?*, GENETICS HOME REFERENCE, GHR.NLM.NIH.GOV, (Dec. 1, 2014) <http://ghr.nlm.nih.gov/handbook/basics/gene>.

of proteins.¹⁶ DNA is wound into the familiar double-helix shape. DNA, which encodes the hereditary information of each cell, is stored in the cell nucleus. The nucleus is the cell's command center that sends directions to the cell to grow, mature, divide (replicate), or die.¹⁷ If something is wrong with the cell, it should receive a signal from the nucleus to initiate cell death (which is for the good of the larger organism, i.e. human).¹⁸

Genetic Mutations and Cancer

When errors occur during the process of copying DNA during cell division, the result is a genetic mutation. A gene mutation is a permanent change in the DNA sequence that makes up a gene. Hereditary mutations are passed generationally and are present throughout a person's life in virtually every cell in the body.¹⁹

Cancers occur when a buildup of genetic mutations in critical genes – those that control cell growth and division or the repair of damaged DNA – allow cells to grow and divide uncontrollably to form a tumor. There are certain genes that have been found to be associated with developing certain types of cancers. BRCA1 and BRCA2 are tumor suppression genes that help repair DNA and play an important role in controlling a cell's life cycle. If a mutation occurs in one of these genes, it can affect the cell's ability to repair DNA and thus result in uncontrolled cell growth, tumors, and cancer.²⁰

¹⁶ National Institutes of Health, U.S. National Library of Medicine, *How Do Genes Direct the Production of Proteins?*, GENETICS HOME REFERENCE, GHR.NLM.NIH.GOV, (Dec. 1, 2014), <http://ghr.nlm.nih.gov/handbook/howgeneswork/makingprotein>.

¹⁷ National Institutes of Health, U.S. National Library of Medicine, *What is DNA?*, GENETICS HOME REFERENCE, GHR.NLM.NIH.GOV, (Dec. 1, 2014), <http://ghr.nlm.nih.gov/handbook/basics/dna>.

¹⁸ See BRUCE ALBERTS, ET. AL, *MOLECULAR BIOLOGY OF THE CELL* (Garland Science, 4th ed. 2002). Accessed via <http://www.ncbi.nlm.nih.gov/books/NBK26873/> (pagination is not available in online accessible excerpt).

¹⁹ National Institutes of Health, U.S. National Library of Medicine, *What is a Gene Mutation and How do Mutations Occur?*, GENETICS HOME REFERENCE, GHR.NLM.NIH.GOV, (Dec. 1, 2014), <http://ghr.nlm.nih.gov/handbook/mutationsanddisorders/genemutation>.

²⁰ National Cancer Institute, *BRCA1 and BRCA2: Cancer Risk and Genetic Testing*, CANCER.GOV, (Jan 22, 2014), <http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA>.

Naturally Occurring DNA Replication and Processes

DNA stores massive amounts of information within it using a complex coding system which utilizes 4 chemical bases that have unique pairing abilities and restrictions: 1) Adenine (A), 2) Thymine (T), 3) Guanine (G), and 4) Cytosine (C). The sequence of these bases results in different outcomes for both building and maintaining a complex organism, like a human being.²¹

The aforementioned bases pair together to form what is known as a “base pair.” The rules of base pairing are as follows. A always pairs with T, and C always pairs with G. There is one exception to this rule, relating to *RNA* which uses Uracil (U) in place of T to pair with A.²²

In naturally-occurring DNA, the process of creating new molecules begins with transcription. DNA naturally consists of both introns and exons. Molecular bonds separate into individual strands of DNA. These then stand alone as single strand DNA templates for forming the other strand, according to base-pairing principles. A complementary RNA strand, known as pre-RNA is formed. Pre-RNA is then naturally spliced by the cell into mRNA, which consists of exons only, meaning that mRNA only encodes for the creation of amino acids.²³

When scientists create DNA synthetically in a laboratory, they begin with an mRNA molecule. Natural bonding properties of nucleotides (C-G), (A-T), (U-A) are used. The result is a new *synthetic* DNA molecule, or cDNA. It is the reverse image of the original DNA molecule, without introns. It also is made up of exons only, meaning that each of its DNA segments only

²¹ See National Institutes of Health, *supra* note 17.

²² See *id.*

²³ Nature Educ., *Ribosomes, Transcription, & Translation*, NATURE.COM, <http://www.nature.com/scitable/topicpage/ribosomes-transcription-and-translation-14120660>, (last visited Dec. 7, 2012, 9:05 AM), (no author provided).

encode for amino acid production. cDNA has applications in developing medical tests where it is easier to detect mutations in these genes by only counting exons.²⁴

DNA Replication and its Applications

DNA naturally has the ability to make copies of itself. This is critical when cells divide, because each new cell needs to have an exact copy of the DNA from the old cell. DNA makes copies of itself and builds proteins through the processes of Transcription and Translation. Transcription is a process where a cell makes an RNA copy of a gene sequence using a molecule known as mRNA. Translation is the process of then translating the sequence of that mRNA molecule to a sequence of amino acids in order to build proteins.²⁵ Segments of DNA that encode for the production of amino acids are known as exons, and segments of DNA that do not encode for amino acid production are known as introns.²⁶

There is also a type of synthetic DNA, which is man-made and assembled in labs, known as cDNA. It is called cDNA because it is complementary, or a mirror image of the original naturally-formed DNA molecule. There are useful applications for using synthetic DNA in medical diagnostic testing. cDNA makes it is easier to detect mutations in genes by creating complementary versions of the DNA that only include exons and then only counting the exons, with an example being 5,500 nucleotides to count in cDNA vs. 80,000 nucleotides to work through in naturally-occurring DNA.²⁷

PATENT LAW OVERVIEW

What is a Patent & Constitutional Basis

²⁴ Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2111, 186 L. Ed. 2d 124 (2013).

²⁵ See Nature Educ. *supra* note 23.

²⁶ See Ass'n for Molecular Pathology, 133 S. Ct. 2107, 2111, 186 L. Ed. 2d 124 (2013), *supra* note 24.

