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Mayo v. Prometheus -- Implications for Diagnostics, Biomarkers, and Personalized Medicine

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What *Should* be Eligible for a Patent?

- 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 U.S.C. § 101

And According to Congress

- "…anything under the sun that is made by man."
  - Senate and House Committee Reports accompanying the 1952 Patent Act

What are the Exceptions to Eligibility?

- Abstract ideas
- Mental processes
- Mathematical formulas
- Laws of nature
- Inventions that clearly do not work (e.g., perpetual motion machines)
- Inventions that are illegal

Mayo Collaborative Services v. Prometheus Laboratories, 566 U.S. __ (March 20, 2012)

- Claims to a method of optimizing 6-thioguanine therapy found to be patent-ineligible
- Opinion written by Justice Breyer
- Unanimous decision
- Two patents at issue, USP 6,355,623 and USP 6,680,302

Sample Claim in *Prometheus*

1. A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

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

(b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

wherein the level of 6-thioguanine less than about 230 pmol per 8 x 10^8 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

wherein the level of 6-thioguanine greater than about 400 pmol per 8 x 10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

The "Law of Nature"

- "[R]elationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm."
- "While it takes human action . . . to trigger a manifestation of this relation in a particular person, the relation itself exists in principle apart from any human action."
- Slip op. at p. 8.

The Decision

- "If a law of nature is not patentable, then neither is a process reciting a law of nature, unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself."

- Slip Opinion at p. 8-9

The "Administering" Step

- "…simply refers to the relevant audience, namely doctors who treat patients with certain diseases with thiopurine drugs. . . . [D]octors used thiopurine drugs to treat patients suffering from autoimmune disorders long before anyone asserted these claims." Slip op. at 9.

The "Determining" Step

- "…methods for determining metabolite levels were well known in the art. . . . Thus, this step tells doctors to engage in well-understood, routine, conventional activity previously engaged in by scientists who work in the field. Purely 'conventional or obvious' 'pre-solution activity' is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law." Slip op. at 10.

The “Wherein” Clauses

- “…simply tell a doctor about the relevant natural laws, at most adding a suggestion that he should take those laws into account when treating his patient. . . . ([R]ather like Einstein telling linear accelerator operators about his basic law and then trusting them to use it where relevant).”

Myriad on Remand after *Prometheus*– What to Expect?

- Three types of claims analyzed by the DCt and the Fed. Cir. in *Myriad* (Fed. Cir. 2011), isolated DNA claims, diagnostic method claims, and claims to a method for screening potential cancer therapeutics – all claims revolve around the "law of nature" that certain mutations in BRCA1 and BRCA2 correlate with an increased risk of breast or ovarian cancers

Myriad "Isolated DNA"Claims

- An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2. USP 5,747,282, claim 1.
- Fed. Cir. Judge Lourie: "isolated" implies that bonds were broken, creating a new chemical entity – patent eligible (2-1 decision, Moore concurring, Bryson dissenting)
- "[T]he claims cover molecules that are markedly different – have a distinctive chemical identity and nature – from molecules that exist in nature." Slip Op. at p. 41.
- All three agree that "cDNA" claims are patent-eligible

Myriad "Isolated DNA" Claims

- Under *Prometheus*, will "isolated DNA" be considered a "product of nature"?

- Relevant Quote from *Prometheus*, "While it takes human action (the administration of a thiopurine drug) to trigger a manifestation of this relation in a particular person, the relationship itself exists in principle apart from any human action." Slip op. at 37-38.

Myriad Diagnostics Claims

- USP 5,709,999:
  - 1. A method for detecting a germline alteration in a BRCA1 gene . . . in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human . . . .
- USP 5,710,001:
  - 1. A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises [ ] comparing a first sequence selected from the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample.
- Fed. Cir: Patent Ineligible even before *Prometheus* decision

Myriad Diagnostics Claims

- "Comparing" and "analyzing" are merely mental steps
- "Myriad's claims do not apply the step of comparing the two nucleotide sequences in a process. Rather, the step of comparing two DNA sequences is the entire process claimed." Slip Op. at p. 50-51.
- "[N]either comparing nor analyzing means or implies 'extracting' or 'sequencing' DNA or otherwise 'processing' a human sample. Id. at 51.
- Likely no change in holding on remand after *Prometheus*, although rationale may swing from "mental steps" to "law of nature"

Myriad Screening Claims

- 20. A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, growing said transformed eukaryotic host cell in the absence of said compound, determining the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and comparing the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic.
- Federal Circuit: Patent Eligible (unanimous)
- Court looked favorably on “growing” and “determining” steps, which are thought to be “central to the purpose of the claimed process.”

Myriad Screening Claims

- Will *Myriad* screening claims survive on remand after *Prometheus*? Uncertain !
- Any weight to be given to the fact that the “transformed cells” are human-made? Not really addressed in the Fed. Cir. opinion
- Would the Supreme Court consider the growth rate of cells in response to a candidate drug to be a “law of nature”?

Where Does the Case Law Leave Us?

- Likely patent-ineligible subject matter
  - Correlations alone (e.g., “wherein presence of mutation X is indicative of increased risk of cancer Y”)
  - Comparisons alone (e.g., “comparing gene X from tumor tissue vs. gene X from normal tissue”); or
  - Correlations and comparisons together with “conventional” or “known” pre- or post-solution activity (e.g., “administering drug X, determining metabolite level in patient and considering modifying dose”)
    - Assume “administering” drug X was known in art and the “considering” step is a mental step that does not require actually modifying the dose

Where Does the Case Law Leave Us?

