Antitrust and Patents in Pharmaceuticals

Antitrust
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Patent PAT.

Protects	machines, inventions
Requires	patentable subject matter, novelty, nonobviousness, utility, enablement
Vests	after application, upon issuance by government
Sustained by	escalating maintenance fees
Lasts	somewhat less than 20 years (from date of issuance to 20 years from date of application)
Theory	incentive to invent and disclose; public goods problem

How is it lost?

©	*Very difficult*
Pat.	Unpaid fees; successful challenge

Defenses include ...

©	Fair use, first-sale
Pat.	Invalidity, first-sale

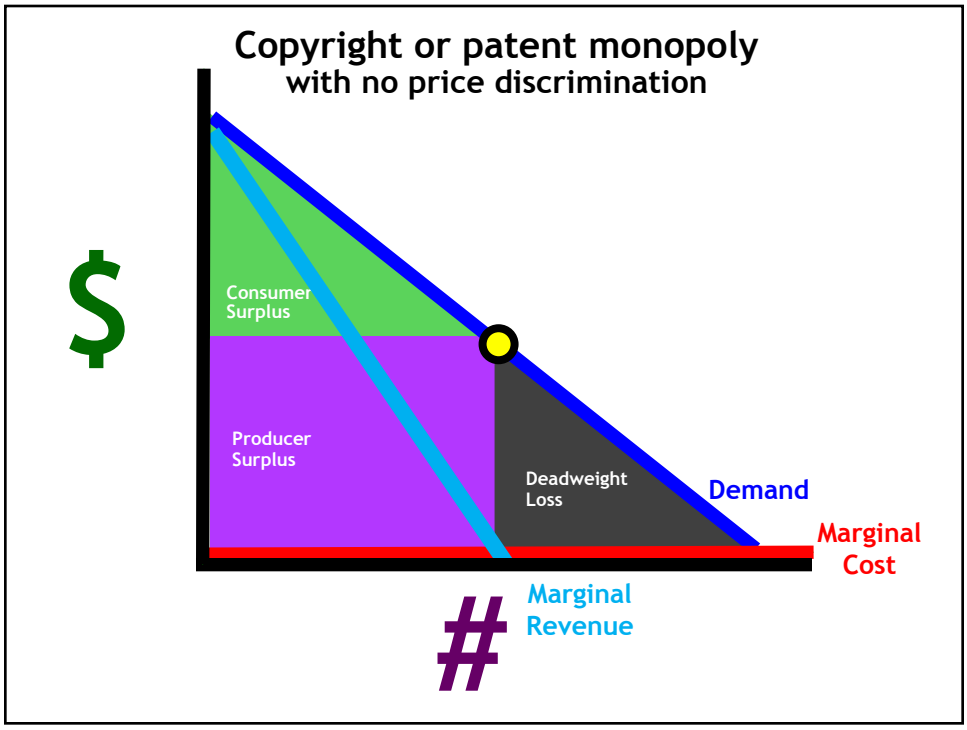
Patent PAT.

Five requirements for a valid patent:

1. patentable subject matter
2. novelty
3. nonobviousness
4. utility
5. enablement