²⁷ *Id.*

A patent is an intellectual property right granted to an inventor, by the government, to exclude others from making, using, or selling the invention throughout the U.S. or importing the invention into the country. It's not actually a right to the invention itself. However, in practice, a patent essentially acts as a federally-backed monopoly of the patented innovation for a limited period of time.²⁸

In the United States, a patent is granted by the federal government in exchange for the inventor disclosing to the public how to create the invention, so that it can be widely reproduced by anyone after the expiry of the patent.²⁹

The concept of the patent was embodied within the U.S. Constitution. Article I, Section 8, Clause 8 provides that "Congress shall have Power... To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."³⁰ Interpreting this clause specifically to patents, it means that Congress shall have the power to promote the progress of science in our country by giving inventors the exclusive right to their discoveries for a limited period of time. The underlying policy behind this constitutional clause is to reward inventors (with a patent) for their time and efforts in developing the invention, in order to encourage technological development in our nation to allow the public to enjoy the use of the innovation and help advance our nation as a whole on the international stage.³¹

Statutory Law: 35 U.S.C.

²⁸ Legal Information Institute, Cornell University Law School, *Patent*, (last visited Dec. 7, 2014, 4:14 PM), <http://www.law.cornell.edu/wex/patent>.

²⁹ *Id.*

³⁰ U.S. CONST. Art. I, § 8 (1787).

³¹ See Susan DeSanti, et. Al., *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, A Report by the Federal Trade Commission, October 2003.

The Constitution bestowed the power upon Congress to do something to promote the Progress of Science. It was then up to Congress to take it from there. Congress then enacted the Patent Act, which it later codified as Title 35 of the U.S. Code (§1-376). 35 U.S.C. governs all aspects of patent law within the United States.³²

Title 35 of the U.S.C. currently has 5 parts. Part I provides for the establishment of the United States Patent and Trademark Office. Part II relates to the patentability of inventions and the grant of patents. Part III applies to the protection of patent rights. Part IV covers the Patent Cooperation Treaty. Lastly, Part V relates to the Hague Agreement, concerning the international registration of industrial designs.³³

There are 3 types of patents available. They are the utility patent, the design patent, and the plant patent. Utility patents are the type of patent typically thought of by a layperson. They relate to the majority of patents in the news. Design patents relate to novel ornamental features that have no function. Plant patents are issued for previously uncultivated plants or novel cultivated plants, provided that the plant reproduces asexually.³⁴

The type of patents at issue in both *Myriad* and *Ambry* are utility patents. Utility patents include the following subject matter: machines, processes, and compositions of matter. The primer claims which will be discussed later are examples of compositions of matter, and the method claims which will be discussed are examples of processes.

³² United States Patent and Trademark Office, *Introduction*, USPTO.GOV, (last visited Dec. 7, 2014, 6:58 PM) <http://www.uspto.gov/web/offices/pac/mpep/mpep-0020-introduction.html>.

³³ Title 35 – Patents, 35 U.S.C. §§1-390 (2012).

³⁴ JUDITH M. TOFFENETTI, *FUNDAMENTALS OF LIFE SCIENCES LAW: DRUGS, DEVICES, & BIOTECH*, 363-364. (2d Ed., 2014).

“Whoever 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.”³⁵

Title 35 U.S.C. lays forth the following basic requirements for patentability: usefulness (the utility requirement)³⁶, novelty (meaning new)³⁷, nonobviousness³⁸, and sufficient disclosure.³⁹ A sufficient disclosure under Section 112 includes four necessary aspects: a written description, enablement⁴⁰, a best mode, and definiteness.⁴¹

Under Section 101, there are four categories of patentable subject matter: process, machine, manufacture, and composition of matter.⁴² A process is a series of acts or steps.⁴³ A Machine is a concrete thing, consisting of parts, or of certain devices and combination of devices.⁴⁴ A manufacture is an article produced from raw or prepared materials by creating new forms, qualities, properties, or combinations.⁴⁵ Compositions of matter relate to all compositions of two or more substances formed from chemical bonds or mixtures.⁴⁶

The subject matter of a patent claim must be directed to one of the four subject matter categories. If it is not, then it is not eligible for patent protection and should be rejected under 35. U.S.C. §101. These have been further defined by judicial interpretations.⁴⁷

³⁵ 35 U.S.C. §101.

³⁶ *Id.*

³⁷ 35 U.S.C. §102.

³⁸ 35 U.S.C. §103.

³⁹ 35 U.S.C. §112.

⁴⁰ *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

⁴¹ United States Patent and Trademark Office, *Guidelines for Examination of Applications for Compliance with the Utility Requirement*, USPTO.GOV, (last visited Dec. 7, 2014, 6:58 PM) <http://www.uspto.gov/web/offices/pac/mpep/s2107.html>.

⁴² 35 U.S.C. §101.

⁴³ *Gottschalk v. Benson*, 409 U.S. 63, 70, 175 USPQ 673, 676 (1972).

⁴⁴ *Burr v. Duryee*, 68 U.S. (1 Wall.) 531, 570, 17 L. Ed. 650 (1863).

⁴⁵ *Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 USPQ 193, 197 (1980).

⁴⁶ *See id* at 197.

⁴⁷ *See* United States Patent and Trademark Office, *supra* note 41.

Administrative Law – The Role of the USPTO

The U.S. Patent and Trademark Office (USPTO) is established under 35 U.S.C. §1.⁴⁸

The USPTO is an agency that falls under the Dept. of Commerce. It has the power to grant and issue patents and trademarks.⁴⁹

35 U.S.C. governs all cases in the USPTO, and the USPTO establishes regulations that govern patent proceedings. The regulations must be in line with the policy set by the Dept. of Commerce and must be consistent with existing law. The primary purpose of the regulations is to advise the public of the rules, based upon the USPTO's interpretation of the statutes. The USPTO's mission includes fostering innovation, competitiveness, and economic growth, as well as guiding policy on intellectual property matters.⁵⁰

The USPTO is made up of different offices. The Patent Office is one of them. The Patent Office examines patent applications and grants patents on inventions if it finds that the inventor is entitled to one. It also publishes and disseminates patent information, records assignments of patents, maintains search files of U.S. and foreign patents, and maintains a search room for public use in examining issued patents and records.⁵¹

Administrative Law – The MPEP

MPEP stands for the Manual of Patent Examining Procedure. This manual is published by the USPTO. It describes the laws and regulations that must be followed when examining patent applications. It also explains the application of these laws & regulations to different

⁴⁸ 35 U.S.C. §101.