- When possible, should practitioners add a treating step in view of *Prometheus*?
- Examples,
  - Increasing effectiveness of known treatment by administering drug to patient exhibiting some “natural phenomenon” (e.g., mutation or level of gene amplification) - Patent-eligible or ineligible?
  - Increasing effectiveness of known drug treatment by administering a *modified* dose to a patient exhibiting some “natural phenomenon” - Patent eligible?

- Caveat: Are diagnostic/personalized medicine claims that include a treating step enforceable?

Enforcing Patents and "Split Infringement"

- *Akamai v. Limelight* (Fed. Cir. 2010)
  - Method claims directed to a content delivery service that permitted a content provider to outsource storage and delivery of discrete portions of its website content
  - Defendant (Limelight) performed all but the "tagging" and "service" steps of the claims
  - Limelight provided a service to customers along with instructions necessary for performing the "tagging" and "service" steps
  - Limelight's standard customer contract required customers to perform steps if they used service

Akamai v. Limelight (continued)

- Patentee (Akamai) asserted that actions of Limelight plus customers constituted infringement
- Federal Circuit disagreed
  - Direct infringement requires performance of all claim elements by a single party
  - Only exception is where one party exercises control or direction over the entire process such that every step of patent claim is attributable to controlling party

Akamai v. Limelight (continued)

- There can only be joint infringement when there is an agency relationship between the parties who perform the method steps or when one party is contractually obligated to the other to perform the steps.
- Neither situation present in *Akamai* as customers act independently and not as agents for Limelight.
- Also, while customers have to perform steps according to form contract *if* they use Limelight's service, there is no contract that obligates customers to use the service.

McKesson v. Epic Systems (Fed. Cir. 2011)

- Method claims directed to personalized web pages for doctors and patients
- Defendant (Epic) licenses software to health care providers.
- Patentee (McKesson) asserted that Epic's licensing of its MyChart software to doctors induced joint infringement of patent by doctors and patients (no single party performed all steps of claim)

McKesson continued

- Majority of panel held no infringement
- As in *Akamai*, holding based on a lack of agency and/or contractual relationship between doctors and patients
- Patients not “controlled or directed” by doctors to use software.

McKesson continued

- Judge Newman's dissent –
  - Patentee not attempting to sue patients and physicians, but seeking to enforce patent against software provider
  - The court's pronouncement of the "single-entity" rule as an absolute rule of law is in error and is contrary to precedent
  - Cases involving infringement by multiple entities should be fact-based decisions according to ordinary rules of tort liability
  - Patents encompassing interactive computer-managed inventions should be enforceable just like any other patent as a matter of policy

Akamai and McKesson

- Both *Akamai* and *McKesson* were three judge panel decisions *and* both are now being re-heard *en banc*
- Oral arguments for Akamai were October 21, 2011.
- Will *en banc* Federal Circuit modify the previous panel decisions and abandon the restrictive “single-entity” rule ?

Akamai and McKesson – What Impact?

- Typical personalized medicine scenarios
  - Physician sends blood to outside clinical laboratory for analysis, diagnostic test performed, results sent back to physician, physician administers or prescribes drug
    - Unlikely that clinical laboratory acts as agent of the doctor or is contractually obligated to perform the test ?
  - Physician and clinical laboratory in one hospital
    - Possible contractual obligation by clinical laboratory with hospital to perform diagnostic test? Are physician and clinical laboratory both agents of hospital? Does the agency relationship need to be between the parties who performed the steps?

Recommendations after *Prometheus*

- For issued patents with potentially patent-ineligible claims after *Prometheus*…
  - If application(s) in family still pending, review specification for limitations that can be added to render claims patent- eligible and pursue in continuation or divisional application
  - If no application pending, consider pros and cons of filing reissue

Recommendations after *Prometheus*

- For newly drafted applications, consider providing support for claims that are patent eligible under *Prometheus and* that avoid the "split infringer" issue in *Akamai* and *McKesson.* Is this possible?
- Some ideas…..

Hint #1: Include Significant "Post-Solution Activity"

- "Post-solution activity that is purely "conventional or obvious," … cannot transform an unpatentable principle into a patentable process." Slip op. at 13 (internal citations omitted)
- Would the "post-solution activity" in the Prometheus '097 patent, "increasing the subsequent dose" be "unconventional" enough?
- Will "post-solution activity" be required? Remains to be seen
- To avoid split infringement:
  - If physician is the "infringer": (a) submit a sample for determination of marker xxx; (b) adjust medication if marker xxx is elevated.
  - If law is the "infringer": (a) assay for the presence of marker xxx; (b) instruct a healthcare provider to adjust medication when marker xxx is elevated.

Hint #2: Include "Several Unconventional Steps"

- The Court distinguished a (way) earlier English case, *Neilson v. Harford* (1841): "law of nature" = hot air promotes ignition better than cold air (as in a furnace).
  - Inserting a receptacle for heated air
  - Heating the air
  - Transferring the heated air to the furnace
- "[T]he claimed process included not only a law of nature but also several unconventional steps . . . That confined the claims to a particular, useful application of the principle." Slip op. at 15.
- Arguably these are all "pre-solution activity."

Hint #3: Avoid "improperly tying up the future use of laws of nature"

- *Gottschalk v. Benson*: claims to a mathematical process for converting binary-coded decimal numerals into pure binary numbers on a general purpose digital computer.
- "[T]he mathematical formula had no substantial practical application except in connection with a digital computer" *Prometheus* Slip Op. at 16 (internal quotes omitted).
- One cannot with one's claim "[tie] up the future use of laws of nature." Id.

Hint #4

- Identify what might be considered a “law of nature,” a “product of nature,” an “algorithm,” etc.
- *Except* for the above, consider whether the rest of your claim is “patentable,” *i.e.*, meets the requirements of §§102, 103, and 112, even before your claim is examined – is your claim “unconventional”?
- If yes, your claim may be deemed “patent eligible.”

QUESTIONS?

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