

## Legal & Regulatory Update

# USPTO guidance on patentable subject matter: Impediment to biotechnology innovation?

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## ABSTRACT

In June 2013, the U.S. Supreme Court issued a unanimous decision upending more than three decades worth of established patent practice when it ruled that isolated gene sequences are no longer patentable subject matter under 35 U.S.C. Section 101. While many practitioners in the field believed that the USPTO would interpret the decision narrowly, the USPTO actually expanded the scope of the decision when it issued its guidelines for determining whether an invention satisfies Section 101. The guidelines were met with intense backlash with many arguing that they unnecessarily expanded the scope of the Supreme Court case in a way that could unduly restrict the scope of patentable subject matter, weaken the U.S. patent system, and create a disincentive to innovation. By undermining patentable subject matter in this way, the guidelines may end up harming not only the companies that patent medical innovations, but also the patients who need medical care. This article examines the guidelines and their impact on various technologies.

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## INTRODUCTION

**I**N JUNE 2013, the U.S. Supreme Court issued a unanimous decision upending more than three decades worth of established patent practice when it ruled that isolated gene sequences are no longer patentable subject matter under 35 U.S.C. Section 101.\* While many practitioners in the field believed that the USPTO would interpret the decision narrowly, the USPTO actually expanded the scope of the decision when it issued its guidelines for determining whether an invention satisfies

Section 101. These guidelines may harm biotechnological innovation by rendering many technologies unpatentable. In this Article, we will examine the guidelines and their impact on various technologies.

## SUPREME COURT DECISIONS REGARDING 35 U.S.C. SECTION 101

Two recent Supreme Court decisions have scrutinized the types of inventions eligible for patent protection under 35 U.S.C. Section 101. In doing so, the Court effectively uprooted decades of well-established precedent that “anything under the sun made by man” is eligible for patent protection.

In *Prometheus v. Mayo*†, for instance, the Court was asked to determine the patent eligibility of method of treatment claims that involved correlating the

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\* 35 U.S.C. Section 101 states, “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.”

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† *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*, 566 U.S. \_\_\_\_ (2012).

effectiveness of the treatment with the amount of a drug metabolite in the blood. The Supreme Court reasoned that the claims were trying to cover a “law of nature” (*i.e.*, the correlation itself), which is not “man-made” and therefore not patent-eligible under Section 101. The Court found that steps of “administering” the drug and “determining” the amount of the metabolite in the blood, *i.e.*, the steps that are performed by man, did not “add enough” to their statements of the correlations to allow the processes they describe to qualify as patent-eligible.” Exactly what constitutes “enough” to meet the Court’s standard is unclear based on the Supreme Court decision.

In *Association for Molecular Pathology (AMP) v. Myriad Genetics*<sup>‡</sup> (also known as the “gene-patent” case), the Supreme Court was asked to decide whether “isolated” genetic sequences are patentable under Section 101. In a unanimous decision, the Supreme Court overturned more than 30 years of established biotech patent practice when it held that isolated DNA sequences are not patent-eligible. Moreover, the Supreme Court upended more than a century’s worth of established patent practice in general when it held that claims directed to an “isolated XYZ substance”, those at the center of the *Myriad* controversy, are no longer acceptable as a valid approach for claiming purified or isolated substances extracted from nature.<sup>§</sup> In handing down its decision, the Supreme Court concluded that “isolation” alone does not go far enough in distinguishing isolated DNA from genomic DNA sequences found in nature. According to the Court, such claims are merely an attempt at protecting “natural phenomena”. The Court did, however, find that synthetically created genetic material, such as complementary DNA (cDNA), is patent-eligible because it is not naturally occurring.

## USPTO’S GUIDANCE FOR DETERMINING SUBJECT MATTER ELIGIBILITY OF CLAIMS RECITING OR INVOLVING LAWS OF NATURE, NATURAL PHENOMENA, & NATURAL PRODUCTS

Following the Supreme Court’s decision, the USPTO issued a set of guidelines for examiners on March 4, 2014<sup>¶</sup> for examiners that expanded the holdings of the

‡ *Association for Molecular Pathology et al., v. Myriad Genetics, Inc.*, 569 U.S. \_\_\_\_ (2013).

§ *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (C.C.S.D.N.Y. 1911)

¶ USPTO, *Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature*,

*Prometheus* and *Myriad* cases to any claim involving a law of nature, natural phenomena or natural product. The guidelines will impact the USPTO’s assessment of patentability of many applications currently pending in the USPTO, and may well impact the validity of many previously issued patents, especially those pertaining to the life sciences and chemistry. Not only have the guidelines undermined the established patent law framework for evaluating subject matter eligibility under Section 101, these guidelines also make the U.S. the only jurisdiction in the world where inventions, such as those claiming isolated DNA, are not patentable.