⁴⁹ United States Patent and Trademark Office, *USPTO Organization*, USPTO.GOV, (last visited Dec. 7, 2014, 7:00 PM) <http://www.uspto.gov/about/offices/index.jsp>.

⁵⁰ United States Patent and Trademark Office, *Mission & Organization of the USPTO*, USPTO.GOV, (last visited Dec. 7, 2014, 7:05 PM) http://www.uspto.gov/about/stratplan/ar/2011/mda_01.html.

⁵¹ United States Patent and Trademark Office, *Office of the Commissioner for Patents*, USPTO.GOV, (last visited Dec. 7, 2014, 7:11 PM) <http://www.uspto.gov/about/offices/patents/index.jsp>.

scenarios and guides patent examiners in the USPTO when reviewing patent applications. It is used and heavily relied upon by patent lawyers and patent agents in their dealings with the USPTO, including claim drafting and prosecution.⁵²

Administrative Law – Prior Examination Guidelines

The USPTO previously issued additional guidelines such as Utility Examination Guidelines 66 Fed. Reg. 1092 (2001). This specific guidance directed patent examiners in reviewing patent applications for genes. “If a patent application discloses only nucleic acid molecular structure for a newly discovered gene, and no utility for the claimed isolated gene, the claimed invention is not patentable... Where the applicant discloses a *specific, substantial, and credible* utility for the claimed isolated and purified gene, the isolated and purified gene composition may be patentable.”⁵³

The Utility Guidelines Training Materials further defined these terms. This training material was recently revised, and includes the following definitions. *Specific* means “particular to the subject matter claimed,”⁵⁴ *substantial* “defines a real world use,”⁵⁵ and *credible* means “a person with ordinary skill in the art would accept that the invention is currently available for such use.”⁵⁶

Judicial Law – The Role of the Courts

Patents are governed by federal law. Federal district courts have original jurisdiction over patent law cases. The U.S. Court of Appeals for the Federal Circuit hears appeals in patent

⁵² 13A Fed. Proc. Forms § 52:4.

⁵³ Utility Examination Guidelines, 66 FR 1092-02 (2001).

⁵⁴ United States Patent and Trademark Office, *Revised Interim Utility Guidelines Training Materials*, (last visited Dec. 7, 2014, 8:55 PM), <http://www.uspto.gov/web/menu/utility.pdf>.

⁵⁵ *Id.*

⁵⁶ *Id.*

law cases. Some cases are ultimately heard by the U.S. Supreme Court, whose ruling is binding on the courts beneath it.⁵⁷

When a patent infringement suit is brought in front of the Court, the Court's role is to interpret the statutes, applying the codified law to the specific set of facts of the case before it. This then sets binding precedent for cases that follow under its jurisdiction.

Over time, the courts have interpreted different aspects of the Patent Act, taking into account such matters as public policy. Historically, there are several judicially recognized exceptions to the four categories of patentable subject matter under 35 U.S.C. 101. These are: laws of nature, physical phenomena, and abstract ideas. If an invention claimed in a patent falls under one of these judicially recognized exceptions to Section 101, then it will not be accepted by the courts as patentable subject matter.⁵⁸

THE MYRIAD DECISION

How the Myriad Case Found its Way to the Supreme Court

Dr. Henry Ostrer, a medical researcher at NY School of Medicine, sent his patients' DNA samples to UPenn's Genetic Diagnostic Laboratory (GDL). Myriad Genetics sent a letter to GDL, telling them they were infringing upon Myriad's patent. GDL then stopped testing and denied patient samples. Myriad went on to sue others performing BRCA testing, preventing any others from providing it.⁵⁹

⁵⁷ See Legal Information Institute, *supra* note 28.

⁵⁸ See Manual of Patent Examining Procedure §2106, (R-11.2013).

⁵⁹ See Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2111, 186 L. Ed. 2d 124 (2013).

Dr. Oster, amongst other interested parties, filed suit, claiming Myriad's patents were invalid under §101. The District Court granted summary judgment to Ostrer on the composition claims, concluding that claims related to cDNA were invalid as products of nature. The Federal Circuit later reversed the District Court's decision. The Supreme Court then granted cert., vacated the judgment, and remanded the case to evaluate standing of petitioners, due to recent decision in *Mayo*.⁶⁰

On remand, the Federal Circuit affirmed the District Court in part and reversed in part, holding that only Ostrer had standing. The Federal Circuit then held that both DNA and cDNA were patent eligible. However, the panel of judges disagreed over why. The Supreme Court agreed to grant Cert. once again to address this issue.

Issues Addressed in *Myriad*

In *Assn. for Molecular Pathology v. Myriad Genetics Corp.*, the Supreme Court addressed two issues before it. The first question addressed was whether a naturally occurring segment of DNA is patent eligible under §101 due to its isolation from the rest of the DNA. The second was whether synthetically created DNA (cDNA) is patent eligible under §101, as it contains the same protein-coding information found in a segment of natural DNA but omits portions of the DNA that do not code for proteins.⁶¹

Justice Clarence Thomas delivered the opinion for the unanimous 9-0 decision. There were two types of composition of matter claims that were reviewed – Myriad's DNA claims

⁶⁰ See *id.*

⁶¹ See *id.*

which related to “genomic” or naturally occurring DNA, and Myriad’s cDNA claims which related to synthetic DNA. The Court did not address the method claims in the case.⁶²

