May 12, 2016

Patent Eligible Subject Matter

Presented to:

PARTNERS HEALTHCARE | INNOVATION

FISH & RICHARDSON

Patent Eligible Subject Matter

- **35 U.S.C. § 101**

TELLS WHAT INVENTIONS ARE ELIGIBLE FOR PATENTING

“ … PROCESS, MACHINE, MANUFACTURE, COMPOSITION …”

DIFFERENT FROM WHAT IS ***PATENTABLE***

- *It must be novel*
- *It must be useful*
- *It must be non-obvious*

Patent Eligible Subject Matter

Judicial Exceptions:

- law of nature
- abstract ideas
- physical [natural] phenomena
- natural products

Why? Concerned about Pre-emption

Alice v. CLS Bank, (upholding the patent "would pre-empt use of this approach in all fields, and would effectively grant a monopoly over an abstract idea")

Judicial History

- *Funk Brothers,* 333 U.S. 127 (1948)
- *Diamond v. Chakrabarty*, 447 U.S. 303 (1980)
- *Bilski v. Kappos*, 130 S.Ct. 3218 (2010)
  - Three types of patent ineligible subject matter: laws of nature, physical phenomena, and abstract ideas.
- *Mayo v. Prometheus*, 132 S.Ct. 1289 (2012)
- *Ass'n for Molecular Pathology v. Myriad Genetics,* 133 S.Ct. 2107 (2013)
- *Alice Corporation v. CLS Bank Int'l* 134 S. Ct. 2347 (2014)

Mayo

Note: No action needed to be taken to meet the wherein clauses.

- **Supreme Court – claims invalid**
  - The '**administering**' step simply refers to the relevant audience … doctors who treat patients with certain diseases with thiopurine drugs.
  - "The '**determining**' step tells the doctor to determine the level of the relevant metabolites in the blood, through whatever process the doctor or the laboratory wishes to use."
  - "The '**wherein**' clauses simply tell a doctor about the relevant natural laws…"
  - Considering the elements together adds nothing (Is this a reference to prior art? Obviousness?)

Myriad

- Supreme Court
  - Naturally occurring DNA segment is a product of nature and not patent eligible.
  - cDNA is patent eligible because it is not naturally occurring (exons/introns??).

- Implications
  - "Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the §101 inquiry."
  - Impact on other "naturally occurring" chemicals - antibodies, hormones, and other proteins, therapeutic RNA, cells, microorganisms, and other biological molecules? Stem cells?
  - Include claims to, e.g., cells and vectors, that contain nucleic acids not present in nature.

How the Courts are Viewing Section 101

Ariosa v. Sequenom (Fed. Cir. 2015)

1. A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises

- amplifying a paternally inherited nucleic acid from the serum or plasma sample and
- detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

How the Courts are Viewing Section 101

Ariosa v. Sequenom (Fed. Cir. 2015)

- It is undisputed that the presence of cell-free fetal DNA ("cffDNA") in maternal blood is a natural phenomenon
- The method ends with paternally inherited cffDNA, which is also a natural phenomenon
- The method therefore begins and ends with a natural phenomenon
- The second step of Mayo requires "something more"
- Use of PCR to amplify and detect cffDNA was well-understood, routine, and conventional
- "The only subject matter new and useful as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum."
- Patent NOT eligible for patent protection

How the Courts are Viewing Section 101

Esoterix Genetic Labs v. Qiagen (U.S. Dt. Ct. MA, September 25, 2015)

- Esoterix sued Qiagen for infringement of U.S. 7,294,468 "Method to Determine Responsiveness of Cancer to Epidermal Growth Factor Receptor [EGFR] Targeting Treatments"
- The discovery is that mutations on the EGFR gene substantially increase the likelihood that specific drugs will be effective in treating non-small lung cancer
- Qiagen filed a Motion to Dismiss under Fed. Rule Civ. Proc. 12(b)(6), for failure to state a claim upon which relief may be granted
- Qiagen argued that the patent covers an unpatentable "law of nature" and that the law is unsettled as to whether the presumption of validity, and, in turn, the "clear and convincing" standard, applies when the issue is one of *Section 101* validity
- The court held that the patent is directed to a law of nature, in that it describes the correlation between a naturally-occurring mutation in a cancer cell, and the likelihood that a particular type of known pharmaceutical compound will be effective

