FDA History and Intellectual Property

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Online Resources

• For the Opioids sessions, videos are available from the HarvardX MOOC, “The Opioid Crisis in America,” http://bit.ly/OpioidX.

Reminders

• Updated syllabus online: http://bit.ly/NUSLDrugLaw

Debates

• Debate 1: Prescription Drug User Fees (September 11, 2019)
• Debate 2: Off-Label Promotion (September 23, 2019)
• Debate 3: OTC Naloxone (October 16, 2019)
• Debate 4: Should the FDA be independent? (October 28, 2019)

All students should come to class prepared to debate if called upon.

Current Events in Drug Law

Debates

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Current Events in Drug Law

Johnson & Johnson loses Oklahoma opioid lawsuit
It’s a landmark ruling and a potentially continuous lid on the opioid industry’s troubles.
@reuterscom

Current Events in Drug Law

U.S. Opioid Damages May Reach $17 Billion, Legal Analyst Says
Monday’s $572 million judgment against Johnson & Johnson suggests future damages across the country could total $17 billion, said one legal expert.
@bloomberg.com

Current Events in Drug Law

FDA clears wearable device to better monitor patients
The Food and Drug Administration has approved a new wearable technology that can measure patients’ heart rate and physical activity.
@healthdata

Current Events in Drug Law

FDA Proposes Graphic Warnings for Cigarette Packages. Will They Work?
The FDA has proposed many graphic warnings for cigarette packs and ads to help curb smoking in the United States. But will they work?
@Healthline.com

Public Comment Brief


• Consult relevant legal, regulatory, and public health material to educate yourself about the context and implications for the proposed action.

• A structured “public comment” brief (5-6 pages) will be due before the start of class on Wednesday, October 2, 2019.
#NUSLDrugLaw on Twitter

• Be sure to tag the following in your tweets: @DrSinhaEsq #NUSLDrugLaw
• Need help getting started on Twitter? Schedule time during office hours!

Final Paper

• The final paper on a pre-approved topic should be 18-24 pages in length and contain appropriately formatted BlueBook references.
• A proposal outlining the topic significance, key questions, expected outcomes and preliminary sources will be due before class on Thursday, September 12, 2019. Please clear the topic with Dr. Sinha prior to beginning the proposal. Use the Hutt book as a resource for project ideas—a lot of great topics not covered in this class.
• The final assignment will be due before 3PM on Friday, November 15, 2019.
Some important laws related to the FDA

- Pure Food and Drug Act (1906) – “snake oil salesmen”
- Food Drug and Cosmetic Act (1938) – elixir sulfanilamide
- Kefauver-Harris Amendment (1962) – thalidomide
- Orphan Drug Act (1983) – rare diseases
- Prescription Drug User Fee Act (1992) – “regulatory capture”
- FDA Modernization Act (1997) – pediatric research
- FDA Amendments Act (2007) – postmarket research (Vioxx)
- Biologics Price Competition and Innovation Act (2009) – biologics

The Market Exclusivity Floor: Regulatory Exclusivity

<table>
<thead>
<tr>
<th>Type of Drug</th>
<th>Baseline</th>
<th>FDA Review Time</th>
<th>Total Approximate Length of Exclusivity Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional (Hatch-Waxman) Drug</td>
<td>5-year</td>
<td>(varies)</td>
<td>6-7 years</td>
</tr>
<tr>
<td>Orphan Drug</td>
<td>7-year</td>
<td>(varies)</td>
<td>8-9 years</td>
</tr>
<tr>
<td>Antibiotic Drug</td>
<td>10-year</td>
<td>(varies)</td>
<td>11-12 years</td>
</tr>
<tr>
<td>Biologics</td>
<td>12-year</td>
<td>(varies)</td>
<td>13-14 years</td>
</tr>
<tr>
<td>New formulation of existing drug</td>
<td>5-year</td>
<td>(varies)</td>
<td>4-5 years</td>
</tr>
</tbody>
</table>

The Market Exclusivity Ceiling: PATENTS

- Issued by the US Patent and Trade Office (USPTO)
- 20 years for inventions that are novel and non-obvious
- Allows inventors to EXCLUDE others (unlike trade secrets)
- Requires COMPLETE DISCLOSURE of invention on the patent itself
- Drug companies often add to their portfolio by evergreening
  - Secondary patents (e.g., salts, metabolites)
  - Tertiary patents (parts of a device)

Patents

- Right to exclude others from making, using, or selling the invention without inventor’s permission
  - NOT a right to make, use, sell, offer for sale or import!
- Time limitation
  - Utility patents → 20 years from filing
  - Design and Plant patents → 14 years from issue
- Geographic limitation to right
  - Patent is effective only in country that grants the patent
Why Grant Patent Rights?