nonexcludable
nonrival


The compensation / incentive problem


Copyright or patent monopoly
with no price discrimination
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Consumer Surplus
Producer Surplus
Deadweight Loss
Demand
Marginal Cost
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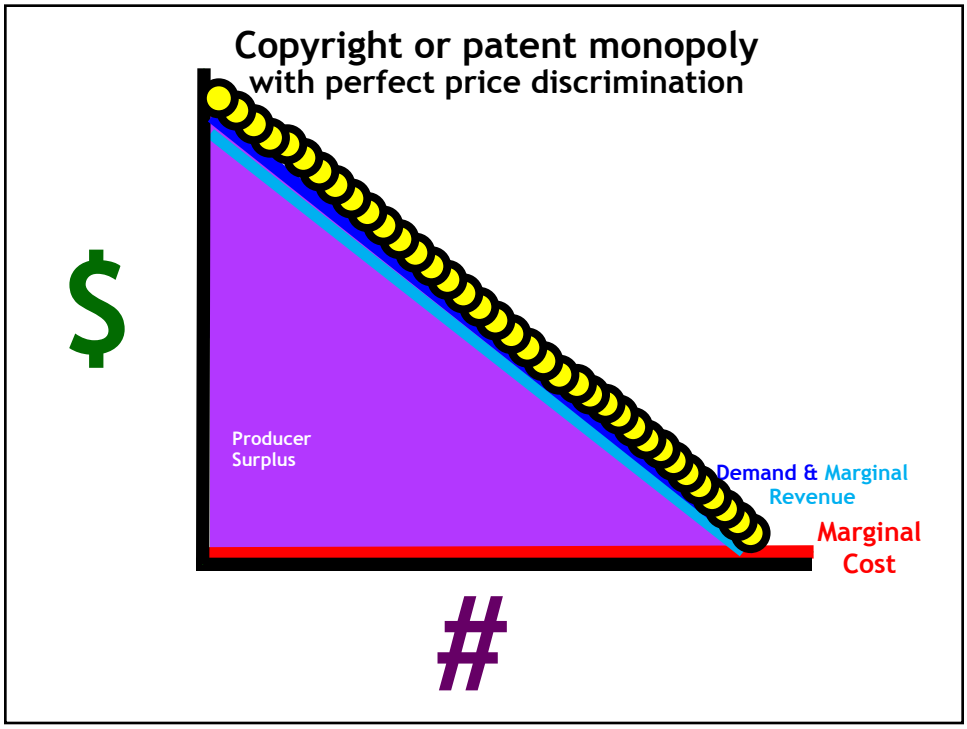
Marginal Revenue


Copyright or patent monopoly
with perfect price discrimination
$
Producer Surplus
Demand & Marginal Revenue
Marginal Cost
#

Licenses with horizontal price conditions

Elhauge's synthesis: "[L]icenses with horizontal pricing conditions are

- legal if the patent is so valuable that the licensee (or licensees) could not make a competitive product without the license, which was true in *General Electric* but demonstrably untrue in *New Wrinkle*. …
- illegal when, as in *New Wrinkle*, (1) the patent is not very valuable and (2) the parties to the licensing agreement have enough market power that the pricing condition could have an anticompetitive effect." (bullets added)

Nonobviousness

Nonobviousness how-to

SCOTUS in *Graham v. John Deere* says:

- Determine the scope and content of the prior art
- Note the differences between the prior art and the claimed invention
- Determine the level of ordinary skill in the art
- Consider secondary factors as well (the "Graham factors"

Graham factors

- Commercial success
- Long-felt but unsolved need
- Failure of others
- Copying of inventor
- Unexpected results
- Skepticism of experts
- Acquiescence
- Adoption by industry

"[W]hen a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious."

KSR v. Teleflex (U.S. 2007) (quoting *Sakraida v. Ag Pro* (U.S. 1976))

