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Honors Thesis

What factors contributed to the development and implementation of the Uruguay Round Agreements Act of 1994? What effects, if any, did the act have in shaping the field of pharmaceutical innovation? What role do investors play in promoting innovation, and what factors influence their investment strategies and decisions?

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Abstract

This study will identify the factors that contributed to the development and implementation of the Uruguay Round Agreements Act of 1994 (the Act, or the URAA of 1994), explore the Act's impact on the field of pharmaceutical innovation, and uncover how investors and market values responded to these changes.

The URAA of 1994, among other things, changed the life of utility patents from 17 years from the date of issue of the patent to 20 years from the filing date. Because the period of monopoly became largely dependent on how fast the patent is approved, investor profits are more difficult to calculate. On the other hand, the Act is claimed to have eliminated the so-called "submarine patents". While many scholars have theorized about the benefits and drawbacks of various provisions of the Act for inventors, investors, and the public, none to my knowledge have approached the topic from a socio-empirical perspective and directly captured the perspective of the stakeholders of the pharmaceutical industry themselves. By interviewing the stakeholders I hope to provide that practical analysis that scholars have omitted from their research projects.

I anticipate that the Act caused investors to be more cautious about investing large amounts into pharmaceutical research due to risks brought by uncertainty about the length of drug exclusivity in the market. I also hypothesize that due to delays related to Food and Drug Administration approval and clinical trials, the actual term of an average patent is significantly lower than the alleged 20 years. Examining how the Act affects the stakeholders is crucial in understanding the socio-economic impact of the URAA of 1994. High costs of launching a drug combined with insufficient time to recoup the costs may discourage inventors, deter investors, and thus impede innovation.

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Introduction

In the contemporary world there is an ongoing tension between protection of innovation in the pharmaceutical industry and dissemination of newly developed drugs that do not have a generic counterpart. Generics are much cheaper and are identical to the original drugs by their chemical structure and therapeutic effects, which allows a considerably larger population to enjoy their benefits. However, it is the original research that drives pharmaceutical market forward and constantly improves existing drugs while working on new formulas. Inventors, who spend years (sometimes decades) developing new medicines and conducting multi-million dollar clinical trials, tend to rely on angel investors and venture capital firms to finance their research. With millions of people in need of low price drugs to treat or curtail life-threatening conditions on one side of the scale, and researchers and investors asking for intellectual property protection and return on their investments on the other side, can social efficiency be achieved?

Every year large venture capital companies and pharmaceutical corporations help advance research and development by investing billions of dollars, expecting their investments to pay off and yield risk-adjusted profit. However, these investments also require some significant trade-offs. When investors take a risk, they must have incentives and be protected under the law. The financial risks are great for most financial sponsors, thus they need to be ensured that they will recover their investment along with a profit margin in order to successfully launch a product. In this case, a certain period of exclusivity is required by investors who specialize in the fields of pharmaceutical research and biotechnology. The number of years required depends on how long it takes for the drug to pay itself off and generate risk-adjusted profit. Although there are other means of financing research and development (university-sponsored, private donations, or charity), in this thesis I discuss investors' role in the pharmaceutical industry.

It has been almost twenty years since the law took effect, and its consequences should now be comparatively easy to observe. Mainly, I seek to discover how changes brought about by the Uruguay Round Agreements Act of 1994 affected investors' willingness to invest in pharmaceutical research, whether investors changed their financing strategy, and whether they believe the new laws seem to have positively affected the rates of innovation in the long run. Additionally, I will conduct interviews of several patent lawyers and record their interpretation of the change in patent law mandated by the URAA of 1994.