Prior Case Law Precedent

Prior case law helped to shape the Court’s view and decision of what is patentable subject matter. *O’Reilly v. Morse* was a case from 1854. Samuel Morse invented the telegraph which used Morse Code to communicate messages at a distance using the electromagnetic force, which Morse had much success in learning how to manipulate toward practical applicability. Morse patented his invention. However, the Court invalidated claim 8 for being overly broad, beyond its particular application of the telegraph.⁶³ The Court was concerned that this would allow Morse to exclude others from making new inventions that Morse had not yet created or even thought of yet.⁶⁴ The court held that patent law does not allow for overly broad patent rights to scientific principles, because this would allow for monopolies that would be unjust to the public and that would defeat the policy purpose behind the patent.⁶⁵

In *Funk Bros. Seed Co. v. Kalo Inoculant Co. (1948)*, the Court held that patents cannot be issued for the discovery of natural phenomena.⁶⁶ The qualities of the bacteria in question were held to be naturally occurring and therefore not patentable subject matter.⁶⁷ The application of the newly-discovered natural principle to the packaging of vaccines was not enough to deserve patentability.⁶⁸

⁶² *See id.*

⁶³ *O’Reilly v. Morse*, 56 U.S. 62, 62, 14 L. Ed. 601 (1853)

⁶⁴ *Id.*

⁶⁵ *Id.*

⁶⁶ *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 68 S. Ct. 440, 92 L. Ed. 588 (1948)

⁶⁷ *Id.*

⁶⁸ *Id.*

Diamond v. Chakrabarty was an important Supreme Court decision in 1980 related to the Biotech field, where the Court reiterated that the laws of nature, physical phenomena, and abstract ideas are not patentable subject matter.⁶⁹ It was decided that although microorganisms in general are a product of nature, a live, *human-made* microorganism is patentable subject matter under §101.⁷⁰ The Court stated that “[c]ongress... recognized that the *relevant distinction* was not between living and inanimate things, but between *products of nature, whether living or not, and human-made inventions*. Here, respondent’s micro-organism is the result of human ingenuity and research.”⁷¹

A more recent relevant decision came in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* (2012). There, the Supreme Court held that Prometheus’ claims, methods of optimizing drug efficacy, were related to laws of nature, and thus were not patent-eligible under 35 USC § 101. This decision was supported by the Court’s basic principles that laws of nature, natural phenomena, and abstract ideas are not patentable. It was held that “[t]o transform an unpatentable law of nature into a patent-eligible *application* of a law of nature requires more than just stating the law of nature while adding the words ‘apply it.’”⁷²

Analysis of *Myriad*

There were two issues addressed by the Supreme Court in *Myriad*. Both involved the patent eligibility of DNA. The first issue was “whether a naturally occurring segment of [DNA] is patent eligible under 35 U.S.C. 101 by virtue of its isolation from the rest of the human

⁶⁹ Diamond v. Chakrabarty, 447 U.S. 303, 100 S. Ct. 2204, 65 L. Ed. 2d 144 (1980).

⁷⁰ *Id.*

⁷¹ *Id.*

⁷² Mayo Collaborative Servs., 132 S. Ct. 1289, 182 L. Ed. 2d 321 (2012).

genome.”⁷³ The second issue involved “the patent eligibility of synthetically created DNA, known as complementary DNA (cDNA), which contains the same protein-coding information found in a segment of natural DNA but omits portions within the DNA segment that do not code for proteins.”⁷⁴ The Court held “that a naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but that cDNA is patent eligible because it is not naturally occurring.”⁷⁵

Nine composition claims from three of Myriad’s patents were at issue in the case. The Court analyzed four claims from Myriad’s U.S. Patent 5,747,282 (the ‘282 patent), stating that they were representative of the collective claims at issue. No method claims were evaluated.

Claim 1 declared a patent on the DNA code that tells a cell to produce BRCA1 amino acids listed in a certain sequence. This claim was invalidated in the case, falling under the “product of nature” exception.

Claim 2 essentially claimed the sequence of cDNA that codes for the BRCA1 amino acids listed in Claim 1. This consisted only of exons in the BRCA1 gene, and so is thus valid, as it was synthetically produced in a laboratory.⁷⁶

Claim 5 claimed isolated DNA from Claim 1, basically asserting a patent on any 15 or more nucleotides in a row in a typical BRCA1 cancer gene. This sounds eerily similar to claiming a patent on breast cancer itself. That specific aspect was not addressed by the Court, but being a subset of Claim 1, Claim 5 also fell under the category of a product of nature, and was therefore invalidated.⁷⁷

⁷³ Ass’n for Molecular Pathology, 133 S. Ct. 2107, 2111, 186 L. Ed. 2d 124 (2013).

⁷⁴ *Id.*

⁷⁵ *Id.*

⁷⁶ *Id.*

⁷⁷ *Id.*

Claim 6 went on to claim a subset of the data in Claim 2, similarly asserting rights over any series of 15+ nucleotides present in the *cDNA* to the BRCA1 gene. Since this corresponded to synthetically created DNA, it remained valid.⁷⁸

While Myriad argued that breaking the covalent bonds connecting a particular segment of DNA to the remainder constituted an innovation that deserved patent protection, the Supreme Court viewed it differently. The Court stated that the process of isolating a nucleic acid does change its structure, by breaking the bonds, but that change itself does not create a *marked difference*⁷⁹ in structure between the isolated portion and its naturally occurring counterpart. This means that although isolating a gene does *technically* create a molecule that is different by virtue of breaking the bonds of the larger molecule, in essence, it is not significantly different, because the nucleotide sequence was not changed.⁸⁰

The Court held that “a naturally occurring DNA segment is a product of nature and is not patent eligible merely because it has been isolated... but *cDNA is* patent eligible because it is not naturally occurring.”⁸¹ In coming to its decision in *Myriad*, the Court cited *Diamond v. Chakrabarty* regarding whether the compound was new “with *markedly different* characteristics from any found in nature.”⁸² The Court held that Myriad’s genomic DNA claim fell within the law of nature exception. Myriad’s genomic DNA claim detailed the extensive process of discovery that Myriad went through, but the court explained that extensive effort alone is insufficient.⁸³

⁷⁸ *Id.*

⁷⁹ *Id.*

⁸⁰ *See id.*

⁸¹ *Id.*

⁸² *Diamond v. Chakrabarty*, 447 U.S. 303, 100 S. Ct. 2204, 65 L. Ed. 2d 144 (1980).