How the Courts are Viewing Section 101

Esoterix Genetic Labs v. Qiagen (U.S. Dt. Ct. MA, September 25, 2015)

- The court noted that the inventors did not invent a new treatment for any cancers, or fundamentally alter an existing treatment
- The court found nothing "transformative" in the method of Claim 1 that amounts to a novel application of the natural law, or that otherwise warrants patent protection (citing *Alice Corp. v. CLS Bank,* 134 S. Ct. 2347, 2354 (2014))
  - First, the "obtaining" step of "[o]btaining DNA from a non-small cell lung cancer tumor sample from the individual" is not inventive
  - Second, the "determining" step relies upon known methods of detecting genetic mutations.
  - Third, the "wherein" step simply recites the natural law in question
- The Court found that, “much like the claims analyzed in *Mayo*, Claim 1 is directed to ineligible subject matter, and is therefore invalid”

How the Courts are Viewing Section 101

Bristol-Myers v. Merck (US Dist. Ct. Delaware, March 17, 2016)

- B-M sued Merck for infringing U.S. 9,067,999 that claims methods of using antibodies that inhibit signals of PD-1, PD-L1 or PD-L2 to activate immunity to lung cancer
- Merck filed a Motion to Dismiss arguing that the patent is directed to a natural phenomenon and the claims do not transform the natural phenomenon into a patent eligible invention
- B-M responded that the claimed method of treatment includes a step of administering a composition of anti-PD-1 antibodies to induce the immune response, which is not a diagnostic step as in *Mayo,* but provides the treatment itself
- The court concluded that material factual disputes exist that cannot be resolved on a motion to dismiss

How the Courts are Viewing Section 101

Bristol-Myers v. Merck (US Dist. Ct. Delaware, March 17, 2016)

- However, the court concluded that the patent touches upon a natural phenomenon by using T cells to activate the immune system, and that the remaining question before the court is whether the claims do significantly more than simply describe these natural relations

- The court said whether the claims amount to an implementation step is a complicated factual determination that the court could better resolve after discovery

- Pursuant to FRCP 12(b)(6), and after having considered the pleadings in the light most favorable to the B-M, the court concluded that Merck had not met its burden to prove by clear and convincing evidence that the patent is invalid on its face under 35 U.S.C. § 101

U.S. Patent & Trademark Office Guidelines

For determining subject matter eligibility

March 2014 – First USPTO Guidance

- Procedure for Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products (Myriad/Mayo)

December 2014 – Revised USPTO Guidance

- 2014 Interim Guidance Patent Subject Matter Eligibility (Myriad/Mayo/Alice)