To determine whether a claim satisfies the requirements of Section 101, the guidelines provide a three-pronged test. First, the test asks whether the claim is directed to one of the four statutory categories: a process, machine, manufacture, or composition of matter. Next, the guidelines ask whether the claim is directed to one of the four judicial exceptions: an abstract idea, a law of nature/natural principle, a natural phenomenon or a natural product. Finally, if the claim is directed to a judicial exception, the guidelines state that the claim is not patentable unless the claim “as a whole recites something significantly different” than the judicial exceptions, and set forth relevant factors for making such assessment, such as reciting something that is non-naturally occurring and markedly different in structure from naturally occurring products, elements/steps in addition to the judicial exception(s) that impose meaningful limits on claim scope, and elements/steps in addition to the judicial exception(s) that include a particular machine or transformation of a particular article. Natural products that must be analyzed under the last step include, but are not limited to: chemicals derived from natural sources (e.g., antibiotics, fats, oils, petroleum derivatives, resins, toxins, etc.); foods (e.g., fruits, grains, meats and vegetables); metals and metallic compounds that exist in nature; minerals; natural materials (e.g., rocks, sands, soils); nucleic acids; organisms (e.g., bacteria, plants and multicellular animals); proteins and peptides; and other substances found in or derived from nature.

In its guidelines, the USPTO provided many examples of how to evaluate whether or not a claim satisfies the requirements of Section 101. Below are several examples demonstrating how examiners may treat claims to compositions, methods of treatment, methods of diagnosing diseases, and methods of manufacture under the guidelines.

Example A relates to a composition reciting a natural product:

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*Natural Phenomena, & Natural Products, March 4, 2014.*  
[http://www.uspto.gov/patents/law/exam/myriad-mayo\\_guidance.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf).

*Claim 2: A bacterium from the genus Pseudomonas containing therein at least two stable energy-generating plasmids, each of said plasmids providing a separate hydrocarbon degradative pathway.*

In this claim, both the stable energy-generating plasmids exist and the *Pseudomonas* bacteria are naturally occurring. Moreover, naturally occurring *Pseudomonas* bacteria containing a stable energy-generating plasmid and capable of degrading a single type of hydrocarbon are known in the art. According to the guidelines, the claim is found to be patent-eligible because the claim as a whole recites something significantly different than naturally occurring bacteria. Although the plasmids alone and the bacterium alone are natural products, the bacterium containing the plasmids is significantly different.

Example B relates to a method of treatment claim:

*Claim 3: A method of treating colon cancer, comprising: administering a daily dose of purified amazonic acid to a patient suffering from colon cancer for a period of time from 10 days to 20 days, wherein said daily dose comprises about 0.75 to about 1.25 teaspoons of amazonic acid.*

In this hypothetical, the guidelines characterize the Amazonian cherry tree as a naturally occurring tree that grows wild in the Amazon basin region of Brazil. The leaves of the Amazonian cherry tree contain a chemical that is useful in treating breast cancer. Applicant has successfully purified the cancer-fighting chemical from the leaves and has named it amazonic acid. The purified amazonic acid is structurally identical to the amazonic acid in the leaves, but a patient only needs to eat about one teaspoon of the purified acid to get the same effects as 30 pounds of the leaves. Applicant has discovered that amazonic acid is useful to treat colon cancer as well as breast cancer. According to the guidelines, the method claim is patent-eligible because the claim includes elements in addition to the judicial exception (e.g., dosage amounts, treatment period limitations) that add significantly more to the judicial exception, and thus the claim as a whole recites something significantly different than the natural product.

Example C relates to an article of manufacture that includes natural products:

*Claim: A fountain-style firework comprising: (a) a sparking composition, (b) calcium chloride, (c) gunpowder, (d) a cardboard body having a first compartment containing the sparking composition and the calcium chloride and a second compartment containing the gunpowder, and (e)*

*a plastic ignition fuse having one end extending into the second compartment and the other end extending out of the cardboard body.*

In this example, the guidelines characterize the calcium chloride as a “natural product” and the gunpowder as a mixture of “natural products.” The guidelines explain that this claim is directed to patent-eligible subject matter “because the claim as a whole recites something significantly different than the natural products by themselves, i.e., the claim includes elements in addition to calcium chloride and gunpowder (the sparking composition, cardboard body and ignition fuse) that amount to a specific practical application of the natural products.”