⁸³ *See id.*

Based upon the Court's opinion, it could be said that there were several flaws in the drafting of the genomic DNA claim. The claims are not expressed in terms of chemical composition. The claims did not rely on the chemical changes that resulted from the isolation of a particular DNA section, but instead focused on the genetic information encoded in the BRCA1 and BRCA2 genes.⁸⁴

However, Myriad's cDNA claim was found to not be a product of nature, and it was held to be patent eligible under Section 101 for that reason. The creation of cDNA results in an exons-only DNA molecule, which is not naturally occurring. The Court found that "the lab technician *unquestionably* creates something new when introns are removed from the sequence."⁸⁵

The Take-away from *Myriad*

In *Myriad*, the Supreme Court agreed 9-0 on two important matters. Naturally occurring gene sequences, and their natural derivative products, are *not* patent eligible. But, the creation of a *new product* in a lab *exempts* that product from being a product of nature. Therefore, gene sequences *refined* by synthetic processes to create molecules that do not occur naturally *are* patent eligible. The dispositive factor in *Myriad* was whether the molecules were *markedly different* from those that occur naturally in nature.⁸⁶

The holding in *Myriad* is contrary to Utility Examination Guidelines 66 Fed. Reg. 1092 (2001). This is because claim 1 of Myriad's '282 patent was invalidated for being a product of nature as genomic DNA. This essentially had the effect of invalidating the Guideline that was inconsistent with the new holding. This meant that the USPTO had to quickly react to this new

⁸⁴ See Ass'n for Molecular Pathology, 133 S. Ct. 2107, 2111, 186 L. Ed. 2d 124 (2013).

⁸⁵ *Id.*

⁸⁶ See *id.*

interpretation of patentable subject matter under Section 101 and revise their policies and guidelines accordingly. The *Myriad* decision may have also resulted in diminishing how much deference should be paid to the USPTO guidelines by practitioners and the courts.⁸⁷

This case resulted in upholding several of Myriad's patent claims, while invalidating others. The reasoning behind the decision will undoubtedly prove to be dispositive in examining future patent applications, as well as in reviewing patent claims which may now be challenged in the courts under the new standard. Claims 1 and 2 of Myriad's '282 patent have a similar relationship as claims 5 and 6 of the '282 patent. Claim 1 and 5 both relate to genomic DNA, and claims 2 and 6 both relate to the complementary cDNA versions of that DNA.

Claim 1 of Myriad's '282 patent was thus invalidated for being a product of nature. Claim 2 of Myriad's '282 patent was upheld for the fact that it related to cDNA. Claim 5 of Myriad's '282 patent was also invalidated as unpatentable genomic DNA, and claim 6 of the '282 patent was upheld as the cDNA version of claim 5. As a result, competitors in the industry, such as Ambry Genetics, saw the potential to market their own products based upon similar naturally-occurring compounds.⁸⁸

Did the Court Get it Wrong?

While the holding in *Myriad* is clearly binding, there is one line of reasoning the Court takes that is difficult to follow. cDNA does not appear to be markedly different from the naturally occurring compound mRNA. The naturally-occurring transcription process results in an mRNA molecule which consists of *exons only*. cDNA also uses natural bonding properties of

⁸⁷ See Carla Mouta & Anthony Tridico, *The Old/New Test for Determining Patentability: Claims Must Be "Substantially Different" from the Judicial Exceptions*, CIPA JOURNAL, (March, 2014), <http://www.finnegan.com/resources/articles/articlesdetail.aspx?news=cffd9fd6-8f66-4b1e-bfc9-82bf6960aa14> (no volume or page number available).

⁸⁸ See Law Firm of Dayrel Sewell, *supra* note 2.

nucleotides to create a new synthetic DNA molecule, the difference being that it is the *reverse* image of the original DNA molecule *without introns*.⁸⁹

The Court focuses on the fact that cDNA was composed of exons only. However, mRNA is also a reverse image of DNA composed of exons only.⁹⁰ The only notable difference appears to be whether uracil or thymine is used in coding, meaning whether the molecule encoding the information is RNA or DNA. This appears to be very similar to natural compounds created by natural phenomena; is it enough to be *markedly different*? It will be interesting to see whether this becomes an issue in either the present *Ambry* case or a future patent challenge.

Interpreting *Myriad* – Going Forward

Inventions derived from nature are increasingly harder to patent now.⁹¹ So, where does the USPTO take it from here? The USPTO responded to *Myriad* by issuing a Guidance.⁹² It also plans to issue a second Guidance, due to industry push-back against the first.⁹³ Although the deference of the courts to the policies of the USPTO seems significantly diminished by the *Myriad* holding, this Guidance will nevertheless be used to examine patent applications going forward. Inventors and companies are worried that they will rely on this Guidance, but that it may be overruled by the Court as the prior Guideline was.

The Biotech industry complains it is “lost at sea” until this is all sorted out. Many companies and practitioners in the Biotech industry are looking forward to *Ambry* to provide

⁸⁹ M.A. Campbell, Copyright 2002 Department of Biology, Davidson College, <http://www.bio.davidson.edu/genomics/method/cDNAproduction.html>.

⁹⁰ See Phillip McClean, *Introns, Exons, & Splicing hn RNA*, NDSU.EDU, <http://www.ndsu.edu/pubweb/~mcclean/plsc731/transcript/transcript4.htm>, (last visited Dec. 7, 2014, 8:08 AM).

⁹¹ Kelly Servick, *Biotech Feels a Chill From Changing U.S. Patent Rules*, 345 SCI. 345, 14 (2014), (discussing the new difficulties in patenting inventions derived from nature).

⁹² Andrew H. Hirshfeld, United States Patent and Trademark Office, 2014 Procedure For Subject Matter Eligibility Analysis Of Claims Reciting Or Involving Laws Of Nature|Natural Principles, Natural Phenomena, And/Or Natural Products. USPTO Memorandum, dated (March 4, 2014).