- Provide incentives for innovation
- Reward invention and success
- Provide financial compensation to cover R&D, opportunity costs, etc.
- Encourage future investment
- Encourage public disclosure of innovations

Inventor

- Must have contributed to the subject matter of the claims
- Joint inventors – each inventor must have contributed to the subject matter of a claim
- Inventorship ≠ Authorship
- Only individuals (not corporations) can be inventors for U.S. patents
  - But rights can be assigned away

First to Invent v. First to File

Inventor with earliest date of invention is entitled to patent (old U.S. system) vs.
Inventor with earliest patent filing date is entitled to patent (rest of world, now current U.S. system)

Filing Date

- Filing Date – earliest date that the application for patent was filed
- Important for determining what counts as prior art
- Important for securing rights to patent
- Important for determining date that patent expires
  - For applications filed on or after June 8, 1995, the patent term is 20 years from the filing date
  - For applications that were filed before June 8, 1995, the patent term is 17 years from the issue date

Enbrel's main patent has already expired. But the drug is now protected by two “submarine patents,” so called because they wended their way through the patent office over a long period of time, hidden from view.

- Even though the inventions involved were made in the early 1990s, the patents were not granted until 2011 and 2012 and last until 2028 and 2029.
- If those patents hold, by 2029, Enbrel will have been on the market without generic competition for 31 years.
Anatomy of a Patent – Front Page

United States Patent

Title: Method of Inducing Aerobic Exercise in a Cat

Abstract: A method of inducing aerobic exercise in an unrestrained cat comprising the steps of:

1. Directing an intense coherent beam of invisible light produced by a handheld laser apparatus to produce a bright highly-focused pattern of light at the intersection of the beam and an opaque surface, said pattern selectively redirecting said beam out of the cat's immediate reach to induce said cat to run and chase said beam and pattern of light around an exercise area.

2. The method of claim 1 wherein said bright pattern of light is small in area relative to a paw of the cat.

GOAL: To provide the reader with enough information to enable one skilled in the art to understand the invention.

Background of the Invention

Summary

Description of the Figures

Description of the Preferred Embodiments

Anatomy of a Patent – Figures

Anatomy of a Patent - Claims

What is claimed is:

1. A method of inducing aerobic exercise in an unrestrained cat comprising the steps of:
   - directing an intense coherent beam of invisible light produced by a handheld laser apparatus to produce a bright highly-focused pattern of light at the intersection of the beam and an opaque surface, said pattern selectively redirecting said beam out of the cat's immediate reach to induce said cat to run and chase said beam and pattern of light around an exercise area.
   - The method of claim 1 wherein said bright pattern of light is small in area relative to a paw of the cat.

2. Types of claims:
   - Independent
   - Dependent

Anatomy of a Patent - Claims
Requirements for Patentability

- **Patentable subject matter**: (35 U.S.C. § 101)
- **Utility**: usefulness (35 U.S.C. § 101)
- **Novelty**: not anticipated in “prior art” (35 U.S.C. § 102)
- **Non-obviousness**: non-trivial extension of the known (35 U.S.C. § 103)
- **Disclosure and enablement**: must describe invention with sufficient particularity to enable one skilled in the art to “practice” it (35 U.S.C. § 112)

Patentable Subject Matter § 101

- 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, subject to the conditions and requirements of this title.
- “Anything under the sun that is made by man”
  - Patentable if made, modified, or transformed by man
  - No morality component in US

What can be patented (utility)

- Process (method)
- Machine
- Manufacture (article)
- Composition of matter (chemical)
- A new use or improvement for any of the above...

A better mousetrap

U.S Patent No. 6,865,843 (2005)

A better mouse


What cannot be patented

- Purely mental processes
- Mathematical Algorithms
- Scientific Principles
- Naturally Occurring Things
- Human Beings
Utility § 101
• 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, subject to the conditions and requirements of this title.
• Test: must be practical and specific, not merely of scientific interest
  • A new compound, gene, or antibody, without any known pharmacological activity or other practical utility, will not normally be patentable.