Nonobviousness

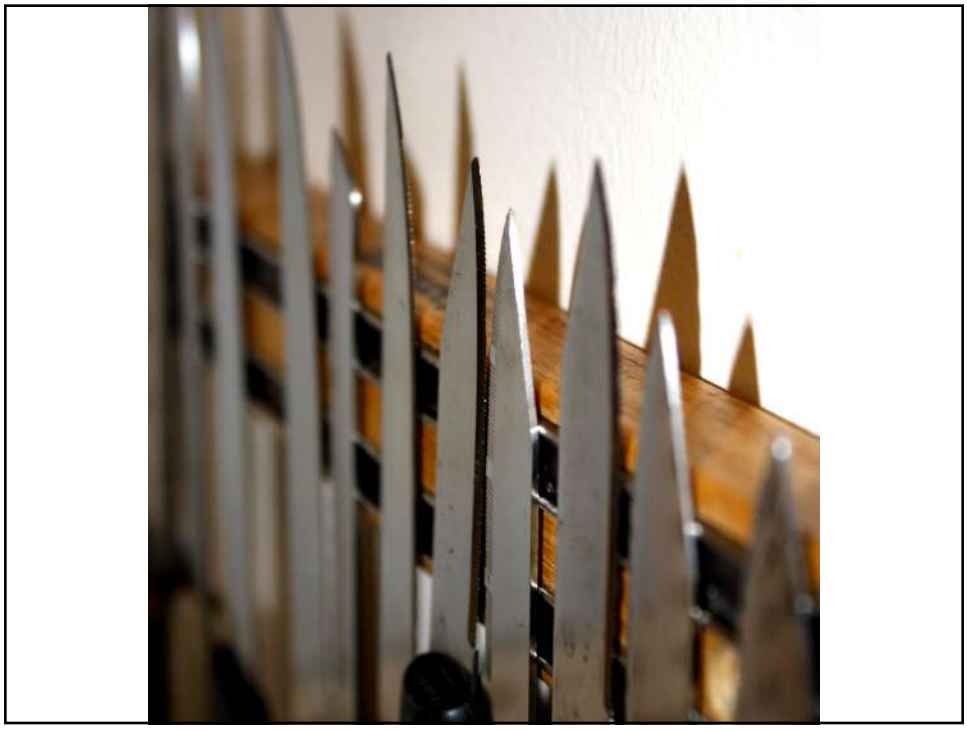
"[A] court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions."

KSR v. Teleflex (U.S. 2007)

Nonobviousness

"Often, it will be necessary for a court to look to interrelated teachings of multiple [prior art references]; the effects of demands ... in the marketplace; and the background knowledge possessed by a [PHOSITA], all in order to determine whether there was an apparent reason to combine. ... [T]he analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a [PHOSITA] would employ."

KSR v. Teleflex (U.S. 2007)



Pharma and patents ...

- There is strong reason to believe that patents do little or nothing to actually induce innovation or commercialization to any significant extent in many or most industries.
- The best example, however, of patents having a powerful inducement effect is in pharmaceuticals. Because of patents, research pharma firms are induced to create new drugs lured by the promise of many billions of dollars in profits enabled by patents.
- Patenting in pharma is also one of the key aspects of the expense of health care in the United States, which is a huge political/economic/social issue of our day.
- This makes patents in the pharma sector worth our special attention.
- What's more, there are complexities to patenting in the pharmaceutical context, including ancillary FDA regulatory exclusivities. This also makes it worth special attention.

Considering the U.S. role in global pharma

- There is a good argument that U.S. patent law (along with neighboring U.S. law in the spheres of antitrust and FDA regulation) is crucial in providing the needed economic inducement for the development of new medicines globally.
- As a general matter, the U.S. has no price controls on drugs, but the rest of the world does.
- Abroad, price controls allow prices to be high enough that it's worth it for the patent-holding pharmaceutical company to sell in that jurisdiction (because marginal cost is far below the allowed price), but arguably the reward is not so great that it significantly contributes to the inducement to develop the new drug in the first place.
- In the U.S., without price controls, prices can be far, far above marginal cost, allowing recoupment of massive R&D costs.
- Thus, arguably, U.S. consumers are paying the drug development costs for the entire world.

The story of a drug ... #1

- **Invention:** Researchers create a new compound that didn't exist before.
- **Preclinical evaluation:** The compound is tested in the lab, such as on cell cultures and animals, to see if it has any pharmacological effect that is potentially useful.
- **IND (Investigational New Drug application):** The research drug firm files an IND with the FDA with preclinical data and a proposed clinical trial design. The FDA decides whether to allow the IND and permit human testing.

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The usefulness threshold for a utility patent is surpassed, if at all, in the preclinical evaluation stage.