⁹³ See Kelly Servick, *supra* note 91.

some clarity. A major concern is whether the Court will support the recent Guidance and help solidify its place in patent law.⁹⁴ In the meantime, the industry must rely on the newest USPTO Guidance in determining whether its patent claims are markedly different from those that are naturally occurring.

Interpreting *Myriad* – USPTO Guidance

This year, the USPTO has changed its policies for examining biotechnology inventions two different times.⁹⁵ And while the first change, on the day that *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013) (*Myriad*), was restricted to Myriad's holding, the USPTO has now taken steps to significantly alter the administrative history surrounding the patenting of biotech inventions in the United States, citing *Myriad* as a "reminder that claims reciting or involving natural products should be examined for a marked difference under *Chakrabarty*."

“Whether effectively a reminder or a new teaching, effective March 4, 2014 the USPTO Patent Examining Corps is instructed to follow a *new procedure* ‘in determining whether a claim reflects a significant difference from that which exists in nature and thus is eligible [subject matter], or whether it is effectively drawn to something that is naturally occurring’ and thus ineligible for patenting.”⁹⁶

The current guidance lists six factors that weigh *in favor* of a claim being markedly different”

“a) Claim is a product claim reciting something that initially appears to be a natural product, but after analysis is determined to be

⁹⁴ See C. Brinkerhoff, *Federal Circuit Hears Arguments In Other Myriad Gene Patents Case*, PHARMA PATENTS BLOG, (Oct. 7, 2014), <http://www.pharmapatentsblog.com/2014/10/07/FEDERAL-CIRCUIT-HEARS-ARGUMENTS-ON-OTHER-MYRIAD-GENE-PATENTS/>.

⁹⁵ See Carla Mouta & Anthony Tridico *supra* note 87.

⁹⁶ *Id.*

non-naturally occurring and *markedly different* in structure from naturally occurring products.

- b) Claim recites elements/steps in addition to the judicial exception(s) that impose meaningful limits on claim scope, i.e., the elements/steps narrow the scope of the claim so that others are not substantially foreclosed from using the judicial exception(s).
- c) Claim recites elements/steps in addition to the judicial exception(s) that relate to the judicial exception in a significant way, i.e., the elements/steps are more than nominally, insignificantly, or tangentially related to the judicial exception(s).
- d) Claim recites elements/steps in addition to the judicial exception(s) that do more than describe the judicial exception(s) with general instructions to apply or use the judicial exception(s).
- e) Claim recites elements/steps in addition to the judicial exception(s) that include a particular machine or transformation of a particular article, where the particular machine/transformation implements one or more judicial exception(s) or integrates the judicial exception(s) into a particular practical application. (See MPEP 2106(II)(B)(1) for an explanation of the machine or transformation factors).
- f) Claim recites one or more elements/steps in addition to the judicial exception(s) that add a feature that is more than well-understood, purely conventional or routine in the relevant field.”⁹⁷

Conversely, the Guidance also lists six factors that weigh *against* a claim being markedly different:

- “g) Claim is a product claim reciting something that appears to be a natural product that is *not markedly different* in structure from naturally occurring products.
- h) Claim recites elements/steps in addition to the judicial exception(s) at a high level of generality such that substantially all practical applications of the judicial exception(s) are covered.

⁹⁷ United States Patent and Trademark Office, *Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products (Guidance)*, March 4, 2014.

i) Claim recites elements/steps in addition to the judicial exception(s) that must be used/taken by others to apply the judicial exception(s).

j) Claim recites elements/steps in addition to the judicial exception(s) that are well-understood, purely conventional or routine in the relevant field.

k) Claim recites elements/steps in addition to the judicial exception(s) that are insignificant extra-solution activity, e.g., are merely appended to the judicial exception(s).

l) Claim recites elements/steps in addition to the judicial exception(s) that amount to nothing more than a mere field of use.”⁹⁸

Each patent claim is to be reviewed under this factor-based analysis, in addition to all other requirements for patentability.

Is the New USPTO Guidance in Line with *Myriad*?

The USPTO incorporated the holding in *Myriad* explicitly into its guidelines for evaluating patent eligibility, focusing on clarifying the *markedly different* aspect. It then developed a six-factor test to be used in determining whether something is markedly different or not.

The Guidance is intended to provide clarity to patent examiners on how to evaluate each patent before it and to ensure that their decisions reflect the holding in *Myriad*. “The fact that a marked difference *came about* as a result of *routine activity* or via human manipulation of *natural processes* does *not prevent* the marked difference from weighing *in favor of* patent eligibility. For example, cDNA having a nucleotide sequence that is markedly different from

⁹⁸ *Id.*

naturally occurring DNA is eligible subject matter, even though the process of making cDNA is routine in the biotechnology art.”⁹⁹

The USPTO appears to have quickly put forth an effort to address the discrepancy between the *Myriad* holding and its past practice of awarding patents to isolated genomic DNA. The six-factor test is a reasonable one, and will provide an additional practical tool to examiners. While further clarifications and expansions to specific Biologic situations are likely to follow, the major substantive points embodied within the Guidance appear to be in line with *Myriad* and should remain in future versions of the Guidance, and it would be reasonable for courts to refer to it for persuasive arguments in *Ambry* and other cases.

Public Response to *Myriad* and the USPTO Guidance

The USPTO has initially received negative feedback on its guidance, which has even been contradictory at times. Some practitioners and legal experts have complained that the guidance does not do enough – that it merely restates *Myriad*. “The USPTO examples do not provide significant additional information helpful to practitioners beyond that which is gleaned from the *Myriad* case, *Myriad* memo, and *Mayo Guidance*. For example, it would have been helpful receive guidance regarding how the USPTO will treat claims to proteins, fusion-proteins, fragments of proteins, and antibodies, a significant fraction of the global biotech industry.”¹⁰⁰ But, the USPTO may have been cautious in going too far, for fear of another guidance being overruled by the Courts and may be waiting out the *Ambry* decision for further clarifications from the courts before it expands too much on the March guidance.