There is an ongoing dispute about the consequences of the Uruguay Round Agreements Act of 1994, with some scholars arguing that its patent-related provisions benefited the inventors and the public (Lemley, 1994: 393), while others suggesting that certain provisions of the Act had a detrimental effect on innovation (Grabowski, 2000: 111). There are several questions that come to mind when considering this topic in the pharmaceutical context. For instance, one would be interested to know how long it takes to launch a drug, how soon investors are compensated, and how they are compensated. What is the formula they use to find out whether an investment has solid potential for profit, and did the formula change with the passage of the Act? To what extent do they rely on the expected profit calculations when making their investment decisions? And, finally, taking into account the answers to questions asked above, another important question arises: has the URAA of 1994 affected the rate of innovation in the pharmaceutical field overall, and if so, positively or negatively? What could be changed to achieve greater efficiency and motivate investors to support research and development of new drugs?

Overview

Professor Robert Cooter touched on this issue in one of my Legal Studies courses at UC Berkeley, and, after reading the book he co-wrote with Professor Thomas Ulen, I decided to research it further. Cooter and Ulen believe that

> In this life cycle of an innovation, the innovation causes a disequilibrium, and the innovator earns extraordinary profits as long as it persists. The reward for innovation thus depends on how long the disequilibrium persists. A quick move to equilibrium gives little reward to the innovator for the resources that it invested and the risk that it assumed. Without legal intervention, competition can quickly destroy the profits from innovation, which results in too little innovation (2011: 114).

Disequilibrium, the polar opposite of equilibrium, means that the supply of the product does not equal the demand. Equilibrium is achieved when supply equals demand, and there is enough product offered in the market for the population demanding it. Under monopoly conditions, the equilibrium is distorted and the demand is much higher than supply, causing prices to skyrocket. However, in the pharmaceutical market, a certain period of exclusivity (or even monopoly) is required in order to help the innovators and investors recoup the tremendous costs involved in research and development. Equilibrium is what the general public would like to see in form of generic drugs that would create healthy competition and drive the market prices down to affordable levels. Not surprisingly, this seems to be a good solution in the short run, but a very dangerous one in the long run because innovators require sponsors to invest in their research, and sponsors in turn seek financial reward for their investment. Products must not only be practical for the public but also innovative in the field. Additionally, if inventors are not sufficiently compensated, it is extremely counterintuitive for them to invest in expensive

research to produce such a new drug and undergo clinical trials required for Food and Drug Administration (FDA) approval. Can regulations help protect intellectual property and promote innovation, or do they impede its success? This project examines the implementation of the Uruguay Round Agreements Act of 1994 and its consequences in relation to research and development in pharmaceutical industry.

Legislative History

Some laws benefit innovation, and some restrict or slow it down. In 1984, United States Congress passed the Drug Price Competition and Patent Term Restoration act of 1984, also known as Hatch-Waxman Act. The Act was seen as a "compromise in the pharmaceutical industry in an effort to balance patent exclusivity against market competition" (Dorsney 2012: xxi). Allegedly catalyzed by a federal court case Roche Products v. Bolar Pharmaceutical, 733 F.2d 858 (Fed. Cir. 1984), the Hatch-Waxman Act introduced amendments to the Federal Food, Drug and Cosmetic Act and the Patent Act of 1984.This law succeeded at relieving the tension between the pharmaceutical pioneers and generic drug producers. This Act allowed development of generics up to the point of commercialization. In other words, the Hatch-Waxman Act "reformed the patent laws to balance incentives for innovation and competition within the pharmaceutical industry" (Thomas 2003: 1). Scholars generally agree that Hatch-Waxman Act not only "effectively establish[ed] a robust generic drug industry in the United States, it [also] deeply impacted pharmaceutical research and development by innovative pharmaceutical firms" (Thomas 2005: 9).

The Uruguay Round Agreements Act of 1994 was a piece of legislation that resulted from the obligation of Congress to comply with the General Agreement on Tariffs and Trade and Agreement on Trade Related Aspects of Intellectual Property Rights (GATT-TRIPs agreement)

(Lemley, 1994: 375). According to Patricia Montalvo, the URAA of 1994 was the first piece of legislation that involved intellectual property issues, which showed "the international commitment to protect intellectual property as well as the growing importance of intellectual property rights as a trade issue" (1996: 141). Among many of its provisions, URAA changed the life of utility and plant (not design) patents from 17 years from the date of issue of the patent to 20 years from the filing date. (USPTO, 20-year Term). According to Seoane-Vazquez et al., "most pharmaceutical patents are classified as utility patents (2009: 171). Utility patents "protect[] apparatus, compositions of matter, or methods of making or using the same" (Wellons 2007: 27). From the investor's point of view, this change was crucial because the effective patent life became variable rather than fixed, and because the 20-year term begins on the day the patent application is filed, it is difficult to calculate its total effective term due to variations in the number of years spent on carrying out additional post-application research, correcting errors, and conducting clinical trials of the drug required to test its therapeutic effects and possible side effects.

