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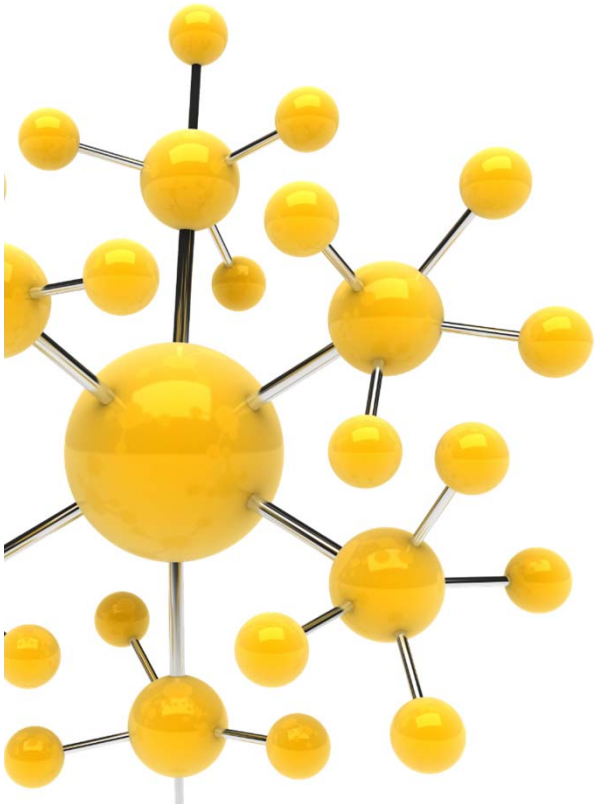

Patent Law Developments in the Biotechnology, Medical Device, and Digital Health Industries

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Updates

1. Patent-Eligibility of Life Sciences Claims After Alice
2. Biosimilar Companies Leveraging IPRs to Clear Path to Market
3. The CRISPR Patent Dispute Rages on Before the Federal Circuit

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1. **Patent-Eligibility of Life Sciences Claims After Alice**
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Mayo Collaborative Servs. v. Prometheus Labs., Inc. (2012)

- Claims: Method of optimizing treatment
  - Administer drug to subject with specified GI disorder, and
  - Determine level of active metabolite of drug in subject
    - Metabolite < 230 pmol = "indicates a need" to increase dose
    - Metabolite > 400 pmol = "indicates a need" to decrease dose

- Invalid under § 101
  - Unpatentable law of nature
  - Relationship b/w [metabolites] in blood and likelihood that dosage will prove ineffective or cause harm

Assoc. for Molecular Pathology v. Myriad Genetics, Inc. (2013)

- Claims:
  - Isolated sequence of BRCA1 gene
  - Isolated cDNA

- cDNA claims not invalid under § 101
  - Isolated DNA = same as that found in nature = unpatentable
  - But, claims to exon-only sequence of cDNA = different from natural DNA = patentable

Alice Corp. v. CLS Bank International (2014): The Alice Two-Step

1. ***Are the claims directed to a patent-ineligible concept?***

2. ***If so, is there an inventive concept such that the claim as a whole covers more than the patent-ineligible concept?***

Post Alice: Genetic Techs. v. Merial

818 F.3d 1369 (Fed. Cir. 2016) (Dyk, Prost, Taranto)

- Rule 12 dismissal
- Claims: Method for detecting genetic variations
  - Amplifying DNA using sequence from non-coding region
  - Analyzing amplified sequence to detect coding region
- Step one fail: Claims cover scientific law
  - Linkage disequilibrium
  - Broad statements of potential applications in spec
- Step two fail: No "inventive concept"
  - DNA amplification and analysis = routine in the art
  - "Detecting the allele" = mental process step

Cleveland Clinic v. True Health Diagnostics

859 F.3d 1352 (Fed. Cir. 2017) (Lourie, Reyna, Wallach)

- Rule 12 dismissal
- Claims: Method for assessing risk of cardiovascular disease
  - Detect levels of MPO enzyme in blood (which is released when artery is damaged)
  - Correlate to CV risk by comparing to MPO levels in healthy subjects
- Step one fail: Relationship b/w MPO levels & CV disease = law of nature
- Step two fail:
  - MPO level detection = “well-known technique”
  - Comparison of MPO levels to control = conventional statistics

Vanda Pharms. v. West-Ward Pharms.