The story of a drug ... #2

- **Clinical testing:** Generally, clinical testing takes place in multiple phases.
  - **Phase I trials: Safety.** The treatment is tested on a small group of people (roughly 20 to 100) to evaluate safety. Answers to get: What's a safe dosage? How is the drug absorbed, metabolized, excreted? What are the side effects?
  - **Phase II trials: Efficacy, plus more safety.** The treatment is given to a larger group of people (up to several hundred) to see if it is effective and to further evaluate safety. These studies are usually randomized, placebo-controlled, blinded.
  - **Phase III trials:** The treatment is given to large groups of people (several hundred to several thousand) to confirm effectiveness and gather more information about side effects, safety, and to compare it to other treatments.

By the way, post-approval, there could potentially be ...

- **Phase IV trials**: To get additional information. Might be conducted by same firm or by other, interested researchers.

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  - **Phase III trials:** …roups of people (several hundre… e… ss and gather mor… sa… to compare it to other treatments.

100%

Phase I: about 70% of drugs pass this phase

~70%

Phase II: about 2/3rd of drugs pass phases 1 & 2

~67%

Phase III: about 70 to 90% of drugs pass this phase

~57%

By the way, post-approval, there could potentially be ...

- **Phase IV trials**: To get additional information. Might be conducted by same firm or by other, interested researchers.

The story of a drug ... #3

- **New Drug Application (NDA):** After clinical testing is done, the drug firm files an NDA with the FDA to try to get the drug approved for marketing.
  - The FDA says, an NDA "is supposed to tell the drug's whole story, including what happened during the clinical tests, what the ingredients of the drug are, the results of the animal studies, how the drug behaves in the body, and how it is manufactured, processed and packaged."
- NDA review: The FDA considers the NDA, and may grant it.
- The average remaining patent term on approval 12 years. Blockbuster drugs may have many billion dollars a year in revenues, with relatively small marginal cost.

The story of a drug ... #4

- **Abbreviated New Drug Application (ANDA):** A generic firm can file an ANDA unsupported by new clinical data, relying on the research pharma company's data. The ANDA will be approved if the generic firm can demonstrate **bioequivalence**.
- "The introduction of generics is a shock to the system for a pharmaceutical company. Prices can drop as much as 20% when the first generic enters the market; with multiple generics, the prices may eventually drop by 80-85%." (Feldman 2018)
- The modern path to generic competition was created by the Hatch-Waxman Act of 1984.

Hatch-Waxman 1/2

a/k/a The Drug Price Competition and Patent Term Restoration Act of 1984

- amended both patent law and food-and-drug law
- provided for patent term extensions to compensate for FDA regulatory approval delays (35 U.S.C. § 156)
- established expedited path for approval of generic drugs that are bioequivalent
  - complaints by generic firms that brand-name firms won't sell them samples for use in needed bioequivalence testing
- created a safe harbor from patent infringement for generic drug companies until the time they request FDA approval

Hatch-Waxman 2/2

- encourages brand-name companies to identify patents covering their drugs—these are listed in the Orange Book
- when a generic drug company seeks FDA approval for an existing drug, they must account for Orange-Book listed patents, either by
  1. saying they will wait until the patent expires
  2. asserting the patents are invalid or don't cover the drug
  - if No. 2, then the generic firm can be sued for infringement
- created new "regulatory exclusivities" – periods of exclusive marketing rights that operate alongside patent protection

Regulatory exclusivities

Some examples:

- 7 year market exclusivity for drugs that treat rare conditions and diseases. (Orphan Drug Act of 1983)
- 5 year exclusivity for drugs that qualify as a "new chemical entity" (NCE) where the FDA hasn't previously approved the active ingredient. During that time, no ANDA applications will be accepted. The period can be reduced to 4 years in some circumstances. (Hatch-Waxman Act of 1984)
- 3 year new clinical study exclusivity period for studies that are essential to FDA approval of an NDA or supplemental NDA. These apply not to the active ingredient (NCE), but to a particular use of the drug. (Hatch-Waxman Act of 1984)
- 180-day generic-drug market exclusivity for being the first generic pharmaceutical firm to file a "paragraph IV certification" challenging the patents on an approved drug. (Hatch-Waxman Act of 1984)

