Prometheus, *Myriad*, and the Future of Biotech Patent Law

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- Nothing in this presentation should be construed to be an admission that any invention or claim is or is not patentable.
- Some liberty has been taken to simplify the opinions and the claims at issue, while retaining the Court's wording and the meaning of the claims as much as possible. Citations and quotation marks have been omitted.

§ 101 and Implicit Exceptions

- 35 U.S.C. § 101 - "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 …."
- Supreme Court's precedents provide three implicit exceptions to § 101's broad principles: Laws of nature, natural phenomena, and abstract ideas are not patentable.
- Such discoveries are "manifestations of . . . nature, free to all men and reserved exclusively to none."

Prometheus' Claim-At-Issue

A method comprising:

(a) administering a drug providing 6-thioguanine to a subject having an immune-mediated gastrointestinal disorder; and

(b) determining the level of 6-thioguanine,

wherein a level less than about 230 pmol indicates a need to increase the amount of the drug, and

wherein a level greater than about 400 pmol indicates a need to decrease the amount of the drug.

Problematic Facts

- Doctors used thiopurine drugs to treat patients before Prometheus' discovery.
- Scientists routinely measured thiopurine metabolite levels to investigate the relationships between the metabolite levels and efficacy and toxicity of thiopurine compounds.
- Methods for determining thiopurine metabolite levels were known in the art.

Prometheus' Holdings

- Phenomena of nature, though just discovered, are not patentable; they are the basic tools of scientific work.
- A process is not unpatentable simply because it contains a law of nature.
- An application of a natural law to a known structure or process may well be deserving of patent protection, but it must come from the application to a new and useful end.
- A process that uses a natural law must contain an "inventive concept" so it is significantly more than a patent upon the natural law itself.

Holding: Claims Not Patentable

- The upshot is that the three steps simply tell doctors to gather data from which they may draw an inference in light of the correlations.
- Claims do not require any particular action; but only make a suggestion that the doctor should take the laws into account when treating patient.
- Claims inform a relevant audience about certain laws of nature; any additional steps consist of routine activity; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts.

Court Explains Only What is Not Sufficient

- To transform an unpatentable law of nature into a patent-eligible application, one must do more than simply state the law and add the words “apply it.”
- Use of well-understood, routine, conventional or purely obvious pre-solution activity is normally not sufficient to transform a law of nature into a patent-eligible application.

Court Explains Only What is Not Sufficient

- The prohibition against patenting abstract ideas cannot be circumvented by "attempting to limit the use of the formula to a particular technological environment."
- Scope of natural law not a factor: preempting even a narrow law of nature can inhibit future research.
- While the "machine-or-transformation" test is an "important and useful clue" to patentability, it does not trump the law of nature' exclusion.

ACLU v. Myriad
(Fed. Cir. Aug. 16, 2012)

Claims to Isolated DNA Are Patentable

- When cleaved, an isolated DNA molecule is a distinct chemical entity (from DNAs in the human body) that is obtained by human intervention.
- "Creating a new chemical entity is the work of human transformation, requiring skill, knowledge, and effort."
- Because isolated DNA is a tangible, man-made composition of matter, defined and distinguished from natural DNA by its objectively discernible chemical structure, it is patentable under § 101.

Certain Method Claims Are NOT Patentable

- A method for detecting a germline alteration in a gene, which comprises analyzing a sequence of the gene.
- A method for screening a sample for a somatic mutation which comprises comparing a first gene sequence from a tumor sample, with a second gene sequence selected from a nontumor sample, wherein a difference in the sequences indicates a somatic mutation in said tumor sample.

Certain Method Claims Are NOT Patentable

- Claims recite nothing more than the abstract mental steps necessary to compare two different nucleotide sequences.
- Although, "Myriad attempts to read into its method claims additional, allegedly transformative steps [extracting DNA from a human sample, and sequencing the DNA molecule,] [t]he claims themselves … do not include …these steps."
- "[T]he claims only recite mental steps, not the structure of physical DNA molecules."

Certain Method Claims ARE Patentable

- A method for screening potential cancer therapeutics comprising: growing a transformed cell containing an altered gene causing cancer in the presence of a potential therapeutic compound, growing said transformed cell in the absence of said compound, determining the rate of growth of said cells and comparing the growth rate of said cells, wherein a slower rate of growth of said cell in the presence of said compound is indicative of a cancer therapeutic.

Certain Method Claims ARE Patentable

- The claim recites a screening method premised on the use of “transformed” host cells.
- Those cells, are not naturally occurring. Rather, they are derived by altering a cell to include a foreign gene, resulting in a manmade, transformed cell with enhanced function and utility.
- The claim thus includes more than the abstract mental step of looking at two numbers and “comparing” two host cells’ growth rates.”

Certain Method Claims ARE Patentable

- By definition, performing even known types of steps on, or to create, novel (*i.e.*, transformed) subject matter is the stuff of which most process or method invention consists.
- If a claimed composition of matter is patent-eligible subject matter, applying various known types of procedures to it is not merely applying conventional steps to a law of nature. The transformed, man-made nature of the underlying subject matter makes the claim patent-eligible.