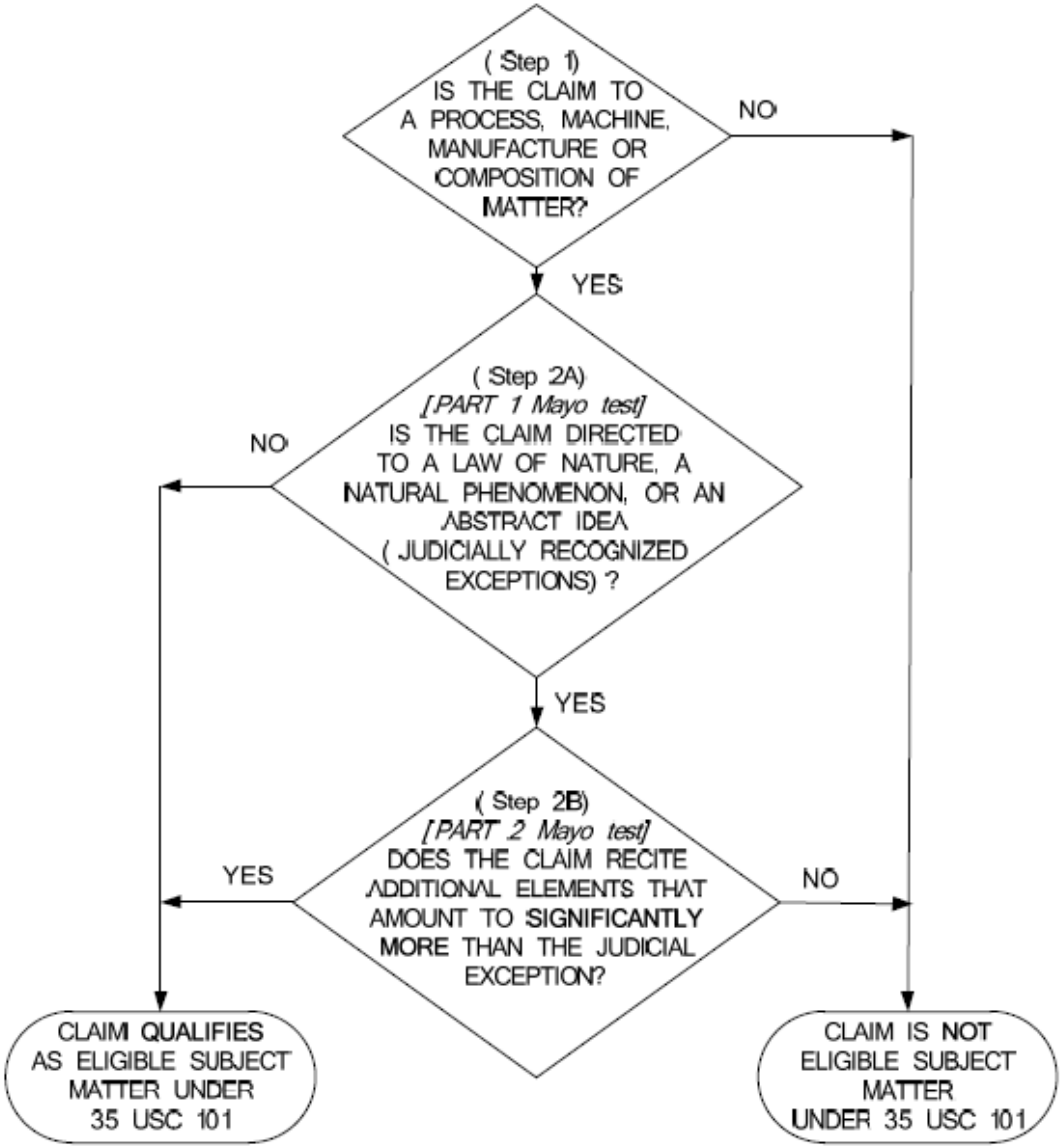
July 2015 Update: Subject Matter Eligibility

- Additional Examples relating to Abstract Idea exception (Myriad/Mayo/Alice) – *no life sciences examples*

May 2016 Update: Subject Matter Eligibility

- Additional Examples relating to Abstract Idea exception (Myriad/Mayo/Alice) –*Life sciences examples!!*

Interim Eligibility Guidance



U.S. Patent & Trademark Office Guidelines

Overall Process: Analysis Under USPTO's Mayo/Alice Framework

1 – Is the claim directed to one of the four patent eligible subject matter categories?

2A – Does the claim recite a judicial exception?

2B - Does the claim as a whole recite something "significantly different"?

U.S. Patent & Trademark Office Guidelines

Does the claim recite "Significantly More" than JE?

- Features or steps that demonstrate that subject matter is markedly different from what exists in nature, or add significantly more to judicial exception
- "Markedly different characteristics can be expressed as the product's **structure, function, and/or other properties**, and will be evaluated based on what is recited in the claim on a case-by-case basis."
- **Improvements to another technology or technological field.**
- Applying the JE with or by use of a particular machine.
- Effecting a transformation or reduction of a particular article to a different state or thing.
- Specific limitation that is not well-understood, routine, or conventional in the field, or unconventional steps that confine to a particular useful application.

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Example 28. Vaccines

- An influenza A viral strain named the “Pigeon flu”
  - Vaccines comprising “live attenuated Pigeon flu virus,” which the specification defines as a live mutant virus that has been attenuated so that it has at least one mutation
  - Vaccines comprising “inactivated Pigeon flu virus,” which the specification defines as a dead virus that is formalin-inactivated, *i.e.*, the naturally occurring Pigeon flu virus was contacted with formalin that causes structural changes to the virus
  - Vaccines comprising Peptide F (a naturally occurring peptide isolated from the Pigeon flu virus) either alone or mixed with a pharmaceutically acceptable carrier such as water
  - Vaccines comprising Peptide F mixed with aluminum salt adjuvants (a well-known class of adjuvants) such as aluminum phosphate ($AlPO_4$)
  - Vaccine delivery devices comprising coated microneedle arrays