Novelty § 102
• A single “prior art” reference
  • “prior art” - any information that has been made available to the public in any form (e.g., patented, described in a printed publication, or in public use, on sale, or otherwise available to the public) before the filing date that might be relevant to a patent’s claims of originality
• Test: is every element of your invention in the prior art reference

Obviousness § 103
• One piece of prior art or combination of 2 or more
• Combination is obvious to one skilled in the art
• Test:
  • Determine scope and content of prior art
  • Determine level of ordinary skill in the art at time the invention was created
  • Determine difference between prior art and claimed invention

Disclosure & Enablement § 112
• Must describe invention with sufficient particularity to enable one skilled in the art to “practice” the invention
• Description defines the invention, providing as much information as possible
• The more detail, the better!

Patentability v. Infringement
• Test for patentability:
  • Patentable subject matter
  • Utility
  • Novel
  • Non-obvious
  • Disclosure and enablement
• Test for infringement: Whether your invention satisfies each and every element of an issued patent claim
• Basic idea: as long as your invention has each limitation/element of the prior art reference, it infringes
• Remember, a patent right is a negative right – it is a right to exclude others from making, using or selling your invention
  • It is not a positive right
• Possible solution:
  • Design around
  • Licensing
**Consequences for Patent Infringement**

- Money Damages
- Injunction
- U.S. Court of Appeals

**Defenses To Patent Infringement**

- Non-infringement: accused product does not literally possess each and every claimed element or its equivalent
- Invalidity: patent is invalid if its claims are unpatentable
- Unenforceable: inequitable conduct
  - Intent to deceive USPTO
  - Material information

**Exceptions**

- Experimental Use: “For amusement, to satisfy idle curiosity, or for strictly philosophical inquiry” *(Madey v. Duke)*
- Safe Harbor: 35 U.S.C. § 271(e)(1) “solely for uses reasonably related to the development and submission of information under a Federal law” *(Merck KGaA v. Integra Lifesciences)*
- Exhaustion: *(Bowman v. Monsanto)*
- Medical Practitioner: 35 USC 287 (c)(1) with respect to a medical Practitioner’s performance of a medical activity

**Congressional Legislation**

- America Invents Act – signed Sept. 16, 2011
- Biggest change to patent law since 1952
- 2 Main Changes
  - Switch from first-to-invent to first-to-file system
  - Expands post-grant opposition review

**Patents in the Supreme Court**

- *Diamond v. Chakrabarty* (1980): “anything under the sun that is made by man” is patentable
- *eBay v. MercExchange* (2006): An injunction should not automatically issue based on a finding of patent infringement (federal court must weigh the four-factor test)
- *KSR v. Teleflex* (2007): obviousness is a matter of common sense
- *Prometheus v. Mayo* (2012): The patent claims say nothing significantly more than “apply the natural laws that they describe” and that simple additional instruction, by itself, is insufficient to transform an otherwise unpatentable claim into a patentable one.
- *AMP v. Myriad Genetics* (2013): Isolated gene sequences (the DNA sequence for the BRCA gene) are not patent-eligible but synthetic sequences (the cDNA sequence) are.
Bayh-Dole Act

- Allowed Universities to retain title to inventions
- Sponsored by:
  - Senator Birch Evan Bayh of Indiana
  - Senator Bob Dole of Kansas

Requirements

University must:
- Provide the federal government with a free license to the invention
- Pursue patenting and commercialization of inventions
- Share a portion of any revenue received from licensing the invention with the inventor
- Give licensing preference to small companies (later modified)
- Requires that the product must be substantially manufactured in the U.S.

Goals of Bayh-Dole

- Promote use and development of federally funded inventions
- Encourage creation and growth of small businesses
- Promote U.S. manufacturing
- Promote and protect government rights in federally funded inventions

Results of Bayh-Dole

- Impact on university patenting/licensing
  - Over 21,856 invention disclosures received by U.S. Universities in 2011
  - Over 19,905 patent applications filed for U.S. Universities in 2011
  - Over 4,700 patents issued by 2011 (compared to 250 before 1980)
  - Over 4,899 license agreements executed in 2011
  - License agreements with 141 different institutions
  - Over $1.8 Billion dollars annually in gross license income received
- “Most inspired piece of legislation to be enacted in America in over a half-century” – The Economist