887 F.3d 1117 (Fed. Cir. 2018) (Lourie, Hughes, Prost dissenting)

- Claims: Method of using iloperidone to treat schizophrenia
  - Determining whether patient is CYP2D6 poor metabolizer (using routine test)
  - Administering 12 mg/day iloperidone if poor metabolizer, or 12 – 24 mg/day if not
- Step one: pass
  - Directed to novel method of administering drug
  - Did not claim relationship b/w metabolization rates and efficacy
  - Mayo didn't require doctor to adjust dose based on test (claims too broad)

Vanda Pharms. v. West-Ward Pharms.

887 F.3d 1117 (Fed. Cir. 2018) (Lourie, Hughes, Prost dissetning)

Mayo

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

(a) administering a drug . . . to a subject having said . . . disorder; and

(b) determining the level of [metabolite] in said subject . . . ,

wherein the level of [metabolite] less than [X] indicates a need to increase the amount of said drug . . . and

wherein the level of [metabolite] greater than [X] indicates a need to decrease the amount of said drug subsequently administered to said subject.

Vanda

A method for treating [schizophrenia] with [a drug] . . . the method comprising the steps of:

determining whether the patient is a CYP2D6 poor metabolizer by:

obtaining . . . a biological sample from the patient; and

performing . . . a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metabolizer genotype; and

if the patient has a CYP2D6 poor metabolizer genotype, then . . . **administering [the drug] to the patient [at dose X]**, and

if the patient does not have a CYP2D6 poor metabolizer genotype, then . . . **administering [the drug] to the patient [at dose Y]**,

wherein [statement of intended result]

Vanda Pharms. v. West-Ward Pharms.

887 F.3d 1117 (Fed. Cir. 2018) (Lourie, Hughes, Prost dissetning)

- Prost Dissent:
  - Claims do not state law of nature, "but do no more than direct the relevant audience to apply it" in a "routine and conventional" manner
  - Differences in Vanda's claims reflect "drafting efforts designed to monopolize the law of nature itself."
  - Majority "conflates" step one and step two
  - Claims merely disclose the natural law that a known side effect could be reduced by administering a lower dose to CYP2D6 poor metabolizers.

Vanda Pharms. v. West-Ward Pharms.

887 F.3d 1117 (Fed. Cir. 2018) (Lourie, Hughes, Prost dissetning)

- Prost Dissent:
  - Footnote 1: Court found claims non-obvious based on unexpectedness of need to adjust dose b/c some people are poor metabolizers
  - "[T]he district court found non-obviousness based on the revelation of the natural law underpinning the claims, not in any other aspect of the claims"

Exergen Corp. v. Kaz USA Inc.

2018 U.S. App. LEXIS 6004 (Fed. Cir. Mar. 8, 2018) (Moore, Bryson, Hughes dissenting)

- Claims: Thermometer that calculates person's core temperature by detecting temp above superficial temporal artery
  - "A method of detecting human body temperature comprising making at least [3] readings per second while moving a radiation detector to scan across a region of skin over an artery to electronically determine a body temperature approximation, distinct from skin surface temperature."
  - Also a corresponding device claim

Exergen Corp. v. Kaz USA Inc.

2018 U.S. App. LEXIS 6004 (Fed. Cir. Mar. 8, 2018) (Moore, Bryson, Hughes dissenting)

- Step one: not addressed by Federal Circuit
- Step two: pass
  - Inventor made discovery and "incorporated that discovery into an unconventional method of temperature measurement."
  - Known in prior art ≠ "conventional, routine, and well-understood"

Exergen Corp. v. Kaz USA Inc.

