PHARMACEUTICAL PATENT LAW

(So, you want to protect your IP?)

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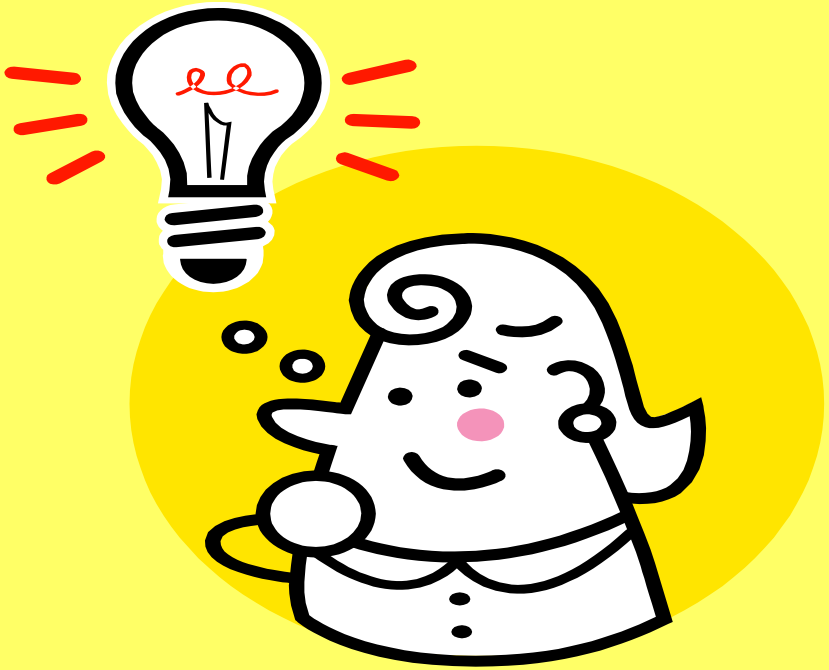
DISCLAIMER

This is NOT legal advise. The main intent of the information provided is to educate pharmaceutical scientists and other readers about patent law so that they may more effectively communicate with their patent attorneys.

Patent law is mostly about



and $


EINSTEIN'S IMPLIFIED
Keep it simple,
not simpler
s.harris

GOAL

To make all of you ditch science and take up patent law

GOAL

To advance the knowledge of patent law among pharmaceutical scientists, both present and FUTURE

SIGNIFICANCE

- **To promote effective communication between pharmaceutical scientists and patent attorneys, who work together to obtain a patent**

- **To understand career opportunities for scientists in patent law.**

“Because there is a general lack of understanding of each culture, these interactions often lead to a cognitive friction that is both disturbing and costly to society.”

A Convergence of Science and Law (National Academy Press, 2001)

http://books.nap.edu/html/science_law/report.pdf

Learning Objectives

1. Introduction to Patent Law Basics

a. Types of Intellectual Property

b. Constitutional and Policy Bases for Patents

c. Patent Rights

d. Parts of a Patent Document

1. Understanding Claims

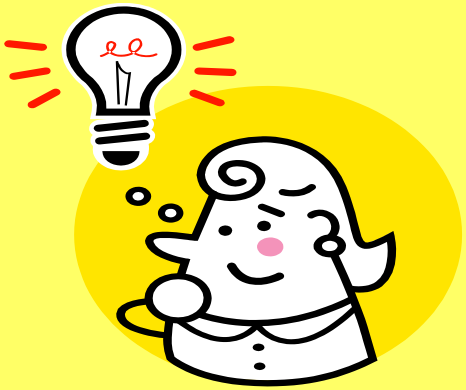
e. Patent Requirements

f. Invention Steps

g. Process to get a patent (patent prosecution)

Learning Objectives (cont'd)

2. Apply case studies from Hatch-Waxman Act litigation (patent battles between generics and innovators) to better understand patent law
3. Discuss potential impact of recent Court decisions on drug development



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INTRODUCTION TO PATENT LAW BASICS

INTELLECTUAL PROPERTY TYPES (PROTECTION)

- **PATENTS**
- **COPYRIGHT**
- **TRADEMARK**
- **TRADE SECRETS**

Why patents?
Policy Basis

United States Constitutional Basis for Patents and Copyrights

Article I, § 8, cl 8

“To promote

the Progress of Science and useful Arts

by securing for limited Times to Authors and Inventors

the exclusive Right

to their respective Writings and Discoveries”

(emphasis added)