Licensing Income

<table>
<thead>
<tr>
<th>Rank</th>
<th>Institution</th>
<th>2011 Research Expenditures</th>
<th>2011 Patents Issued</th>
<th>2011 Licensing Income</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Northwestern U.</td>
<td>$484,149,349</td>
<td>67</td>
<td>$191,541,162</td>
</tr>
<tr>
<td>2</td>
<td>U. of California System</td>
<td>$1,016,491,941</td>
<td>195</td>
<td>$182,049,620</td>
</tr>
<tr>
<td>3</td>
<td>Columbia U.</td>
<td>$732,942,000</td>
<td>88</td>
<td>$146,220,950</td>
</tr>
<tr>
<td>4</td>
<td>New York U.</td>
<td>$429,782,000</td>
<td>94</td>
<td>$132,925,577</td>
</tr>
<tr>
<td>5</td>
<td>Princeton U.</td>
<td>$253,940,000</td>
<td>111</td>
<td>$155,206,000</td>
</tr>
<tr>
<td>6</td>
<td>Massachusetts Inst. Of Technology (MIT)</td>
<td>$1,490,429,000</td>
<td>174</td>
<td>$122,000,000</td>
</tr>
<tr>
<td>7</td>
<td>U. of Washington/Health Res.</td>
<td>$66,017,000</td>
<td>15</td>
<td>$79,281,885</td>
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<tr>
<td>8</td>
<td>Stanford U.</td>
<td>$594,489,877</td>
<td>164</td>
<td>$55,074,577</td>
</tr>
<tr>
<td>9</td>
<td>U. of Texas System</td>
<td>$1,113,841,832</td>
<td>156</td>
<td>$57,725,000</td>
</tr>
<tr>
<td>10</td>
<td>U. of Wisconsin-Madison/WARF</td>
<td>$1,153,985,000</td>
<td>155</td>
<td>$41,721,291</td>
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<tr>
<td>11</td>
<td>Duke U.</td>
<td>$975,246,000</td>
<td>67</td>
<td>$41,811,872</td>
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<tr>
<td>12</td>
<td>U. of Michigan</td>
<td>$340,926,757</td>
<td>79</td>
<td>$37,054,745</td>
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<tr>
<td>13</td>
<td>U. of Florida</td>
<td>$295,166,000</td>
<td>60</td>
<td>$29,493,522</td>
</tr>
<tr>
<td>14</td>
<td>Harvard U.</td>
<td>$833,200,000</td>
<td>60</td>
<td>$13,813,327</td>
</tr>
</tbody>
</table>

All Totals: $55,074,821,326 | 4,296 | $1,813,968,412
Licensing Income

• University patenting growing before 1980, and no change in slope after legislation
• May have hastened patenting and licensing by universities that had previously avoided these practices
• Universities patenting less important innovations
• Universities are bad licensors
  • Median income: $1.13 million
  • Licensing returns modest compared to investment

Stanford v. Roche (2011)

• Facts: Dispute over patents covering diagnostic tests for HIV infection, originally owned by Stanford University, and HIV diagnostic tests sold by Roche.
• When the researcher joined the faculty of Stanford, he, like all scientific personnel at companies and research institutions, signed an agreement in which he agreed that his employer would own any inventions he made.
• Holding: The Supreme Court held that U.S. patent rights have always (since 1790) initially vested in "the inventor" and that the non-specific language of the Bayh-Dole Act does nothing to change the original setup

March-In Rights

• Government has right to “require the contractor [university], an assignee or exclusive licensee of a subject invention to grant a non-exclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such a request, to grant such a license itself.”
• Allows the government to ignore the exclusivity of a patent and practice the invention itself, or have a third party practice the invention on the government’s behalf

Requirements

• Government must justify why action is necessary
  • Contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use
  • Needed to alleviate health or safety needs
  • Meet requirements for public use specified by Federal regulations

Examples of March-In Rights

• Government never has exercised its March-In Rights
• Anthrax attacks of 2001
  • Bayer had patent rights to the drug ciproflaxin, which was used to treat anthrax
  • As the anthrax scare continued and fear of a full-blown epidemic increased, the federal government contemplated marching in and acquiring Bayer’s patent rights to the drug ciproflaxin in order to benefit the health and safety of the public
In the Case of Xalatan

• Facts:
  • Pfizer had patent to glaucoma drug
  • Sold in U.S. at 2-5 times the prices in other high income countries

• Result:
  • NIH denied petition; Pfizer has met the standard for achieving practical application
  • No evidence that health and safety were not adequately met by Pfizer
  • NIH should not address the issue of whether drugs should be sold in the U.S. for the same price as they are sold in Canada and Europe, only Congress

In the Case of Norvir

• Facts:
  • Abbott Labs had patent to ritonavir (Norvir), used in treatment of AIDS
  • Abbott raised the price of Norvir by 400% in U.S.
  • Abbott refused to license Norvir to another company for purpose of providing protease inhibitors co-formulated with ritonavir

• Result:
  • NIH denied the petition
  • Abbott has met the standard for achieving practical application
  • No evidence that health and safety were not adequately met by Abbott
  • NIH should not address the issue of drug pricing, only Congress

Any questions?

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