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Trends in Biotech Cases

- Biotech/Pharma patent cases have been outpacing others in growth since the mid-nineties
- Biotech/Pharma cases have the second highest median damages awards
- The Supreme Court has addressed patentable subject matter in three of the past four terms

*Source: PWC 2013 Patent Litigation Study
Study: Biotech Sector Ripe for Patent Trolling

Chelsea Allison, The Recorder
February 14, 2014

A study released Friday by UC-Hastings professor Robin Feldman and Harvard Fellow Dr. Nicholson Price predicted that biopharmaceutical companies will become a growing target of patent monetizers.

Their paper, Patent Trolling: Why Bio & Pharmaceuticals Are at Risk, examined life sciences patents—ranging from methods of treatment to active drug ingredients and dosage forms—of five
Patentable Subject Matter
“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.”
“Anything under the sun that is made by man…”
“The Court has long held that this provision contains an important *implicit* exception. Laws of nature, natural phenomena, and abstract ideas are not patentable.”
A Historical Perspective

- **Funk Bros. Seed Co. v. Kalo Inoculant Co.** (1948)
  - Novel mixture of bacterial strains – NOT PATENTABLE (phenomena of nature)

- **Parker v. Flook** (1978)
  - Application of concept/formula must itself be novel – NOT PATENTABLE (abstract idea)

- **Diamond v. Diehr** (1981)
  - Novel application of concept/formula – PATENTABLE

- **Gottschalk v. Benson** (1972)
  - Concept/formula not tied to application – NOT PATENTABLE (abstract idea)

- **Mayo v. Prometheus** (2012)
  - Concept/formula must be tied to something more than field of use

- **Bilski v. Kappos** (2010)
  - Novel application of concept/formula – PATENTABLE

- **Ass’n for Molecular Pathology v. Myriad** (2013)
  - Concept/formula must be tied to something more than field of use
• New discovery: Specific concentrations of metabolites, 6-TG and 6-MMP, that indicated that dosage of a thiopurine drug was either too high or too low

• But claims covering methods of administering thiopurine drugs using this discovery are not patentable
1. A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

(a) **administering** a drug … to a subject having said immune-mediated gastrointestinal disorder; and

(b) **determining** the level of [the drug],

**wherein** the level of [the drug less than a certain amount] indicates a need to increase the amount of said drug subsequently administered to said subject and

**wherein** the level of [the drug above a certain amount] indicates a need to decrease the amount of said drug subsequently administered to said subject.
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*wherein* the level of [the drug above a certain amount] indicates a need to decrease the amount of said drug subsequently administered to said subject.

- “[T]o consider the three steps as an ordered combination *adds nothing to* the laws of nature that is not already present when the steps are considered separately.”

- “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 … [do more than] monopolize the law of nature itself.”
New discovery: Precise location of two human genes, mutations that can substantially increase the risks of breast and ovarian cancer (BRCA1 and BRCA2 genes on chromosomes 17 and 13)

But, claims covering the isolated DNA sequence are **not patentable**

However, claims covering synthetically created complementary DNA (cDNA) **are** patentable
1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.

2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.

6. An isolated DNA having at least 15 nucleotides of the DNA of claim 2.

- “[Myriad] found an important and useful gene, but separating that gene from its surrounding genetics material is not an act of invention”
- “Nor are Myriad’s claims saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a nonnaturally occurring molecule...the claims understandably focus on the genetic information encoded in the BRCA1 and BRCA2 genes.”
Myriad – cDNA is an “Act of Invention”

- Creation of cDNA results in an exons-only molecule that is not naturally occurring

- Despite Petitioner’s argument that “[t]he nucleotide sequence of cDNA is dictated by nature, not by the lab technician,” the Supreme Court held that the cDNA is patentable because “the lab technician unquestionably creates something new when cDNA is made.”
New discovery: Cell-free fetal DNA (cffDNA) is detectable in maternal serum or plasma samples

But, Sequenom’s method of non-invasive pre-natal diagnosis based on this discovery is **not patentable**
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.