A patent is property right granted by the US government to an inventor

Property Right

to exclude others from:
making,
using,
offering for sale or selling
the invention or

importing the invention for a limited time

in exchange for public disclosure of the invention

Simply stated:

An utility US patent is a limited-time monopoly granted by the government (20 years from effective filing date of the patent application)

Inventor may

sell

bequeath

transfer (assign) or

license

the patent to anyone

Types of Patents (Subject Matter)

1. Utility
2. Plant
3. Design

Types of Utility patents

1. Machine
2. Manufacture (e.g., oil eating bacteria)
3. Composition of Matter (e.g., NCE)
4. Process

What is patentable? (35 U.S.C. § 101)

Whoever invents or discovers

any new and useful

process, machine, manufacture or composition of matter, or

any useful improvement thereof

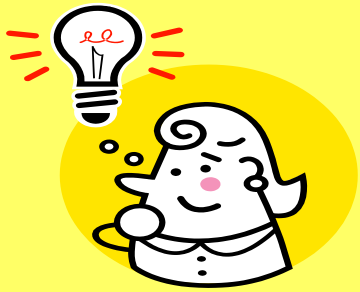
may obtain a patent

What is patentable? (Utility Patents)

"anything under the sun that is made by man"

- **Diamond v. Chakrabarty, 447 U.S.. 303 (1980)**

Requirements for a patent



Patent law: a “nano” review

- 35 U.S.C. § 101: “Utility” or Useful
- 35 U.S.C. § 102: “Novelty ” or New
- 35 U.S.C. § 103: “Nonobviousness”

Patent Requirements

1. Allowed by statue
2. Useful

Patent Requirements (cont'd)

3. Novel

in relation to "prior art"

What is prior art?

Concept:

What is known pertinent to the invention at the time of invention?

Patent Requirements (cont'd)

4. Non-obvious (to whom?)

to a person of ordinary skill in the art (POSITA) from the prior art (at the time of the invention)

.

35 U.S.C. § 103:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

INVENTION STEPS

(PATENT)

1. Conception

2. Reduction to Practice

Conception is the formation in inventor's mind of a definite and permanent idea of the complete and operative invention

Example

The conception of a chemical compound requires the inventor

to have a mental picture of its structure

to define it by its method of preparation, its physical or chemical properties

Reduction to Practice (RTP)

ACTUAL – MAKING THE INVENTION

CONSTRUCTIVE – FILING YOUR PATENT APPLICATION

Key Parts of a Patent Document (Describing the Invention)

DOCUMENT DETAILS

1. Title
2. Background
3. Summary
4. Drawings (e.g., structures)
5. Detailed description (where the science goes)
6. Claims

- 37 CFR 1.77

Major Sections of a Patent Document/Application

- **SPECIFICATION**
- **CLAIMS**

SPECIFICATION

“DETAILS” OF YOUR INVENTION

35 U.S.C. 112 (¶ 1)

1. WRITTEN DESCRIPTION
2. ENABLEMENT
3. BEST MODE

35 U.S.C. 112 Specification (¶ 1)

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Understanding and Importance of Claims

Claim Drafting is Vital

To coin a phrase, the name of the game is the claim

- Giles Rich, then Chief Judge of the Federal Circuit (CAFC), ***The Extent of the Protection and Interpretation of Claims-American Perspectives*****, 21 Int'l Rev. Indus. Prop. & Copyright L., 497, 499 (1990)**

Claim Drafting is Vital (cont'd)

"It is a 'bedrock principle' of patent law that the claims of a patent define the invention to which a patentee is entitled the right to exclude"

- Philips v. AWH Corp. 415 F. 3d 1303 (Fed. Cir. 2005)

Patent claims define boundaries of an invention ("metes and bounds")

Infringement: Like Trespassing

35 U.S.C. 112 (¶ 2)

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

CLAIMS

WHAT IS/ARE YOUR INVENTION(S)?

METHOD FOR TREATING PAIN BY ADMINISTERING 24 HOUR ORAL OPIOID FORMULATIONS

- **US Patent No. 5,672, 360**
- **Issued : 9/30/1997**
- **Inventors: Richard S. Sackler, Robert F. Kalko and Paul Goldenhelm**
- **Assignee: Purdue Pharma L.P.**

Claims

What is claimed is:

- **1. A method of effectively treating pain in humans comprising orally administering to a human on a once-a-day basis an oral sustained release dosage form containing an opioid analgesic or salt thereof which upon administration provides a time to maximum plasma concentration (Tmax) of said opioid in about 2 to about 10 hours and a maximum plasma concentration (Cmax) which is more than twice the plasma level of said opioid at about 24 hours after administration of the dosage form, and which dosage form provides effective treatment of pain for about 24 hours or more after administration to the patient**

Claims (cont'd)

2. The method of claim 1, wherein Tmax occurs in about 2 to about 8 hours after oral administration of said dosage form

3. The method of claim 1, wherein Tmax occurs in about 6 to about 8 hours after oral administration of said dosage form

Claims (cont'd)

4. The method of claim 1 wherein the said opiod analgesic is morphine sulfate

Meaning of words often the grounds for patent infringement dispute

Which word is open to interpretation?