2018 U.S. App. LEXIS 6004 (Fed. Cir. Mar. 8, 2018) (Moore, Bryson, Hughes dissenting)

- Court denied JMOL on § 101 defense
- Step two = question of fact = deference
- No special verdict questions re: § 101 defense
- Does Seventh Amendment require facts underlying 101 analysis to be decided by jury?

Exergen Corp. v. Kaz USA Inc.

2018 U.S. App. LEXIS 6004 (Fed. Cir. Mar. 8, 2018) (Moore, Bryson, Hughes dissenting)

- Hughes Dissent:
  - Step one: fail
    - Claims "merely calculate a law of nature using conventional, commercially available technology"
    - Law of nature here was relationship b/w core body temp and forehead skin temp
  - Step two: fail
    - Claimed invention = using preexisting temperature detector to take conventional and routine measurement of forehead skin temperature
    - "[T]he Majority opinion erroneously conflates step two with a novelty inquiry"

*Hope for Diagnostic and Treatment Method Claims Post-*Alice

- Federal Circuit has upheld claims directed to
  - (1) specific treatment steps, and
  - (2) patent-ineligible concepts applied via a novel method
- For patent-drafters:
  - Claim particularized treatment steps
  - Specific dosing regimens
  - Performance of novel measurement steps

Forthcoming PTO Guidance

- Director Iancu:
  - "Distorted legal conclusions" about patent eligibility "must end"
  - Working on **further** guidance and soliciting public input
    - Better define "abstract ideas" :
      - Mathematical concepts
      - Methods organizing human activities (basic economic/marketing/sales tools)
      - Mental processes
    - Improper incorporation of obviousness and written description issues into § 101 analysis

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Biosimilar Companies Leveraging IPRs to Clear Path to Market

- Record number of post-grant petitions filed against biopharma drug patents in 2017
  - **251** biopharma-related PTAB petitions filed in 2017
    - Up from **179** filed in 2016
  - Biopharma = **11%** of all post grant petitions in 2017
  - Biopharma IPR petitions nearly **double** since 2014

Biosimilar Companies Leveraging IPRs to Clear Path to Market

- Significant rise in challenges to biologics patents
  - **70** IPRs against biologics in 2017
    - Fewer than **20** the previous two years
  - Petitions focused on Blockbuster biologics:
    - Herceptin®
    - Humira®
    - Rituxan®
- Why?
  - Biosimilar developers' incentive to challenge blocking patents before filing a marketing application
  - No need for Art. III standing for biosimilars to file IPRs

Biosimilar Companies Leveraging IPRs to Clear Path to Market

- BUT, Art. III standing required to appeal
- ***Momenta v. BMS***, No. 17-1694 (Fed. Cir. argued Dec. 5, 2017) will clarify when biosimilar companies have standing to appeal
- Background: PTAB upheld validity of BMS patent covering Orencia
  - Momenta had invested $$ in developing biosimilar, appealed
- Relevant precedent:
  - *Sandoz v. Amgen*, 773 F.3d 1274 (Fed. Cir. 2014): Biosimilar that has not filed marketing application does not meet Art. III justiciability requirement to bring DJ action
  - *Phigenix v. Immunogen*, 845 F.3d 1168 (Fed. Cir. 2017): no standing to appeal IPR where challenger alleged only hypothetical licensing injury
    - Estoppel provisions of IPR statute ≠ injury in fact

Momenta v. BMS, No. 17-1694 (Fed. Cir. argued Dec. 5, 2017)

- Momenta:
  - Requirement of marketing application specific to DJ action
  - Estoppel effect of 35 U.S.C. § 315(e) creates injury in fact where party is engaged in activity that would give rise to future suit
- BMS:
  - No injury because claims based on speculative infringement liability, hypothetical economic injury
  - Bypassing BPCIA pathway for challenging brands
- Parties filed supplemental arguments in light of:
  - *Altaire Pharms, Inc. v. Paragon BioTeck, Inc.*, 889 F.3d 1274 (Fed. Cir. 2018) (Art. III standing without seeking FDA approval to market)
  - *JTEKT Corp. v. GKN Auto., Ltd.*, 898 F.3d 1217 (Fed. Cir. 2018) (no Art. III standing where no substantial risk of future infringement)