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Vaccines – Claim Analysis

- 1. A vaccine comprising live attenuated Pigeon flu virus.
  - Has at least one mutation that reduces its virulence as compared to naturally occurring Pigeon flu virus.
  - Eligible – Because the live attenuated virus has markedly different characteristics from what exists in nature, it is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.
- 2. A vaccine comprising inactivated Pigeon flu virus.
  - Structurally altered by formalin so it can no longer reproduce
  - Eligible - Because the inactivated virus has markedly different characteristics from what exists in nature, it is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

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Vaccines – Claim Analysis

- 3. A vaccine comprising: Peptide F; and a pharmaceutically acceptable carrier.
  - The broadest reasonable interpretation (BRI) of the claim is Peptide F mixed with water.
  - Natural Product (*Step 2A:YES)*
  - The mixture of these two naturally occurring components is novel and does not occur in nature; compare to its naturally occurring components
  - There is no indication that mixing these components changes the structure, function, or other properties of the peptide or water - each component continues to have the same properties in the mixture as it had alone.
  - Ineligible - Using a carrier in a peptide vaccine was well-understood, routine & conventional prior to applicant's invention and at the time of filing the application, so the mixing of the peptide and carrier, when recited at this high level of generality, does not meaningfully limit the claim.
    - *Funk Brothers Seed Co. v. Kalo Inoculant Co*., 333 U.S. 127, 131 (1948)

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Vaccines – Claim Analysis

- 4. A vaccine comprising: Peptide F; and a pharmaceutically acceptable carrier selected from the group consisting of a cream, emulsion, gel, liposome, nanoparticle, or ointment.
  - BRI includes an emulsion comprising Peptide F mixed with small uniform droplets of cottonseed oil that are homogenously dispersed in water
  - Natural Product (*Step 2A:YES)*
  - Do not occur together in nature, compare to naturally occurring components
  - Cream has different structural and physical characteristics than its naturally occurring components: semi-solid, adhere to a patient's skin or mucous membranes longer
  - Eligible - The cream's changed form and adherence are marked differences in structural and physical characteristics as compared to the natural counterparts, and therefore the cream is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

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Vaccines – Claim Analysis

- 5. A vaccine comprising: Peptide F; and an immuno-effective amount of an aluminum salt adjuvant.
  - BRI includes a mixture of Peptide F with a sufficient amount of aluminum phosphate to increase the vaccine's immunogenicity
  - Natural Product (*Step 2A:YES)*
  - Substances do not occur together in nature, so compare to naturally occurring components
  - Immunogenicity of the mixture is different (higher) than the mere "sum" of the immunogenicity of the individual components
  - Eligible - The mixture's changed immunogenicity is a marked difference in functional characteristics as compared to the natural counterparts, and therefore the mixture is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

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Vaccines – Claim Analysis

- 6. A vaccine comprising: Peptide F; an immuno-effective amount of an aluminum salt adjuvant; and a pharmaceutically acceptable carrier.
  - BRI includes a mixture of Peptide F, a sufficient amount of aluminum phosphate to increase the vaccine's immunogenicity, and water.
  - Natural Product (*Step 2A:YES)*
  - Aluminum phosphate does occur naturally in combination with water, so compare to Peptide F, and the naturally occurring water/aluminum phosphate combination
  - Eligible - The mixture's changed immunogenicity is a marked difference in functional characteristics as compared to the natural counterparts, and therefore the mixture is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

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Vaccines – Claim Analysis

- 7. A vaccine delivery device comprising a microneedle array that is coated with a vaccine comprising Peptide F.
  - Natural Product (*Step 2A:YES)*
  - peptide does not have any characteristics (structural, functional, or otherwise) that are different from the naturally occurring peptide in its natural state, so is a "product of nature" exception
  - Prior to applicant's invention, and at the time the application was filed, coated microneedle arrays were known to most scientists in the field, but were not routinely or conventionally used to administer vaccines
  - Conventional delivery device was a pre-filled syringe
  - **An application of the exception with a particular manufacture that is not a conventional delivery device, and thus is more than a mere instruction to "apply" the peptide (the exception) using a well-understood, routine or conventional device in the field.**
  - Eligible - recitation of the coated microneedle array yields a claim as a whole that amounts to significantly more than the "product of nature" exception itself (*Step 2B: YES*).