Claim 2.

A touch probe . . . the probe generating a trigger signal when said sensing tip contacts an object . . .

[Renishaw PLC v. Marposs Societa' Per Azioni 158 F.3d. 1243 (Fed. Cir. 1998)]

Process to get a patent (patent prosecution)

Patenting process (cont'd)

Drafting an application requires special knowledge and style

Patenting process (cont'd)

File application with USPTO (United States Patent and Trademark Office) with full disclosure of invention

Patenting Process (cont'd)

Patent application is reviewed by the USPTO, i.e., examiner(s); this part is analogous to a review of a scientific paper or grant application.

Applicant has a limited number of opportunities to rebut examiner's statements (claim rejection).

A patent is issued if the application in its revised form meets all the legal and technical requirements.

Rejections at the examiner level can be challenged at higher levels within the USPTO and/or in the courts

Changes in Patent Law

America Invents Act of 2011

Change from:

"First to Invent" to "First to File"

Implication:

File your patent application as soon as possible

Hatch-Waxman Act
(where drug and patent laws meet)

DRUG PRICE COMPETITION AND PATENT TERM RESTORATION ACT OF 1984

H-W POLICY ISSUES

To Protect Intellectual Property

- ***Encourage Innovation (new drugs)***

Foster Competition

- ***Consumer Benefit (generic drugs)***

Patents and H-W ACT

- New Drug Applications (NDAs) are required to include:
  - patent number and
  - expiration date of any patent that claims either
    - the drug (active ingredient and/or composition or formulation) or
    - method of use (i.e., indication)

Patents and H-W Act (cont'd)

FDA is required to list the submitted patent information in its "Orange" book

Approved Drug Products with Therapeutic Equivalence Evaluations

H-W Certifications

A generic company (the ANDA/503(b)2 applicant) must certify that drug :

- **I) has not been patented;**
- **II) patent has expired;**
- **III) patent will expire on a given date and that generic will not be marketed prior to that date; OR**
- **IV) patent is not infringed or invalid**
  - **(where the action is)**

Paragraph IV Certification

Generic company:

- **must notify innovator about ANDA filing**
- **must explain:**
  - **why generic product will not infringe innovator patent OR**
  - **why innovator patent is invalid**

Under the H-W Act, filing such an ANDA is open to infringement challenges by the patentee.

THE PROZAC® CASE
(Pharmacologists Beware!)

One Drug – fluoxetine

Its three uses: antidepressant, antianxiety, serotonin reuptake inhibitor (same mechanism of action)

Three patents – one patent for each use

Courts to Eli Lilly: You only have one invention!

THE PROZAC® CASE
INVALIDITY-DOUBLE PATENTING

FACTS

- fluoxetine (active ingredient of Prozac)
- Barr Labs submitted ANDA in December 1995 for generic fluoxetine with ¶ IV certification
- Lilly brought action alleging Barr's ANDA application infringed its patents

Obviousness-type Double Patenting

"[T]he extension of exclusive rights through claims in a later patent that are not patentably distinct for claims in an earlier patent." (emphasis added)

(222 F.3d at 985)

Issue for Court of Appeals for the Federal Circuit (CAFC)

222 F.3d. 973 (2000) – Part I

To determine whether claim 1 of the '895 patent (issued April 19, 1977) covers subject matter claimed in claim 7 of the '549 patent (issued December 2, 1986)

A method of blocking the uptake of serotonin by brain neurons in animals comprising the administering to said animal of fluoxetine (claim 7, "549" patent)

A method of treating human suffering from depression which comprises administering to said human of an effective antidepressant dose of fluoexitine (claim 1, "895" patent)

Issue for CAFC
251 F.3d 955 (2001) – Part II

To determine whether claim 1 of the ‘213 patent (issued May 20, 1986) covers subject matter claimed in claim 7 of the ‘549 patent (issued December 12, 1986)

A method of blocking the uptake of serotonin by brain neurons in animals comprising the administering to said animal of fluoxetine (claim 7, '549 patent)

A method for treating anxiety in a human subject in need of such treatment which comprises the administration to such human an effective amount of fluoxetine or norfluoextine or pharmaceutically acceptable salts thereof (claim 1, '213 patent)

Decision

The subject of claim 7 of the ‘549 patent is obvious because it is covered by the claims from the ‘895 and ‘213 patents.