Literature Review

There is an ongoing dispute about the consequences of the Uruguay Round Agreements Act of 1994. Some scholars argue that its patent-related provisions benefited the majority of the inventors and the public (Lemley, 1994: 393, and Sukhatme 2013: 1), while others suggest that certain provisions of the Act had a detrimental effect on innovation (Grabowski, 2000: 111). In this literature review I summarize some pertinent changes in legislation followed by the main benefits and disadvantages relevant to the patent law provisions, as they have impacted the pharmaceutical industry. The intention of this overview is to familiarize the reader with the most recent context of the law related to patents and innovations. I will then introduce the scholarly

opinions and arguments that support the provisions mandated by the Uruguay Round Agreements Act of 1994 and opinions of scholars that believe that the Act brought more problems than solutions. I will critique authors' claims as well as their reasons for supporting or objecting to the URAA of 1994 in the context of pharmaceutical development, specifically. Then, I will explain how the scholars' arguments contribute to my work and how the scholarly works are missing an important link in their arguments in the context of pharmaceutical research and development. Finally, I will show how my research will improve the understanding of the consequences of the Act. In the course of this literature review I will raise several questions that I hope to find answers to by conducting additional socio-legal research that will include but is not limited to interviewing patent attorneys and venture capital representatives. I will also run "Net Present Value" calculations to show how the value of an average drug changes in response to increases or reductions in the total number of years of effective patent protection.

According to Mark Lemley, in general, the changes brought by the GATT-TRIPS benefit the average patentee while hurting only a small portion of patentees. He suggests that out of those 1.5 % that are disadvantaged, half are suspected to be "submarine patents" (1994: 393). However his data shows statistics for patents overall, and are not targeted to pharmaceutical patents, for which there is little to no evidence of submarine patents. Therefore, the discussion may miss an important part of the process – the time it takes to conduct clinical trials and obtain the FDA approval for a drug. The time it takes for the patent to be approved is irrelevant when not looking at the bigger picture – in total it takes about 10 years to conduct the necessary trials, file an application for a patent, and obtain approval for a drug from the FDA, provided the process stays free from major errors that would cause setbacks.

Professor Lemley is William H. Neukom Professor of Law at Stanford Law School, the Director of the Stanford Program in Law, Science and Technology, and the Director of Stanford's LLM Program in Law, Science and Technology. He also teaches classes on intellectual property, computer and internet law, patent law, and antitrust law. Professor Lemley agreed to provide a more recent update and express his opinion about the changes URAA caused for pharmaceutical patents. He believes that "due to PTO backlog issues prosecution overall takes more time than it did 20 years ago." However, Professor Lemley adds that despite the delays, "the length of effective patent term has increased for pharmaceutical companies because inventors can claim extensions to compensate for FDA regulatory delays." He agrees that pharmaceutical prosecution is generally longer than that of other industries, but believes that it's because pharmaceutical companies choose to use continuations to extend the time in prosecution.

Henry Grabowski, Professor of Economics at Duke University, sees the increase in patent life from two angles. He believes that marginal social benefit is achieved by "increasing patent life [which] will cause some NCEs that would not have been developed to now be introduced" (Grabowski, 2000: 100). Marginal social cost occurs because " longer patent life will simply postpone the onset of generic price competition" (Grabowski, 2000: 100). Dr. Sukhatme adds, "a patent should be valid only as long as necessary to incentivize innovation and no longer" (2013: 4). Like Professor Cooter, Professor Grabowski believes that "[w]hen these marginal gains just equal the marginal costs, the patent life is optimal" (2000: 100). When looking at effective patent life of utility patents, one should keep in mind an important difference – the cost of research and development in the pharmaceutical industry is much higher than it is in other industries, thus making investments riskier. Investors require assurance that they will receive their "risk-adjusted return on its capital" (2000: 100).