The President and CEO of the Biotechnology Industry Organization, BIO, made a public statement of BIO’s view of the *Myriad* decision. BIO viewed the confirmation that cDNA is

⁹⁹ *Id.*

¹⁰⁰ See Carla Mouta & Anthony Tridico *supra* note 87.

patentable subject matter as an important in providing a “needed certainty for research-driven companies that rely on cDNA patents for investment in innovation.”¹⁰¹ But, BIO was disappointed in the court’s decision on the patentability of genomic DNA. “In other respects, however, the Supreme Court’s decision today represents a troubling departure from decades of judicial and Patent and Trademark Office precedent supporting the patentability of DNA molecules that mimic naturally-occurring sequences. In addition, the Court’s decision could unnecessarily create business uncertainty for a broader range of biotechnology inventions.”¹⁰² The statement went on to criticize the decision further, claiming that this decision makes the U.S. the only developed country with such a restricted view on patenting and that it showed the nation’s indifference toward our global position in terms of scientific development. Then, BIO disputed the concept behind the term “gene patent” arguing that it is “misleading, because patents cannot cover the genes that exist in humans, plants, animals or microbes. Patents have never conferred ownership over genes.”¹⁰³ BIO went on to argue that the broader patent rights that have been available in gene patenting had led to “an unprecedented explosion of research and scientific publication”¹⁰⁴ over the past 25 years.

The Biotech industry also appears to be unhappy with the latest USPTO Guidance, and has been openly pushing back on the USPTO, arguing that the policies promulgated by it are beyond what the Supreme Court intended. The industry is upset that what they took for granted, in terms of patentability, over the past years is now no longer valid.¹⁰⁵ This means that

¹⁰¹ Roy Zwaylen, *Myriad Supreme Court Decision: BIO’s Statement*, PATENTLY BIOTECH BLOG FROM BIOTECH NOW, (June 13, 2013), <http://www.biotech-now.org/public-policy/patently-biotech/2013/06/myriad-supreme-court-decision-bios-statement>.

¹⁰² *Id.*

¹⁰³ *Id.*

¹⁰⁴ *Id.*

¹⁰⁵ See Kelly Servick, *supra* note 91.

companies that have outlaid capital for R&D related to products that they had assumed to be patentable may have done so in what may now turn out to be a wasted investment.

The industry is free to express its displeasure and criticisms of the Guidance, but some of their complaints of the USPTO are more emotional than rational. The USPTO had to react quickly, and it needed to do so in a way that was in line with the *Myriad* holding, yet did not overstep the bounds of *Myriad*. The rules of the biotech patent game are changing, and the USPTO didn't want to get it wrong again. The USPTO was put in a difficult situation after *Myriad*, and this guidance was a first step toward providing some clarity to its examiners and to the industry. Although not yet a comprehensive document that addresses all situations, the industry is probably better off with some method of determining how to ascertain whether something is markedly different than being left by the Court with no guidance at all. Historical claim drafting methods of first drafting a broad claim and then following it by narrower claims can still provide some level of protection for applicants of new patents during this time period of uncertainty.

Just because it doesn't make for good business doesn't mean that the interpretations are wrong. Different policies are at odds here, and those proponents of making potentially life-saving genetic testing more affordable and accessible for patients likely welcome the recent decision in *Myriad* and its subsequent interpretations and expansion by the USPTO. Although making something harder to patent may negatively impact the initial R&D involved in developing a new useful invention for society, has the positive effect of becoming more widely available for use and enjoyment by the public if it is not patent protected. This means a lot to patients, cancer survivors, their friends & family, and those potential future users of such services.

AMBRY

Ambry v. Myriad – Where We Are Now

After Ambry offered similar genetic testing services, Myriad sued for a preliminary injunction against Ambry over its claims not invalidated by the Supreme Court in *Myriad*.¹⁰⁶ The District Court denied the injunction, because Ambry raised a substantial question of Myriad's claims being ineligible products of nature.¹⁰⁷ The Federal Circuit is reviewing the claims of the case that were not invalidated by the Supreme Court's 2013 ruling. The *Ambry* case is currently before the Federal Circuit, which must abide by the Supreme Court's ruling in *Myriad* and apply that holding to the facts of the present case before it.¹⁰⁸

“On October 6, 2014, the Federal Circuit heard oral arguments in a case involving the claims of the Myriad gene patents that were not invalidated by the Supreme Court's 2013 decision. The Federal Circuit is reviewing the district court's denial of Myriad's motion for a preliminary injunction against Ambry Genetics Corp., based on the finding that Ambry had “raised a substantial question” as to whether Myriad's “Primer Claims” and “Method Claims” are directed to “patent [in]eligible products of nature and abstract ideas.”¹⁰⁹ The two main issues at stake are the “correct implementation of the test for patent eligibility”¹¹⁰ and the “application of the test to probes and primers.”¹¹¹

¹⁰⁶ John Conley, *District Court Denies Myriad's Preliminary Injunction Against Ambry*, GENOMICSLAWREPORT.COM, (March 18, 2014), <http://www.genomicslawreport.com/index.php/2014/03/18/district-court-denies-myriads-preliminary-injunction-against-ambry/>.

¹⁰⁷ *In re BRCA1-, BRCA2-Based Hereditary Cancer Test Patent Litig.*, No. 2:13-CV-00640-RJS, 2014 WL 931057 (D. Utah Mar. 10, 2014).

¹⁰⁸ See Law Firm of Dayrel Sewell *supra* note 2.

¹⁰⁹ See C. Brinkerhoff *supra* note 94.

¹¹⁰ See Law Firm of Dayrel Sewell *supra* note 2.

¹¹¹ *Id.*

Although the USPTO's guidelines are not binding on the Federal Circuit, the Court will likely consider them as persuasive material, given that the USPTO wrote the recent March 4th Guidance based on its interpretation of the holding in *Myriad*. The Federal Circuit will rely on *Myriad* for the legal rule that genomic (naturally occurring DNA) is not patentable and that cDNA is patentable subject matter, but it will need help from the March 4th Guidance to then apply the specific facts of the claims in *Ambry* to determine whether the claims in question are markedly different from naturally occurring product or process.