USPTO INTERIM GUIDELINES JULY 5, 2012

Issued in light of *Mayo v. Prometheus*

A Three-Step Inquiry (abbreviated)

- Is it a process claim?
- Does the claim have a natural principle or correlation as a limiting feature of the claim?
- Does the claim include additional elements so that it claims significantly more than the natural principle itself?

Step 1: Is it a process?

- Product claims seem to be immune
- Make sure you look at isolated or purified limitations (and guess what the S.Ct. will do)
- Kit claims/system claims

Step 2: Does it recite a natural principle, etc.?

- “If a natural principle is not a limitation . . . [it] requires no further analysis”
- Hey, can I write a claim without saying WHY I am doing the steps?
- Who said that a wherein clause with a conclusion was limiting anyway?
  - “wherein a level above X indicates A”
  - “wherein the presence of X indicates Y”

Step 3: Additional elements present that limit use of natural principle

- Natural principle must be applied
- Post-solution activity that is not "integrated" with natural principle is insufficient (like recording data on a chart)
- Routine, conventional activity previously engaged in by those in the field is insufficient

Example 2 from Guidelines

- There is a naturally occurring correlation between a patient having rheumatoid arthritis and their level of rheumatoid factor IgM.
- Increased levels of factor = increased binding of an anti-IgM antibody = diagnosis of RA.
- Anti-IgM antibody XYZ does not occur in nature and is novel and non-obvious.
- Assays M and N can be used for comparing the anti-IgM antibody to a control sample, but are not routinely used together.

Claims from Guidelines

- 1. A method of determining the increased likelihood of having or developing rheumatoid arthritis in a patient, comprising the steps of:
  - obtaining a serum sample from a patient;
  - contacting the serum sample with an anti-IgM antibody; and
  - determining that the patient has rheumatoid arthritis or an increased likelihood of developing rheumatoid arthritis based upon the increased binding of the anti-IgM antibody to IgM rheumatoid factor in the serum sample. (Reminder – man-made antibody)

Claim 2 from Guidelines

- 2. The method of claim 1 further comprising:
  - providing a positive control sample; and
  - contacting the positive control sample with an anti-IgM antibody,
  - wherein the step of determining that the patient has rheumatoid arthritis or increased likelihood of developing rheumatoid arthritis comprises a step of comparing the anti-IgM antibody in the serum sample to the positive control sample.

Claim 3 from Guidelines

- 3. The method of claim 1 or 2, wherein the anti-IgM antibody is antibody XYZ.

Hypothetical Claims

Patentable or Not?

- What if the discovery relates to auto-antibodies to proteins XX and XY, previously known to exist but its association with RA was not known? Thus both the auto-A/B and proteins exist in nature?

A method for determining the risk of developing RA comprising manufacturing a reagent that can be used to identify the presence in a sample of auto-antibodies to one or more biomarkers selected from proteins XX and XY, contacting said reagent with a sample from a patient.

Patentable or Not?

A kit for determining the risk of developing RA comprising a solid support comprising one or more biomarkers, or antigenic fragments thereof, wherein the one or more biomarkers are selected from proteins XX and XY.

Patentable or Not?

A method for enhancing the photosynthesis of a crop by increasing carbon dioxide assimilation comprising:

applying to the surface of said crop highly reflective, finely divided particulate materials having a median size below 3 microns,

wherein the particles as applied allow for the exchange of gases.

Tessenderlo Kerley, Inc. v. OR-Cal, Inc.
(N.D. Cal. 6/05/12)

- Holding: Motion for summary judgment of invalidity is denied without prejudice. Discovery is needed to determine whether the claimed application of finely divided particulate materials with certain claimed properties to certain horticultural crops was well-understood, routine, conventional activity previously engaged in by researchers in the field.

Patentable or Not?

A method for detecting a paternally inherited nucleic acid from a maternal sample, comprising:

obtaining a non-cellular fraction of the blood sample,

amplifying a paternally inherited nucleic acid from the fraction, and

performing nucleic acid analysis on the amplified nucleic acid to detect paternally inherited fetal nucleic acid.

Aria Diagnostics, Inc. v. Sequenom, Inc.
(N.D. Cal. 7/5/12)

- Ariosa [f/k/a Aria] argued patent does no more than combine conventional techniques of amplifying and detecting certain paternally-inherited fetal DNA, with the "discovery" of the natural phenomenon that this DNA exists in maternal blood.
- Patent itself described fractionation, amplification, and detection as "standard" in the field.
- Holding: Ariosa raised a substantial question as to whether claims were directed to patent ineligible subject matter, therefore, motion for P.I. denied.

Patentable or Not?

A method of immunizing a subject with a disease-causing organism-associated immunogen comprising

(I) Screening immunization schedules, by (a) immunizing two groups according to two different immunization schedules, and (b) comparing the immunization schedules to identify the one that has the lower risk of inducing a chronic immune mediated disorder; and

(II) immunizing said subject according to the schedule identified as having the lower risk.