Example D relates to a composition reciting multiple “natural products”:

*Claim: An inoculant for leguminous plants comprising a plurality of selected mutually non-inhibitive strains of different species of bacteria of the genus Rhizobium, said strains being unaffected by each other in respect to their ability to fix nitrogen in the leguminous plant for which they are specific.*

Rhizobium bacteria are naturally occurring nitrogen-fixing bacteria. While the prior art shows that all Rhizobium species were mutually inhibitive, the Applicant had discovered that there are particular strains that do not exert a mutually inhibitive effect on each other, and sought to patent mixtures of such strains. Following the Supreme Court’s 1948 decision in *Funk Brothers*<sup>\*\*</sup>, the guidelines hold that this claim is not patent-eligible because “none of the natural products recited in the claim are markedly different.” Rather, the guidelines explain that “[t]he specification describes that applicant has not changed the bacteria in any way, but instead has simply combined various strains of naturally occurring bacteria together.” The guidelines further state that no other factors in the claim support patent-eligibility, “i.e., there is nothing in the claim other than the bacteria.”

Example E also relates to a composition reciting multiple “natural products”:

*Claim 1: A pair of primers, the first primer having the sequence of SEQ ID NO: 1 and the second primer having the sequence of SEQ ID NO: 2.*

<sup>\*\*</sup> *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948).

In this example, SEQ ID NOs: 1 and 2 are naturally occurring DNA sequences found on a human chromosome. According to the guidelines, this claim is not patent-eligible, because the structural difference “is not significant enough to render the isolated nucleic acid markedly different, because the genetic structure and sequence of the nucleic acid has not been altered.” The guidelines further mention that the function of the recited primers is essentially identical, stating “the first and second primers have the same function as their natural counterpart DNA, i.e., to hybridize to their complementary nucleotide sequences.” Interestingly enough, the guidelines fail to address the fact that primers, unlike naturally-occurring DNA, can function to amplify target DNA.

Example F relates to a method of diagnosing a disease:

*Claim: A method for determining whether a human patient has degenerative disease X, comprising: obtaining a blood sample from a human patient; determining whether misfolded protein ABC is present in the blood sample, wherein said determining is performed by contacting the blood sample with antibody XYZ and detecting whether binding occurs between misfolded protein ABC and antibody XYZ using flow cytometry, wherein antibody XYZ binds to an epitope that is present on misfolded protein ABC but not on normal protein ABC; and diagnosing the patient as having degenerative disease X if misfolded protein ABC was determined to be present in the blood sample.*

According to the guidelines, this claim is patent-eligible because the claim as a whole recites something significantly different than the natural principle, i.e., the claim includes elements in addition to the judicial exceptions (e.g., contacting the blood sample with a specific novel antibody XYZ, and detecting binding using flow cytometry) that amount to a practical application of the natural principle.

## RESPONSE TO THE GUIDELINES

The guidelines were met with intense backlash. Many argue that they unnecessarily expand the scope of the *Myriad* and *Mayo* cases in a way that could unduly restrict the scope of patentable subject matter, weaken the U.S. patent system, and create a disincentive to innovation.

As a result of the negative publicity it received, the USPTO decided to rethink its approach and agreed to

host a public forum on May 9, 2014, at the USPTO headquarters in Alexandria, Virginia, to solicit feedback from organizations and individuals on its recent guidance memorandum.<sup>††</sup> Based on the feedback it received, the USPTO may revisit the guidelines. Moreover, the guidelines do not have the force of law. Thus, a cautious approach should be applied when relying on the guidelines.

In the meantime, however, the guidelines represent the USPTO’s current thinking regarding how examiners are instructed to examine certain types of patent claims. To the extent that prosecution cannot be delayed until the revised guidelines are issued, it is helpful to have a good understanding of the guidelines, as they are likely to present hurdles for a broad range of biomedical technologies. Below are examples of rejections that have already been issued since the guidelines were announced.

## STATE OF CLAIMS IN VIEW OF THE GUIDELINES

Following the release of the guidelines, many claims have been rejected as allegedly not satisfying the requirements of Section 101. Below are several examples of claim rejections that have recently been issued applying the guidelines.

### Pharmaceutical Compositions:

*A composition comprising Compound X or a fragment thereof and X % by weight of Component Y.*

According to the Examiner, since Compound X is a “natural product” and Component Y could be a “natural product”, there is nothing “in addition to the judicial exceptions” that would render the overall claim patent-eligible.<sup>‡‡</sup>

<sup>††</sup> USPTO, *Guidance For Determining Subject Matter Eligibility Of Claims Reciting Or Involving Laws of Nature, Natural Phenomena, & Natural Products*, March 4, 2014, [http://www.uspto.gov/patents/law/exam/myriad-mayo\\_guidance.pdf](http://www.uspto.gov/patents/law/exam/myriad-mayo_guidance.pdf).

<sup>‡‡</sup> Courtney C. Brinckerhoff, *The New USPTO Patent Eligibility Rejections Under Section 101*, PharmaPatentsBlog, published May 6, 2014, accessed <http://www.pharmapatentsblog.com/2014/05/06/the-new-patent-eligibility-rejections-section-101/>.