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Diagnosing and Treating Julitis – Claim Analysis

- 1. A method of detecting JUL-1 in a patient, said method comprising:
  - a. obtaining a plasma sample from a human patient; and
  - b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody.
- Eligible - These steps do not recite or describe any recognized exception.
  - *See, e.g.*, Mayo Collaborative Svcs. v. Prometheus Labs., 566 U.S. __, 132 S. Ct. 1289, 1297 (2012) (recited steps of administering a drug to a patient and determining the resultant level of 6-thioguanine in the patient "are not themselves natural laws"). Accordingly, the claim is not directed to an exception (*Step 2A: NO*), and is eligible.
- ***Focused on*** a process of detecting whether JUL-1 is present in a plasma sample, and not on the nature-based products; no 2B analysis anyhow

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Diagnosing and Treating Julitis – Claim Analysis

- 2. A method of diagnosing julitis in a patient, said method comprising:
  - a. obtaining a plasma sample from a human patient;
  - b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody; and
  - c**. diagnosing** the patient with julitis when the presence of JUL-1 in the plasma sample is detected.
- A correlation or relationship between the presence of JUL-1 in a patient's plasma and the presence of julitis in the patient = a judicial exception (*Step 2A: YES*)
- Any detection technique with any generic anti-JUL-1 antibody
- Ineligible - additional elements as a combination also adds no other meaningful limitations to the exception not already present when the elements are considered separately… Even when viewed as a combination, the additional elements fail to transform the exception into a patent-eligible application of that exception. Thus, the claim as a whole does not amount to significantly more than the exception itself *(Step 2B: NO).*

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Diagnosing and Treating Julitis – Claim Analysis

- 3. A method of diagnosing julitis in a patient, said method comprising:
  - a. obtaining a plasma sample from a human patient;
  - b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with a porcine anti-JUL-1 antibody and detecting binding between JUL-1 and the porcine antibody; and
  - c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.
- Law of Nature/Abstract idea like claim 2 (*Step 2A:YES)*
- No evidence that porcine antibodies were routinely or conventionally used to detect human proteins such as JUL-1, so use is an unconventional step that is more than a mere instruction to "apply" the correlation and critical thinking step (the exception) using well-understood, routine or conventional techniques in the field.
- Eligible - The recitation of detecting JUL-1 using a porcine anti-JUL-1 antibody yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*).

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Diagnosing and Treating Julitis – Claim Analysis

- 4. A method of diagnosing julitis in a patient, said method comprising:
  - a. obtaining a plasma sample from a human patient;
  - b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with antibody mAb-D33 and detecting binding between JUL-1 and antibody mAb-D33; and
  - c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.
- Law of Nature/Abstract idea like claim 2 (*Step 2A:YES)*
- Antibody mAb-D33 was not routinely or conventionally used to detect human proteins such as JUL-1, so use is an unconventional step that is more than a mere instruction to "apply" the correlation and critical thinking step (the exception) using well-understood, routine or conventional techniques in the field.
- Eligible - The recitation of detecting JUL-1 using a porcine anti-JUL-1 antibody yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*).

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Diagnosing and Treating Julitis – Claim Analysis

- 5. A method of diagnosing and treating julitis in a patient, said method comprising:
  - a. obtaining a plasma sample from a human patient;
  - b. detecting whether JUL-1 is present in the plasma sample;
  - c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected; and
  - d. administering an effective amount of topical vitamin D to the diagnosed patient.
- Law of Nature/Abstract idea like claim 2 (*Step 2A:YES)*
- Steps a and b by themselves do not add significantly more
- Use of topical vitamin D was NOT widely prevalent in the field
- Eligible - recitation of administering topical vitamin D yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*)

May 2016 USPTO Guidelines

Diagnosing and Treating Julitis – Claim Analysis

- 6. A method of diagnosing and treating julitis in a patient, said method comprising:
  - a. obtaining a plasma sample from a human patient;
  - b. detecting whether JUL-1 is present in the plasma sample;
  - c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected; and
  - d. administering an effective amount of anti-tumor necrosis factor (TNF) antibodies to the diagnosed patient.
- Law of Nature/Abstract idea like claim 2 (*Step 2A:YES)*
- Steps a and b by themselves do not add significantly more
- Use of anti-TNF antibodies to treat a patient diagnosed with julitis was well-understood, routine and conventional activity engaged in by doctors in the field