“[T]he only inventive part of the patent is that the conventional techniques of DNA detection known at the time of the invention are applied to paternally inherited cffDNA as opposed to other types of DNA. Thus, the only inventive concept contained in the patent is the discovery of cffDNA, which is not patentable.”
Preemption of all practical uses of the abstract idea or law of nature has been a consideration – See Gottschalk v. Benson, 409 U.S. 63, 71-72 (1972)

However, Ariosa took it further, stating “[i]f the alternative methods are not commercially viable, then the effect of the patent in practice would be to preempt all uses of the natural phenomenon.”
However, Dolly herself is an exact genetic replica of another sheep and does not possess markedly different characteristics from any [farm animals] found in nature. Dolly’s genetic identity to her donor parent renders her unpatentable.”

Is the Claim Patent Eligible?

- Basic discovery vs. “act of invention” – patentable claim must encompass something new and specifically address the new thing created
- Must “add enough” to the phenomenon or law of nature – cannot simply say, in effect, “apply it”
- Must have “markedly different characteristics” from what already exists in nature
- Regardless of how great the discovery, must add something more than “well-understood, routine, conventional” steps to a natural phenomenon, concept, or law of nature
- Must not preempt use of (commercially viable) alternatives?
Safe Harbor Exception to Patent Infringement
Agenda

- Background of the Safe Harbor
- Types of Protected Inventions
- Types of Protected Activity
35 U.S.C. § 271(e)(1)  
The “Safe Harbor”

“It shall not be an act of infringement to make, use, offer to sell, or sell . . . a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.”
The “Dual Distortions” Prior to the Safe Harbor Provision

Actual Patent Term

FDA Approval

Effective Patent Term

FDA Approval
“From the perspective of R&D pharmaceutical corporations, for instance, the law giveth, section 156, and the law taketh away, section 271(e)(1).”

*AbTox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997).
Defining the Patented Invention

Drugs\(^1\)

Medical Devices\(^2\)

Research Tools\(^3\)

\(^1\) Eli Lilly and Co. v. Medtronic, 496 U.S. 661 (1990).
\(^2\) Proveris Scientific Corp. v. Innovasystems, Inc., 536 F.3d 1256 (Fed. Cir. 2008).
The Safe Harbor
The Safe Harbor

Drugs
Expansion #1: Medical Devices

- **Eli Lilly & Co. v. Medtronic Inc.**, 496 U.S. 661 (1990)
  - The safe harbor:
    - includes (class III) medical devices
    - protects all “patented inventions” subject to a “Federal law which regulates the manufacture, use, or sale of drugs”
    - invokes “an entire scheme of regulation”—not just the drug provisions in FDCA
- **AbTox Inc. v. Exitron Corp.**, 122 F.3d 1019 (Fed. Cir. 1997)
  - extended to class II medical devices
Expansion #1: Medical Devices
Expansion #2: Reasonably Related

- **Preclinical** research reasonably related to submitting information to the FDA is protected **even if** never provided to the FDA
- But basic research is not protected
Expansion #2: Reasonably Related

Drugs
Medical Devices
Pre-Clinical, Clinical
Gate #1: Research Tools

- *Proveris v. Innovasystems*, 536 F.3d 1256 (Fed. Cir. 2008)
  - optical spray analyzer (OSA)
  - for testing aerosol sprays for drug delivery, used for FDA submissions
  - not subject to regulatory approval
  - no patent term “distortions”
  - not protected by safe harbor
Gate #1: Research Tools

- Drugs
- Medical Devices
- Pre-Clinical, Clinical

*Research Tools*
Gate #2: Post-Market Activity

- Post-market activity *may* be protected
- Activity must be *required* for continuing FDA approval
Gate #2: Post-Market Activity
Putting It All Together

- **Protected:**
  - drugs and devices
  - preclinical and clinical activities
  - “reasonably related” to FDA submission
  - post-market activities if required for maintaining FDA approval, but not if for “routine” submissions

- **“Research tools” not subject to regulatory approval are not necessarily protected by the safe harbor.**
  - OSAs: lab equipment not protected under Proveris.
  - What about other “tools” – proteins? ASRs?
Follow-On Biologics Regulatory Approval Pathway: Legislation and Implementation
Agenda

- Background on the BPCIA
- Implementation to Date
- Open Issues and Pharmacy Substitution
- Recent and Upcoming FDA Actions
The Biologics Price Competition and Innovation Act of 2009

- Creates an abbreviated licensure pathway for biological products found to be “biosimilar to” or “interchangeable with” an FDA-licensed reference product.