"Evergreening" of pharmaceuticals (1/3)

- "[D]rug makers do all they can to soften the blow of losing market monopoly. Some strategies ... involve what is known as 'evergreening'. [In] its broadest connotation [the term means] trying to refresh one's monopoly protection on a drug." (Feldman 2018)
- Techniques include filing for new patents on new formulations (e.g., extended release), new methods of use, new dosage schedules, new combinations with other ingredients, etc. This often includes very weak patents unlikely to survive challenge, for instance for lacking nonobviousness.

"Evergreening" of pharmaceuticals (2/3)

- How does having secondary patents help the research pharma firm?
  - Marketing efforts to encourage use of new formulations, trying to move prescribers and buyers with direct-to-consumer advertising and working to get doctors to prescribe the newer formulations.
  - All patents are listed in the Orange Book by the research pharma firm, and then to get FDA approval, the generic challenger must defeat all listed patents—which can be expensive, even when patents are weak.
  - Research pharma companies often enter settlements with would-be generic challengers to delay market entry, staving off competition and keeping prices high. The legality of this is an active area in antitrust law.

"Evergreening" of pharmaceuticals (2/3)

- How does having secondary patents help the research pharma firm?
  - Marketing efforts to encourage use of new formulations, trying to move prescribers and buyers with direct-to-consumer advertising and working to get doctors to prescribe the newer formulations. ← arguably benign (absent effects of delaying improvements and "market failure" w/r/t advertising)
  - All patents are listed in the Orange Book by the research pharma firm, and then to get FDA approval, the generic challenger must defeat all listed patents—which can be expensive, even when patents are weak. ← arguably economically inefficient
  - Research pharma companies often enter settlements with would-be generic challengers to delay market entry, staving off competition and keeping prices high. The legality of this is an active area in antitrust law. ← arguably economically inefficient and highly socially pernicious

“Evergreening” of pharmaceuticals (3/3)

- "Many ... evergreening strategies involve applying for new patents. Even if the patents are of questionable validity, the process of challenging them through Hatch-Waxman litigation is expensive and lengthy for a generic, again allowing years of additional profits for the brand-name company. If companies are able to ... justif[y] obtaining new patents or exclusivity protections, these companies [may avoid the drop-off in profits from patent expiration]. Our data suggest that this is occurring in a widespread manner throughout the industry.” (Feldman 2018)
- “In short, despite the quaint theory that competitors will enter after a pharmaceutical patent expires, the reality is quite different. Numerous strategies and opportunities exist that allow companies to extend their protection and prolong the period of market monopoly for their drugs.” (Feldman 2018)

Sources:

- FDA, *What Are the Different Types of Clinical Research?*, https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research
- *The Hatch-Waxman Act: A Primer*, September 28, 2016, Congressional Research Service
- Robin Feldman, *May Your Drug Price Be Evergreen,* 5 Journal of Law and the Biosciences 590 (2018).

Biologics

- The foregoing stuff about Hatch-Waxman and Paragraph IV certifications, as well as stuff about the FDA's Orange Book (which came up in FTC v. Actavis) applies to what are called "small-molecule drugs."
- For instance, aspirin is a small-molecule drug. It's chemical forumla is $C_9H_8O_4$. Chemically speaking, it's pretty simple. It can be synthesized through age-old chemistry means.
- Adalimumab ("Humira") is a "biologic." It's a huge biological molecule made up of subparts of amino acids. You can't meaningfully describe it with a chemical formula, but the formula would look like $C_{6428}H_{9912}N_{1694}O_{1987}S_{46}$.
- Biologics have different regulatory law than small-molecules. But it works similarly, and it creates similar incentives for patent-holding originators, generic ("biosimilar") challengers, and settlements. Instead of the Paragraph IV certification, you have the "patent dance" described in the case.

but let's go back ...