Phases of drug development

There are 4 phases in clinical trials, each consisting of different goals and posing unique challenges. Pfizer's official website describes the 4 stages in detail:

Phase 1 is referred to as a "Safety study", and usually takes about one year. During that phase researchers attempt to test the drug using the lowest dose at first, gradually increasing it until they see first adverse effects. This is a very important stage because if the adverse effects are serious, the whole drug development may be shut down. This phase does not require too many subjects for clinical testing. Human subjects are usually healthy individuals who do not have the disease that the drug is intended to treat. Subjects' clinical response, drug absorption, and tolerance are closely monitored by an investigator (Phases of Development, 2013).

During Phase 2, researchers engage in testing the effectiveness of the drug by administering it to actual patients who have the condition that the drug is intended to treat. This phase usually requires a few hundred human subjects, although in some cases fewer than 100 subjects can be accepted (for instance, orphan drugs). Besides testing the efficacy of the drug, information about risks, side effects, and other possible outcomes are recorded. Patients are drawn from multiple locations, often even from different countries (Phases of Development, 2013). At the end of this phase, researchers should be able to determine the optimal dosage, as well as the most appropriate delivery method (injection, pills, or capsules etc).

Phase 3 involves testing the medicine in larger population, usually ranging from several hundred to several thousand participants. It's common to conduct the testing using the randomized, double-blind method. Double-blind method means that during drug testing neither the physician nor the human subjects know whether they are ingesting placebos or the drug being tested. During this phase, a risk-benefit analysis is done as well as data collected about the

medicine that will be used in the labeling (Phases of Development, 2013). After phase 3 is complete, an approval is issued if the FDA believes, in fact, the benefits of the drug outweigh the disadvantages. Even after this degree of testing, many drugs are rejected.

Immediately after phase 3 is complete, registration of the drug takes place. Inventors need to fill out an application with their country's health regulatory authority. In the United States, one would file a New Drug Application (NDA) with the United States Food and Drug Administration (FDA) (Phases of Development, 2013). The purpose of this step is to prove safety and efficacy of the drug, describe the clinical trial results, quality data, and manufacturing process. Only after this step is successfully completed can a new medicine be sold in the market.

There is also a phase 4, which is called "post-marketing studies". This phase takes place after the regulatory approval has been issued, and involves collection of additional information about risks, benefits, and optimal use of a drug. It may last years and involve thousands of human subjects (Phases of Development, 2013).

Benefits of and Arguments for the Uruguay Round Agreements Act of 1994

URAA of 1994, among other things, introduced a significant improvement. The act suggested ridding of the "first-to-invent" system that had ruled in the United States prior to 1994 and replacing it with the more common worldwide "first-to-file" system. According to Seoane-Vazquez et al, this new system that has been predominant in other countries "encourages early filing of patent applications" which in turn "allows inventors to obtain an earlier date of invention relative to potential competitors and establish the right of priority over the invention" (2009: 171). Although most of the provisions specified in the URAA of 1994 took effect on June 8, 1995, the "first-to-file" provision was passed on September 16, 2011 when President Obama

signed the Leahy-Smith American Invents Act (AIA) (US House 2011). The AIA took effect on March 16, 2013. The "first-to-file" system introduces a few important changes in the way patents are filed. On the one hand, because of the high costs to hire a patent attorney to assist with drafting and filing a patent application, the new system seems to favor large scale pharmaceutical corporations over smaller scale businesses that engage in pharmaceutical research. On the other hand, it eliminates the time-consuming and often unproductive task of trying to figure out who was the original inventor, or in other words, who was first. It is difficult to determine the overall effect of this particular provision due to multiple variables, but the following scenario can illustrate the importance of this change. It also makes the application filing procedure less complex overall because (roughly) the patent landscape in the US will mirror that of other countries.