Classen Immunotherapies, Inc. v. Biogen IDEC (D. Md. 8/9/12)

- The Classen patent states that prior to its invention, chronic immune mediated diseases, such as diabetes mellitus, were not considered vaccine complications.
- Thus, the record contains no evidence that the claims involve "well-understood, routine, or conventional activity."
- Holding: Defendant's motion to dismiss Plaintiff's Complaint due to unpatentability is denied.

Patentable or Not?

1. A method of detecting cancer X comprising:

   obtaining a tissue sample from a patient at risk of cancer X,

   measuring/detecting the level of marker Y in said sample,

   wherein the presence of marker Y indicates the presence of cancer X.

- Is this patentable?
- How can we improve this claim?

Patentable or Not Patentable?

- What if we eliminate the law from the claim:

1. A method ~~of detecting cancer X~~ comprising:

   obtaining a tissue sample from a patient ~~at risk of cancer X~~, **and**

   measuring/detecting the level of marker Y in said sample.

   ~~wherein the presence of marker Y indicates the presence of cancer X.~~

Patentable or Not Patentable?

1. A method of treating cancer X comprising:

   obtaining a tissue sample from a patient at risk of cancer X,

   measuring/detecting the level of marker Y in said sample,

   administering treatment Z to said patient when marker Y is present in said sample.

- Is this patentable?
- How can we improve this claim?

Patentable or Not?

A method of treating prostate cancer in a patient comprising

administering to the patient a therapeutically effective amount of a compound that reduces expression of Gene X,

wherein one or more cancerous tumors in the patient's prostate are reduced in size or have their growth suppressed.

Patentable or Not?

A method of screening for drugs useful in treating prostate cancer, comprising

administering a compound to cultured prostate cancer cells,

wherein death or reduced proliferation of said cells indicates said compound is useful in treating prostate cancer.

Patentable or Not?

A method of determining whether a subject has an increased risk of developing prostate cancer, comprising

determining if nucleotide #43 in the protein coding sequence of Gene X (Seq. ID #1) in such subject is uracil,

wherein if nucleotide #43 is uracil, the subject has an increased risk of developing prostate cancer.

Patentable or Not?

An isolated nucleic acid having at least ten nucleotides of the human protein coding sequence of Gene X (Seq. ID#1).

Practice Pointers

- Tie method claims to the use of particular “man-made” article such as isolated nucleic acid(s) or transformed cells.
- Set forth in patent/argue that it was not routine/conventional to amplify, detect, measure, etc. nucleic acids with the claimed sequence(s).
- Draft claims with different levels of breadth and specificity; include kit and other classes of claims.
- Include step requiring some affirmative action.

Practice Pointers

- Avoid stating natural law in a separate, easily identifiable “Wherein” clause.
- Disclose multiple applications of the natural law and use separate claims for particular applications, e.g., treatment on one disease only.
- Set forth specific parameters. *See* Justice Kagan quote from Oral Argument.

Prometheus Oral Argument

- JUSTICE KAGAN: What [the claims] haven't done is say at a certain number, you should use a certain treatment; at another number, you should use another treatment. So, I guess the first question is, why didn’t [Prometheus] file a patent like that? Because that clearly would have been patentable. Everybody agrees with that.

Post-*Prometheus* Decisions

Case	Court/ Date	Abstract Idea/ Natural Law	Holding
CLS Bank v. Alice *(103 U.S.P.Q.2d 1297)*	Fed. Cir. 7/9/12	Abstract Idea	Patentable
ACLU v. Myriad *(103 U.S.P.Q.2d 1681)*	Fed. Cir. 8/16/12	Natural Law	Mixed
Nazomi v. Samsung *(No. C-10-05545 RMW)*	N.D. Cal. 3/21/2012	Abstract Idea	Patentable
Smartgene v. Advanced Biological *(No. 08-00642 (BAH), 2012 BL 75942)*	D.D.C. 3/30/2012	Abstract Idea	Ineligible
Advanced Software Design v. Fiserv *(No. 4:07CV185 CDP., 2012 BL 120333)*	E.D. Mo. 5/15/2012	Abstract Idea	Patentable
Tessenderlo Kerley v. OR-Cal *(No. C 11-04100 WHA, 2012 BL 139021)*	N.D. Cal. 6/5/12	Natural Law	Discovery Needed

Post-*Prometheus* Decisions

Case	Court/ Date	Abstract Idea/ Natural Law	Holding
Aria Diagnostics v. Sequenom *(No. 3:11-cv-06391-SI, 2012 BL 181998)*	N.D. Cal. 7/5/12	Natural Law	P.I. Denied – Subst. Q. Invalidity
Classen v. Biogen IDEC *(No. WDQ-04-2607., 2012 BL 203163)*	D. Md. 8/9/12	Natural Law	Possibly Patentable
CyberFone v. Cellco *(No. 11-831-SLR, 2012 BL 208079)*	D. Del. 8/16/12	Abstract Idea	Ineligible
OIP Tech. v. Amazon.Com *(No. C-12-1233 EMC)*	N.D. Cal. 9/11/12	Abstract Idea	Ineligible
RMail v. Amazon.com *(No. 2:10-cv-00258-JRG)*	E.D. Tex	Is § 101 a permissible litigation defense?	Pending