Industry & Invention
Pharma

Utility Patents and Regulatory Exclusivities in Pharmaceuticals

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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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Review

Specific Utility

Examples from diagnostics:

Ex. 1: Applicant makes a general statement of diagnostic utility, such as diagnosing an unspecified disease.

➔ Insufficient.

Ex. 2: Applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition.

➔ Sufficient to identify a specific utility.

Specific Utility in the Therapeutic or Pharmacological Context

Nelson v. Bowler, 626 F.2d 853 (CCPA 1980):

- Nelson satisfied the practical utility requirement in identifying the synthetic prostaglandins as pharmacologically active compounds.

Specific Utility in the Therapeutic or Pharmacological Context

Nelson v. Bowler, 626 F.2d 853 (CCPA 1980):

"Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility."

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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: about 70 to 90% of drugs pass this phase

~57%

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).