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Diagnosing and Treating Julitis – Claim Analysis

- 6. continued…
- "When the additional elements are viewed **as a combination,** however, the additional elements (steps a, b and d) amount to a claim as a whole that adds meaningful limits on the use of the exception (the correlation and critical thinking step). The totality of these steps including the recitation of a particular treatment (administration of an effective amount of anti-TNF antibodies) in step d integrate the exception into the diagnostic and treatment process, and amount to more than merely diagnosing a patient with julitis and instructing a doctor to generically "treat it."
- Eligible - the administration of anti-TNF antibodies, when considered as a combination with the other additional elements, yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*)
- !!!!!!!!!!

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Diagnosing and Treating Julitis – Claim Analysis

- 7. A method of treating a patient with julitis, the method comprising administering an effective amount of anti-TNF antibodies to a patient suffering from julitis.
- The claim is focused on a process of practically applying the product to treat a particular disease (julitis), and not on the product *per se*
- Eligible - The recited step of administering antibodies to a patient suffering from julitis does not recite or describe any recognized exception. *See, e.g.*, Mayo, 132 S. Ct. at 1297 (recited steps of administering a drug to a patient and determining the resultant level of 6-thioguanine in the patient "are not themselves natural laws"). Thus, the claim is not directed to an exception (*Step 2A: NO*).

May 2016 USPTO Guidelines

Example 30. Dietary Sweeteners

- “Texas mint” plant that has a thin liquid sap containing about 10% texiol (a newly discovered glycoside similar to rebaudioside A)
- Lower in calories and tastes sweeter than table sugar, but it has a bitter aftertaste
- Preferred dietary sweetener comprising 1-5% texiol and at least 90% water
- Dietary sweetener comprising texiol mixed with water and Compound N (a natural flavor excreted from mushrooms and having a mild umami taste); Compound N neutralizes the bitter aftertaste
- Dietary sweetener solid gel formulation comprising 5% texiol mixed with water and/or fruit juice and sufficient pectin to provide a solid gel.
- Dietary sweetener comprising texiol in granular form for use by consumers, produced by grinding or milling or controlled crystallization
- Dietary sweetener comprising texiol in a controlled release formulation

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Dietary Sweeteners – Claim Analysis

- 1. A dietary sweetener comprising:
  - texiol; and
  - water.
- 2. A dietary sweetener comprising:
  - 1-5 percent texiol; and
  - at least 90 percent water.
- 3. A dietary sweetener comprising:
  - 1-5 percent texiol;
  - at least 90 percent water; and
  - 1-2 percent Compound N.
- 4. A dietary sweetener comprising:
  - 5 percent texiol;
  - water, fruit juice, or a combination of water and fruit juice; and
  - sufficient amounts of pectin to provide a solid gel.
- 5. A dietary sweetener comprising:
  - granular particles of texiol having a particle diameter of X10 of 80 microns and X90 of 300 microns.
- 6. A dietary sweetener comprising texiol in a controlled release formulation.

May 2016 USPTO Guidelines

Example 31. Screening For Gene Alterations

- Discovered the “wild-type” sequence of the human BRCA1 gene (*i.e.*, the typical sequence of the gene in humans), and naturally occurring alterations from the wild-type sequence that are correlated with an increased likelihood of developing breast or ovarian cancer.
- Hybridization and Amplification were routine
- Scanning Near-field Optical Microscopy (SNOM) to study DNA hybridization had been discussed in several articles in widely-read scientific journals, but scientists were not commonly or routinely using SNOM to study DNA hybridization
- Cool-Melt PCR, which has a 20-fold higher sensitivity of mutation detection, known and used by a few scientists in the field, later became standard

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Screening For Gene Alterations – Claim Analysis

- 1. A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises comparing germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject. (Mayo claim)
  - The step of comparing could be performed by a human using mental steps or basic critical thinking, so an abstract idea (*Step 2A: YES*)
  - Ineligible - A single step of comparing, along with a wherein clause... no other elements/steps recited in the claim. The claim as a whole does not amount to significantly more than the abstract idea of comparing information (*Step 2B: NO*).