Barr wins!

The Prilosec® Case
(Attention Formulators!)

Facts

- Omeprazole – active ingredient of Prilosec® (acid labile)
- Kremers Urban Development Co. (KUDCo.) submitted ANDA for generic omeprazole with ¶ IV certification
- Patent holder Astra Aktiebolag, owner of US Patents Nos. 4,786,505 (the '505 patent and 4,853,230 (the '230 patent) filed an infringement suit against KUDCo.

Prilosec® Case (cont'd)

Claim 1 of the '505 patent states (in part):

- **An oral pharmaceutical preparation comprising:**
- **(a) a core region comprising an effective amount of a material selected from the group consisting of omeprazole plus an alkaline reacting compound, an alkaline omeprazole salt plus an alkaline reacting compound and an omeprazole salt alone; (emphasis added). . .**

Prilosec® Case (cont'd)
222 F. Supp.2d 423 (S.D.N.Y. 2002)

- **The main issue:**
  - **Did the Kremers Urban Development Co. (KUDCo) formulation contain an alkaline reacting compound (ARC)?**

Prilosec® Case (cont'd)

- **Formulation Differences**
  - **Core Composition**
- **KUDCo microtablet has 3 parts:**
  - **a core, a subcoat and enteric coat**
  - **The court concluded that the subcoat and the enteric coat of the microtablet do not differ from the '505 patent**

Prilosec®Case (Cont'd)

DECISION (affirmed by CAFC in 2003)

The Court held that KUDCo product did not infringe the '505 patent because the KUDCo microtablet was "designed around" the '505 patent by developing a formulation that did not require an ARC in its core

KUDCo wins!

Prilosec Case (cont'd)

- **There were 3 other generic companies that had also filed ANDAs**
  - **Andrx Pharmaceuticals, Cheminor Drugs, and Genpharm, Inc.**

They all were found to infringe on several of the claims of the Astra patent(s)

Impact of Case Law on Drug Development

Case Law Topics

1. Patentable Subject Matter ("101" issues)
2. Safe Harbor Provisions
3. Obviousness (Obvious to Try) ("103" issues

TOPICS

1. Patentable Subject Matter (“101” issues)

Patentable Subject Matter ("101" issue)

"[L]aws of nature, natural phenomena, and abstract ideas are not patentable"

(e.g. $E = mc^2$)

***Diamond v. Diehr*, 450, U.S. 175, 185, (1981)**

Mayo v. Prometheus

(566 U.S. ___ (2012) (Supreme Court case)

FACTS:

Mayo Clinic used diagnostic tests sold by Prometheus Laboratories based their two patents: U.S. No. 6,355,623 (the '623 patent), and 6,680,302 (the '302 patent)

Mayo stated in 2004 that it planned to market its own version of a similar diagnostic test.

Prometheus filed infringement suit against Mayo

Mayo v. Prometheus (cont'd)
(566 U.S. ___ (2012)

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Mayo v. Prometheus (cont'd)

The Court examined claim 1 of the '623 patent (considered "typical"), which states:

"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-thioguanaine in said subject having said immune-mediated gastrointestinal disorder,

"wherein the level of 6-thioguainine less than about 230 pmol per $8x10^8$ 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 $8X10^8$ indicates a need to decrease the amount of said drug subsequently administered to said subject."

Mayo v. Prometheus (cont'd)

Mayo Clinic's test used a slightly higher concentration (450 pmol per $8X10^8$ red blood) for toxicity. Therefore, its method does infringe the '623 patent.

Mayo v. Prometheus (cont'd)

District Court concluded that claims of the '623 patent, which deal with concentration-effect relationships, belong to natural laws, and thus, were not patentable.

Mayo v. Prometheus (cont'd)

CAFC: Reversed lower court ruling. Using the "machine or transformation" test.

Mayo v. Prometheus (cont'd)

A process can patented, only if

(a) "it is tied to a particular machine or apparatus, or

(b) it transforms a particular article into a different state or thing."