## Vaccines:

*A pharmaceutical composition, comprising: a peptide having an amino acid sequence that is at least 90% identical to SEQ ID NO.: 1, and a pharmaceutically acceptable carrier. [SEQ ID NO.: 1 is a naturally occurring protein or fragment thereof]*

According to the Examiner, a claim directed to a vaccine is rejected because neither the peptide nor the carrier is structurally different from a natural product.

## Antibodies:

*An isolated polynucleotide comprising a nucleotide sequence which encodes an antibody heavy chain variable region (VH) polypeptide comprising the amino acid sequence SEQ ID NO.: 9 or SEQ ID NO.: 10, wherein an antibody comprising said VH polypeptide can specifically bind to Antigen X. [SEQ ID NO.: 9 refers to a humanized sequence and SEQ ID NO.: 10 refers to a murine sequence]*

The Examiner rejected reference to SEQ ID NO.: 10 on the grounds that the murine sequence is not structurally different than the sequence found in nature. SEQ ID NO.: 9, on the other hand, satisfied the guidelines because humanized sequences are engineered.

## Methods of Making

*A method of making a composition comprising Compound X and Component Y, comprising providing Compound X and Component Y [at specified relative amounts].*

The Examiner rejected this claim because all of the claim language relates to “natural products” and so there is nothing “in addition to the judicial exceptions” on which to base patent eligibility.<sup>55</sup>

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<sup>55</sup> Courtney C. Brinckerhoff, *The New USPTO Patent Eligibility Rejections Under Section 101*, PharmaPatentsBlog, published May 6, 2014, <http://www.pharmapatentsblog.com/2014/05/06/the-new-patent-eligibility-rejections-section-101/>.

## Methods of Treatment

*A method of treating Disease X in a subject, comprising administering to the human the composition according to claim 1.*

The Examiner rejected this claim because it is directed to a natural product and recites nothing in addition to the dosage exceptions. This method claim differs from Example B, claim 3, which includes elements in addition to the judicial exception (e.g., dosage amounts, treatment period limitations) that add significantly more to the judicial exception.

## Methods of Diagnosing Disease

*A method of diagnosing Disease X in an individual suspected of having disease X, comprising the steps of: a) measuring the level of expression of Genes Y and Z in a biological sample from the individual; b) comparing the level of expression of Genes Y and Z in the biological sample to the level of expression of Genes Y and Z in a control sample from an individual without Disease X, wherein a decreased level of expression of Gene Y and an increased level of expression of Gene Z in the biological sample relative to the control sample is indicative of the individual having Disease X, thereby diagnosing Disease X in the individual.*

Referring to the guidelines, the Examiner rejected this claim because as a whole it was directed to a law of nature/natural principle and allegedly did not recite something “significantly different” than the law of nature/natural principle. Here, the “natural principle” is “expression of Genes Y and Z that correlate with the presence or absence of Disease X.” The Examiner reasoned that the claim does not practically apply the natural principle in a significant way, but instead was drawn to conventional, routine, and well-understood method steps. Accordingly, the claims do not recite something “significantly different” than the natural principle, but rather “simply inform” the natural principle to one performing routine active method steps and do not amount to significantly more than the natural principle itself.

## FUTURE OF BIOTECHNOLOGICAL INNOVATION

Instead of encouraging development of biomedical inventions by promoting strong patent protection, the guidelines may create hurdles for biotechnology and pharmaceutical companies when it comes to patenting and protecting their products. Not only has USPTO guidance in view of the *Prometheus* and *Myriad* decisions unsettled the more than thirty years of established patent law framework for determining patent eligibility under Section 101, it also made the U.S. the only jurisdiction in the world to exclude whole groups of inventions that are patentable elsewhere.

The weakening of patent protection in this way could impact life sciences companies of all sizes. Established companies with marketed products may face greater competition as their ability to rely on patents to deter competitors is diminished. Startup and clinical stage companies, on the other hand, may struggle to attract the necessary financing for conducting research and development without key patents protecting their assets. As a result, many potentially life-saving technologies may never be developed. The USPTO guidelines could

therefore stifle innovation because companies may choose to imitate rather than to innovate, and investors may not want to continue to fund the research and development that is required to bring products to market. Finally, contrary to public policy encouraging disclosure of patented inventions, the USPTO's guidelines may encourage secrecy as some companies may forgo seeking patent protection entirely in favor of retaining their innovations as trade secrets, where possible.

## CONCLUSION

Patents in the biotechnology and pharmaceutical areas protect many important technological developments, including vaccines, drugs and diagnostic tests. As such, they are important in the development and delivery of healthcare. Over the last two years, however, the Supreme Court and now the USPTO have taken actions that threaten to diminish the value of these patents. By undermining these patents, these changes reduce incentives for discovery of new innovative medicines, which may end up harming not only the companies which patent their innovations, but also the patients who need medical care.