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Screening For Gene Alterations – Claim Analysis

- 70. The method of claim 1, wherein said comparing BRCA1 sequences further comprises:
  - hybridizing a wild-type probe to a BRCA1 gene isolated from said sample; and
  - detecting the presence of a hybridization product by measuring conformational changes in the probe that are indicative of hybridization to the BRCA1 gene with scanning near-field optical microscopy.
- Eligible - the recitation of detecting hybridization using SNOM yields a claim as a whole that is significantly more than the judicial exception itself (*Step 2B: YES*).

May 2016 USPTO Guidelines

Screening For Gene Alterations – Claim Analysis

- 75. A method for hybridizing BRCA1 sequences comprising:
  - hybridizing a wild-type probe to a BRCA1 gene isolated from a tissue sample from a human subject; and
  - detecting the presence of a hybridization product by measuring conformational changes in the probe that are indicative of hybridization to the BRCA1 gene with scanning near-field optical microscopy.
- Eligible - the claim is not directed to an exception (*Step 2A: NO*)

May 2016 USPTO Guidelines

Screening For Gene Alterations – Claim Analysis

- 80. The method of claim 1, wherein said comparing BRCA1 sequences further comprises:
  - amplifying by Cool-Melt PCR all or part of a BRCA1 gene from said sample using a set of primers to produce amplified nucleic acids; and
  - sequencing the amplified nucleic acids.
- Although Cool-Melt PCR was used by a few scientists in the field to amplify nucleic acids at the time the invention was made and the application was filed, use by only a few scientists does not make the technique routine or conventional in the field as a whole.
- Eligible - Reciting using Cool-Melt PCR yields a claim as a whole that is significantly more than the judicial exception itself (*Step 2B: YES*).

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Screening For Gene Alterations – Claim Analysis

- 85. A method for amplifying BRCA1 sequences comprising:
  - amplifying by Cool-Melt PCR all or part of a BRCA1 gene from a tissue sample from a human subject using a set of primers to produce amplified nucleic acids; and
  - sequencing the amplified nucleic acids.
- Eligible - claim is not directed to an exception (*Step 2A: NO*)

Patent Drafting/Litigation Considerations

- Avoid red-flag terms in spec: e.g., routine, conventional, well-understood, well known (conflict with enablement!).
- Define some terms (e.g., “pharmaceutically acceptable carrier”) to exclude natural products, if possible (but Europe!).
- Extract from inventors any structural and/or functional differences between claimed product and natural product; put in specification!
- Include structure in claims, at least to the extent consistent with business objectives.

Patent Drafting/Litigation Considerations

- If you have a novel reagent, consider eliminating from the claims (or at least one claim set) any comparing/correlation steps (e.g., “method for detecting X using novel antibody Z”).
  - Set forth any novel primers/probes etc., deposit or sequence antibodies
- Use preemption framework to draft claims of realistic scope.
- Use claim features that are “more than well-understood, purely conventional or routine” (if possible)

Patent Drafting/Litigation Considerations

- Consider spelling out particular steps/reagents in otherwise established procedures: e.g., set out primers, nucleotides, use of Taq polymerase, heating steps, cooling steps, number of cycles, etc., rather than simply reciting “PCR” (same re flow cytometry, mass spectrometry etc.) (as perverse as this might seem).
- For combinations of “natural” products, be proactive in framing the functional difference perspective, and argue the examiner must look at the “claim as a whole”.

Patent Prosecution Tips

- ✓Still a significant amount of uncertainty.
- ✓Interview, Interview, Interview.
- ✓Use the Interim Guidance and Examples.
- ✓Respond in Writing
  - ✓Address both steps of the Mayo/Alice analysis

    (1) Is the claim *directed* to a patent-ineligible concept or product? Markedly Different?

    (2) Does the claim recite additional elements that amount to significantly more than the judicial exception?
- ✓Keep a continuation pending!