In re Bilski, 545 F3d. 934,954 (Fed. Cir. 2008) (en banc)

Mayo v. Prometheus (cont'd)

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Mayo v. Prometheus (cont'd)

Supreme Court in reversing CAFC said:

While "the 'machine-or-transformation' test is an '*important and useful clue*' to patentability, we have neither said or implied that the test trumps the 'law of nature' exclusion"

Mayo wins!

Case Law Topics

1. Patentable Subject Matter ("101" issues) 
2. Safe Harbor Provisions
3. Obviousness (Obvious to Try) ("103" issues

Safe Harbor Provisions

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States 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. (emphasis added) (35 U.S.C. 271(e)(1))

Safe Harbor Provisions (cont'd)

Enacted by Congress primarily to overrule Roche v. Bolar (733 F.2d. 858) (Fed. Cir. 1984)

Applying patent law*, Bolar was found by CAFC to have infringed Roche's patent on flurazepam because it initiated ANDA studies before the expiry of the patent.

*** . . . "whoever without authority . . . uses . . . any patented invention, within the United States during the term of the patent therefor, infringes the patent ." 35 U.S.C §271(a)**

Merck v. Integra
543 U.S.193 (2005)

FACTS

1. Integra Life Sciences owns several (5) patents covering the “RGD” peptide.
2. Scripps researcher discovers that a cyclic RGD (EMD 66203) peptide provided by collaborator Merck can inhibit tumor growth in chickens (inhibition of angiogenesis)

Merck v. Integra (cont'd)

FACTS (cont'd)

3. Scripps then focused on developing EMD peptides as a potential drug candidates.
4. Integra files patent infringement suit against Merck and Scripps.

Merck v. Integra (cont'd)

District Court Holding

1. Merck and Scripps infringed Integra's Patents
2. Awarded $15 million in damages, later reduced to $ 6.375 million

Merck v. Integra (cont'd)
331 F.3d 860 (Fed. Cir., June 6, 2003)

CAFC (2-1 split)

1. **Affirmed lower court's ruling on infringement**
2. **Remands to lower court to reconsider infringement award because Integra purchased all the infringing patents from Telios for $20,000,000.**

Merck v. Integra (decision)

543 U.S.193 (2005)

Supreme Court overturned patent infringement ruling of lower courts, stating:

> **Congress did not limit § 271(e)(1')s safe harbor to development of information for inclusion in a submission to the FDA; nor did it create an exemption applicable only to research relevant to filing an ANDA for approval for a generic drug. . .”**

Merck wins!

Case Law Topics

1. Patentable Subject Matter ("101" issues) 
2. Safe Harbor Provisions 
3. Obviousness (Obvious to Try) ("103" issues

Obviousness (Obvious to try)

"When there is a design need or market pressure to solve problem, and there are a finite number of identified, predictable solutions, a person of ordinary skill has a good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103." (emphasis added)

-KSR INT'L CO. *v*. TELEFAX INC. 550 U.S. 398, 421 (2007)

Bayer Pharma v. Barr Laboratories (575 F3d. 1341) (2009)

FACTS:

Barr filed an ANDA to market a generic version of Yasmin®.

Bayer files suit under the Hatch-Waxman Act alleging that Barr's product will infringe its U.S. Patent No. 6,787,531 (the '531 patent)

Bayer Pharma v. Barr Laboratories (575 F3d. 1341) (2009)

Claim 1, representative of the '531 patent:

A pharmaceutical composition comprising from about 2 mg to 4 mg of micronized drospirenone particles, about 0.01 mg to about 0.05 of 17α-ethynlestradiol, and one or more pharmaceutically acceptable carriers, the composition being in an oral dosage form exposed to the gastric environment upon dissolution and the composition being effective for oral contraception in a human female. (emphasis added)

Drospirenone Pharmacokinetic Properties

1. Poorly water soluble (hence, micronized)
2. Acid labile (isomerizes at pH 1, in vitro)
3. Absorbed equally well in-vivo (with or without enteric coating)
4. Similar to spirorenone (prior art)

Decision

The ‘531 patent is invalid for obviousness

Barr wins!

Summary of Court Cases On Drug Development

1. Supreme Court decisions have:
   a. broadened the scope of the safe harbor provisions, making it "easier" to avoid infringement when using patented information for drug development
   b. raised the standards of obviousness, making patenting an invention more difficult

CONCLUSIONS

Pharmaceutical scientists with a good understanding of patent law should be able to:

1. **better design their research for patenting purposes**
2. **communicate more effectively with patent attorneys**
3. **have an edge in the competitive job market (“a second skill set”)**

Questions?