…Or Perhaps We'll See a Sharp Decline in Biopharma IPR Challenges

- **Proposed Legislation**: Hatch-Waxman Integrity Act of 2018
  - Sen. Hatch proposed amendment to new CREATES Act
    - Biosimilars/generics can only challenge brand patents in district court using abbreviated regulatory approval pathway if they do not file IPR/PGR
  - Purpose: to prevent IPR/PGR process from undercutting purpose of Hatch-Waxman Act, which created a patent-challenge process for generics/biologics

> Section 5(d) amends the PHS Act to require that applications submitted to FDA under 351(k) of the PHS Act include, with respect to any patent that is, or that could be, included in the list of potentially infringed patents to be supplied by the reference product sponsor, a certification that neither the biosimilar applicant nor any party in privity has filed, or will file, a petition to institute an IPR or PGR challenge of that patent. Section 5(d) also requires that the Secretary of

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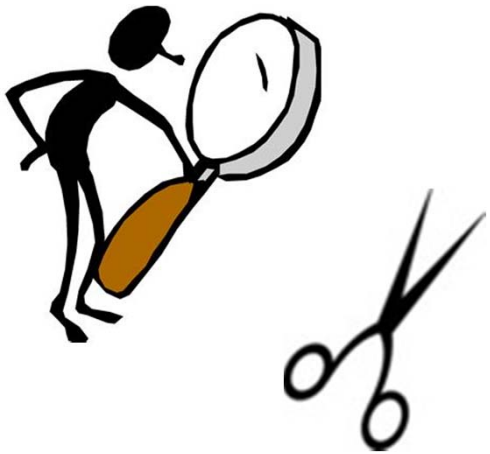
The CRISPR Patent Dispute Rages On

- CRISPR = Clustered Regularly Interspaced Short Palindromic Repeats
  - CRISPR Cas9 = gene editing enzyme, targets and cuts genetic material
    - Fix errors in genome
    - Add/remove genes
    - Turn genes on/off
  - Process:
    - Guide RNA finds target gene
    - CRISPR Cas9 enzyme cuts DNA



History of the CRISPR Patent Dispute

- 2012 – Scientists at UC create CRISPR system for gene editing, publish in *Science*
- 2013 – Scientists at Broad Institute develop improved CRISPR Cas9 system for eukaryotic cells, publish in *Science*
- 2014 – Broad is granted patents on its technology (eukaryotic)
- 2016 – UC initiates interference proceeding at USPTO
- 2017 – PTO finds Broad's work not obvious over UC's, and claims not directed to same invention. *No interference in fact*.
  - UC appeals to CAFC
- 2018 – CAFC hears oral arguments in April
  - UC argues PTO committed legal error, ignored evidence
  - Broad argues PTO was right given unpredictability in art

Regents of the University of California v. Broad Institute

No. 17-1907 (Fed. Cir. Sept. 10, 2018)

- *Affirmed*: Substantial evidence supported no interference in fact
  - UC and Broad applied for distinct patents on CRISPR technology.
  - UC's claimed invention does not render Broad's patents obvious
    - Broad's expert testified differences between prokaryotic and eukaryotic systems render application of CRISPR in eukaryotes unpredictable
    - No reasonable expectation of success in applying CRISPR-Cas9 in eukaryotic cell

CRISPR Technology – Continued Research and Licensing

- To date, CRISPR has been available for continuing research through licensing
  - Freely available to nonprofits and academic institutions via AddGene
  - Commercial licensing $$$
- Moving forward, third parties may wish to license from both entities to cover use in both prokaryotic and eukaryotic cells
- Potential for cross-licensing between UC and Broad to reduce cost for potential licensees
- Remaining uncertainty: UC's patent applications still pending before USPTO

Thank you

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