- Let's go back to the essential economic concepts at the heart of FTC vs. Actavis.
- Remember:
- Economics is all about incentives.
- Decisions are made at the margins (marginal analysis). And the yardstick for whether something is good or bad is societal welfare (consumer surplus, producer surplus, and lack of deadweight loss).
- And antitrust law cares about (although it depends on who you are talking to) both consumer welfare and overall economic efficiency.

Hexetron -w- Econopharm re Glornox

Hexetron claims glornox is protected by the '222 patent, which expires about two years from today. Hexetron makes $10B a year in revenues from glornox. The marginal cost is almost zero. Econopharm wants to manufacture glornox and files a paragraph IV certification challenging the '222 patent as invalid for being nonobvious (and there's a 50% chance a court will agree). The court's decision will come down very soon (after a bunch of money is spent on lawyers). Here are two possible settlements:

(A) Econopharm drops the challenge, and Hexetron will allow Econopharm to make glornox one year from today. Until then, Econopharm will refrain. Econopharm figures this path will give it $675M in additional revenue versus having to wait two years.

(B) Hexetron will pay Econopharm $675M for Econopharm to drop the challenge and to wait two years to market glornox.

What's the difference between these two settlements? (Use your economics!) Should Hexetron offer and agree to either of these settlements? Should Econopharm? Should one party agree to neither and push forward with the litigation/challenge? Does it make any difference to overall societal welfare?

(X) The challenge never existed:

Econopharm gets $0; Hexetron gets $20B.

(Y) The challenge/litigation plays out:

Compared to (X): Econopharm expects to gain $675M (50% of $1.35B) less some legal fees; Hexetron expects to lose a bit less than $10B. You can call it $10B for simplicity. (Or you could say $9.325B: 50% of $20B is $10B, but it would get back about $675M in authorized-generic revenues, plus some legal fees.)

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Compared to (X): Econopharm gets $675M and saves on legal fees. Hexetron loses out on about $9.3B in producer surplus. Consumers gain about $9.3B in consumer surplus.

Compared to (Y): Econopharm and Hexetron are indifferent, except for saving on fees. Consumers are indifferent.

(B) Hexetron will pay Econopharm $675M for Econopharm to drop the challenge and to wait two years to market glornox.

Compared to X: Econopharm gets $675M. Hexetron gets $19.325B.

Compared to Y: Econopharm is indifferent, except for saved legal fees. Hexetron is up by $9.325B (the expectation value of the possible loss of the litigation). Great for Hexetron! Consumers are out $9.325B.

Compared to A: Econopharm is indifferent. Hexetron loves B compared to A, because it is up by about $9.325B! Consumers are out $9.325B compared to A.

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In reality, Econopharm is probably not going to accept B. They'll hold out and extract a substantial additional payment from Hexetron over and above $675M because they'll know how to negotiate and they'll know B vs. Y is going to be worth billions to Hexetron. <u>But, all of this depends on there being some barrier to other firms coming along and threatening Hexetron in the same way Econopharm did.</u>

Compared to A: Econopharm is indifferent. Hexetron loves B compared to A, because it is up by about $9.325B! Consumers are out $9.325B compared to A.

Some takeaways from *Actavis*

- "The likelihood of a reverse payment bringing about anticompetitive effects depends upon its size, its scale in relation to the payor's anticipated future litigation costs, its independence from other services for which it might represent payment, and the lack of any other convincing justification." *Actavis,* p.198
- "[W]hen the net reverse payment (i.e., payment net of the value of any return services) exceeds the patent holder's anticipated litigation costs, that fact: (1) shows market power, (2) obviates the need to inquire into the patent merits, and (3) indicates that the settlement exclusion period exceeds what is merited by the expected patent odds." EE, p.200.
- "A reverse-payment settlement causes anticompetitive harm if, without the reverse payment, the parties would have either (a) reached a no-payment settlement with an earlier entry date or (b) continued a patent litigation that would have produced an earlier expected entry date." EE, p.203.