Applying *Myriad* to the Current *Ambry* Case

The *Myriad* claims at issue are different than those brought in the first case. The primer claims discussed in *Ambry* are composition of matter claims. Specifically, these are claims 16 and 17 of the '282 patent and claims 29 and 30 of the '492 patent, which are similarly structured.

Claim 16 claims "a pair of single-stranded DNA primers for determination of a nucleotide sequence of a BRCA1 gene by a polymerase chain reaction, the sequence of said primers being *derived from human chromosome 17q*, wherein the use of said primers in a polymerase chain reaction results in the synthesis of DNA having all or part of the sequence of the BRCA1 gene." Claim 17 goes on to claim "the pair of primers of claim 16 wherein said BRCA1 gene has the nucleotide sequence set forth in SEQ ID NO:1." This claim structure is similar to that used in the claims at issue in *Myriad*, with claim 1 of the '282 patent claiming "an isolated DNA coding for a BRCA1 polypeptide which has the amino acid sequence set forth in SEQ ID NO:2," and claim 2 claiming "the isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1." The similarity of how the claims were written is an important fact for the court to consider in determining the validity of the current claims at issue.

Myriad's Arguments

Myriad Genetics argued that the Federal Circuit and the Supreme Court have both “previously acknowledged that Myriad was entitled to patent some applications of their newly-discovered gene sequence and tools designed specifically to utilize that sequence.”¹¹² Myriad also put forth an argument about its primer claims, arguing that “primer pairs are patent subject matter eligible under 35 U.S.C § 101 because the pairs are structurally and functionally different than a single fragment of DNA.”¹¹³ Regarding the method claims, Myriad argued that “as a whole, the method of screening for alterations on the BRCA genes involves steps of the method claims, when considered together, effect an improvement in a technical field – by using Myriad’s probes and primers that Myriad invented.”¹¹⁴

Myriad Genetics further argued that the Supreme Court’s decision in *Myriad* was narrow and does not cover the points at issue in the present case. Myriad maintains that the probes and primers are distinct from naturally occurring DNA and possess a novel utility due to human manipulation. According to Myriad, the BRCA1 probe was not conventional at the time of patenting, and the Primer Claims have a different utility than what is found in nature.¹¹⁵

Ambry's Arguments

According to Ambry, a primer is just a segment of DNA, and when cDNA is not distinguishable from genomic DNA, it is not patentable. Ambry puts forth multiple arguments based on the case *CLS Bank Int’l v. Alice Corp. Pty.*, a 2012 Third Circuit decision. Ambry argues that the primer claims fail under *Alice*, as they are “a generic component used to amplify a person’s gene sequence to access the sequence information for the patent-ineligible sequence

¹¹² See Law Firm of Dayrel Sewell, *supra* note 2.

¹¹³ *Id.*

¹¹⁴ *Id.*

¹¹⁵ See C. Brinkerhoff *supra* note 94.

comparison.”¹¹⁶ RNA primers act in a way that mirrors and mimics nature by creating the starting point to build the 2nd strand of DNA. Furthermore, all other steps in the claims were routine and conventional. Ambry contends that the primer claims are not patent eligible because they are a product of nature, as a segment of naturally occurring DNA.¹¹⁷ Regarding method claims, Ambry again argues its point under *Alice*, asserting that “the combination of unpatentable subject matter and a generic physical application is no more patent eligible than a claim reciting only the unpatentable subject matter.”¹¹⁸

Analysis of the Primer Claims

The primer claims are claims for compositions of matter according to 35 U.S.C. §101. Under *Myriad*, genomic DNA is not patent eligible, and cDNA is patent eligible. Following the USPTO Guidance, the Primers are not markedly different. The analysis is conducted by following this chain of logic: Do the primer claims appear to be *product claims* reciting something that *appears to be a natural product* that is *not markedly different in structure* from naturally occurring products? Yes, according to factor 1. The genes *appear to be* segments of DNA that are *not markedly different in structure from naturally occurring* genomic DNA.

The next question is whether *Myriad* added a new and useful improvement to those aspects that are naturally occurring and those steps that are already known in the industry. The answer is no, according to factor 4. The claim *recites elements* that appear to be *well-understood, purely conventional, and routine* in the field of genetic engineering.¹¹⁹ Therefore, these claimed primers have sequences that correspond to portions of the *naturally occurring gene sequences*, so they should be found *not to be patent eligible* under 35 U.S.C. Section 101

¹¹⁶ See Law Firm of Dayrel Sewell, *supra* note 2.

¹¹⁷ See *id.*

¹¹⁸ *Id.*

¹¹⁹ See M.A. Campbell, *supra* note 89.

and its interpretation in *Myriad*. However, since the claims at issue here have similar structure to those in *Myriad*, if the material in claims 17 and 30 relate to cDNA, as they appear to, then they will be upheld, but claims 16 and 29 will not.

The Method Claims

Method Claims involve a different inquiry under Section 102 case law, due to the fact that these claims involve a novelty matter. The Supreme Court said in *Myriad* that they weren't addressing the Method Claims.

The *Myriad* decision will not provide any precedent for the Method Claims at issue in *Ambry*. So, *Ambry* may very well be the next patent law case that will end up before the Supreme Court as a method question. Since *Myriad* did not address methods claims, the Court will likely rely on the USPTO Guidance in conjunction with other case law as the best way to evaluate the method claims at issue in *Ambry*, which involve a product of nature.

CONCLUSION

While it may not be the last piece of the puzzle of applying the new interpretation of patentable subject matter to specific Biotech patent quandaries, *Ambry* will likely solidify the fact that genomic DNA does not deserve patentability when they invalidate patent '282 claim 16 and patent '492 claim 29. If the court finds that claim 17 of the '282 patent and claim 30 of the '492 patent relate to cDNA, then Federal Circuit must hold these claims to be valid in order to stay in line with the Supreme Court precedent in *Myriad*. So long as the holding in *Ambry* is consistent with the recently decided *Myriad* which came from the current Justices, then the Supreme Court would not have any reason to grant cert., and this battle will stop here. And though it may not be the outcome that many genomic patent-holding companies in the Biotech

industry would hope for, it will likely send a clear message that the rules have changed, narrowing the scope of patentable subject matter under Section 101.