- Establishes two types of follow-on biologics:
  - Biosimilar
  - Interchangeable
Key Features of the Law

• Application for a biosimilar or interchangeable biologic:
  - Must treat the same condition as the reference product; have the same mechanism of action (if known) as the reference product; have the same route of administration, dosage form, & strength as the reference product; be manufactured, processed, packed, or held in a facility that meets standards designed to assure that the biological product continues to be safe, pure, and potent.
Key Features of the Law

• Provides exclusivity to the reference product and first interchangeable product under certain conditions.
  – Reference products:
    • No follow-on biologic applications for 4 years.
    • No follow-on biologic approvals for 12 years.
  – First Interchangeable Products: no subsequent interchangeable approved for earlier of:
    • 1 year after commercial marketing;
    • 18 months after resolution of patent suit;
    • 42 months after approval, if patent suit instituted & ongoing; or
    • 18 months after approval, if no patent suit instituted.

• Establishes a detailed procedural framework for addressing patent disputes.
Implementation to Date

- To date, FDA has issued five draft guidance documents.
  
  - **Scientific Considerations in Demonstrating Biosimilarity to a Reference Product**
    - Provides an overview of FDA’s approach to determining biosimilarity and discusses important scientific considerations in demonstrating biosimilarity.
  
  - **Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product**
    - Details analytical factors to be considered in evaluating biosimilarity; intended to aid in completion of an application’s CMC section.
  
  - **Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009**
    - Answers common questions on both administrative and substantive issues.
  
  - **Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants**
    - Describes procedures for requesting / conducting meetings with FDA regarding follow-on biologic product development.
  
  - **Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product**
    - Discusses clinical pharmacology studies for biosimilar products as part of a stepwise approach to developing the data needed to support a demonstration of biosimilarity.

- These draft guidances focus solely on biosimilarity; none addresses the standards for interchangeability.
Implementation to Date

• No applications have yet been approved.

• As of February 2014:
  – No applications have been submitted.
  – 36 follow-on biologic programs are in development.
  – 21 INDs have been submitted.
  – Multiple BPD Type 4 meetings have been held.
Many questions remain unanswered in FDA’s implementation of the BPCIA:

- FDA has not yet defined the standards that will be applied to establish interchangeability.
- FDA has not yet established the method(s) by which it will approve names for labeling and marketing of follow-on biologics.
- Concerns that the BPCIA’s data requirements are time and resource intensive, creating a regulatory burden.
- Debate over the proper interpretation of, and potential changes to, the length of the exclusivity periods established in the statute.

Many states are considering legislation regarding pharmacy substitution.

- Some have already enacted laws restricting substitution.
- Over 10 other states are considering, are soon expected to consider, or have considered and declined to advance such laws.
Recent and Upcoming FDA Actions

- Numerous citizen petitions have been submitted to FDA regarding the naming of follow-on biologics.
- Recent listening sessions have been held with interested parties regarding follow-on biologics nomenclature.
- FDA intends to issue guidance regarding follow-on biologics nomenclature prior to approving any applications.
- Full implementation of the BPCIA is expected to take several more years.
Takeaways

- Interchangeability standards and nomenclature are critical issues, yet FDA has not yet provided guidance.
- Pharmacy substitution policies may shape the economic viability of follow-on biologics and the utility of the pathway.
- Companies should stay abreast of FDA activities and seize opportunities to offer input on implementation.
- Companies with early-stage product candidates should meet with FDA to assess the feasibility of, and requirements for, licensure.
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