Subject Matter Eligibility

Useful Materials

USPTO established a website:

http://www.uspto.gov/patents/law/exam/interim_guidance_subject_matter_eligibility.jsp

Case Law:

- *Diamond v. Chakrabarty*, 447 U.S. 303 (1980)
- *Bilski v. Kappos,* 130 S.Ct. 3218 (2010)
- *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. __, 134 S.Ct. 2347, 110 USPQ2d 1976 (2014)
- *Association for Molecular Pathology v. Myriad Genetics, Inc.,* 569 U.S. __, 133 S.Ct. 2107, 106 USPQ2d 1972 (2013)
- *Mayo Collaborative Serv. v. Prometheus Labs., Inc.*, 566 U.S. __, 132 S.Ct. 1289, 101 USPQ2d 1961 (2012)
- *Ariosa Diagnostics, Inc. v. Sequenom, Inc. (*Fed. Cir. 2015)

Thank you!

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Placental Tissue Graft

1. A dehydrated, laminated tissue graft consisting essentially of one or more washed and/or substantially cleaned amnion layers and one or more washed and/or substantially cleaned chorion layers

- wherein at least one of the amnion layers contains its fibroblast cell layer, and
- Further wherein the amnion layer and the chorion layer are directly laminated to each other.

Visualizing Placental Tissue Graft

1. A method for permitting direct, visual determination of the orientation of a placental tissue graft by user,

wherein the placental tissue graft has a first side and a second side, said method comprising:

- placing an asymmetric label on a portion of at least one side of said tissue graft, which label visibly distinguishes one side from the other side, thereby permitting direct, visual determination of the orientation for application of said tissue graft; and ascertaining the orientation of the placental tissue graft by direct visual determination.

Primer Sequences

1. A kit for determining the methylation status of at least one CpG dinucleotide, the kit comprising:

- at least one first nucleic acid primer at least 8 nucleotides in length that is complementary to a bisulfite-converted nucleic acid sequence comprising a CpG dinucleotide at position 373378 of chromosome 5 within the aryl hydrocarbon receptor repressor (AHRR) gene, wherein the at least one first nucleic acid primer detects either the unmethylated CpG dinucleotide or the methylated CpG dinucleotide.

What you need to know: Bisulfate treatment of a nucleic acid sequence deaminates unmethylated cysteine residues to uracil residues.

Quantifying Metabolites

- 1. A method for quantifying at least one metabolite in a biological sample comprising the steps of:

  (a) providing one biological sample obtained from a patient on a prescribed medication regimen, wherein the sample comprises at least one test metabolite, ***wherein in the sample is urine***;

  (b) providing one set of known normative data specific to a reference metabolite, wherein the set of data is collected from a population that is on a prescribed medication regimen;

  (c) contacting the biological sample with an analytical device;

  (d) detecting the presence of at least one test metabolite in the biological sample with the device, wherein the device is capable of measuring the concentration of the test metabolite in the sample;

  (e) normalizing the biological sample to adjust for changes in the patient's hydration status by determining the metabolite/creatinine ratio of the patient; and

  (f) quantifying the concentration of at least one test metabolite in the biological sample by comparing a ratio between the concentration of the test metabolite from the patient to the set of known normative data specific to the reference metabolite concentration.

Mayo plus administration

- 1. A method of treating pain in a renally impaired patient, comprising the steps of:

a. providing a solid oral controlled release dosage form, comprising:

i. about 5 mg to about 80 mg of oxymorphone or a pharmaceutically acceptable salt thereof as the sole active ingredient; and

ii. a controlled release matrix;

b. measuring a creatinine clearance rate of the patient and determining it to be (a) less than about 30 m[L]/min, (b) about 30 mL/min to about 50 mL/min, (c) about 51 mL/min to about 80 mL/min, or (d) above about 80 mL/min; and

c. orally administering to said patient, in dependence on which creatinine clearance rate is found, a lower dosage of the dosage form to provide pain relief;

wherein after said administration to said patient, the average AUC of oxymorphone over a 12-hour period is less than about 21 ng•hr/mL.

Proteins make it all OK????

- 1. A method of in vitro diagnosis which discriminates between exposure of a subject to Mycobacterium tuberculosis and vaccination with the Bacille Calmette Guerin strain of Mycobacterium bovis, the method comprising testing for the presence of CD4 T lymphocytes that respond to MTBN4, wherein the presence of the CD4 T lymphocytes that respond to MTBN4 indicates that the subject has been exposed to Mycobacterium tuberculosis, and wherein CD4 T lymphocytes from a subject vaccinated with the Bacille Calmette Guerin strain of Mycobacterium bovis but not exposed to Mycobacterium tuberculosis do not respond.