Two inventors, A and B, had been working on a drug that will cure cancer. Both drugs have identical formula and structure. Inventor A, however, filed a patent application on May 1, 2012. Inventor B filed his on May 3, 2012. Under the first-to-invent system, if B can prove that he invented the drug before A, B's patent application will be valid. However, under the new rule, because inventor A filed his patent application earlier than B, he is entitled to the patent. Inventors are thus incentivized to file their patent applications as early as possible to avoid situations in which others take credit for their work. Once the patent is filed, no one else can claim that he or she invented the drug first. Proving who filed a patent application first is considerably easier than figuring out who owns the original idea.

Another important improvement is a new "scheme [that] will eventually eliminate the possibility of submarine patents" (Thomas 2005: 282). Submarine patents were such patents whose review was intentionally delayed in order to extend the exclusion and monopoly. These

patents were intentionally vague and were customized to match the existing successful innovations within an industry later on and collect royalty payments. Such patents often surfaced years later when the conditions were more favorable and marketing the invention was easier. For example, one inventor that used to delay the approval of his patents was Jerome H. Lemelson. He used the loopholes in the system to delay the mechanism of processing his purposely-vague patents and thus created submarine patents. He then "modified the application to match the industry, and let[] it issue in the middle of a fully developed industry that he has contributed nothing to before forcing these companies to pay him royalties" (Montalvo 1996: 157). Lemelson holds about 500 patents in the United States on various inventions (Lemley 1994: 379). Now that the new rule is in place (measurement of patent life from the filing date rather than issue date), it is counterproductive for drug manufacturers to delay the approval of their patents because it shortens the patent life. However, the line between a broad and narrow patent is blurry and thus complicates determining whether the patent is a legitimate one. In addition, there are few, if any, of such situations in life science.

Neel Sukhatme, Ph.D. Candidate in Economics argues that the URAA caused "pharmaceuticals patentees [to] [speed] up patent prosecution significantly" (2013: 1). Because they lose precious time everyday they wait to respond, they tend to act quicker in order to keep their effective patent life as long as possible. Furthermore, the URAA Act "provides the inventor with a thirty-six month window within which to obtain a patent grant, thus extending the life of a patent in 80% of the cases" (Montalvo 1996: 156). A footnote from Tripp and Stokley provides statistical information gathered from the USPTO: [the average pendency of] "chemical applications is 19.7 months", which results "in an average patent term of 18 years and five months from issue, under the new 20 year term" (1995: 315). This data sounds assuring,

however, some are skeptical about the real-life situation in the pharmaceutical field. Dr. Josh Bloom, who is the director of chemical and pharmaceutical sciences at the American Council on Science and Health, believes that the actual patent life for pharmaceutical innovations is "effectively about 11 years after accounting for development time" (Bloom 2012). Hence, in life science, earlier issuance may have some advantages in terms of business clarity, but it is not a major advantage because of FDA delay. Conversely, the end of the patent term may become much more a focus. Although it is important to acknowledge some advantages of this Act, it is equally imperative to list several provisions that, according to some scholars, are not beneficial to the innovators, particularly in life science.

Disadvantages of and Arguments Against the Act

One of the main things that innovators as well as investors seem to find harming to their business turns out to be one of the provisions discussed above as a benefit. It is the change in the way patent life is measured. Before June 8 1995 (the provision's effective date), the patent life was measured from the date it was issued. However, the life of patents filed on or after that date was going to be measured from the date the earliest application was filed. As Dr. Bloom has already pointed out, in reality effective patent life is much shorter than calculated. He also argues that "bringing one new drug to the market takes roughly 14 years, at a cost of about $1.3 billion" (Bloom 2012). Because "[f]inancing [is] always difficult for start-up business [and] is further complicated by the tremendous risks and long lead time involved in bringing a product from concept to market" (Wellons and Ewing 2007: xxxii), rational investors will be less willing to take the risk if the life of the patent is not long enough to recoup the costs and make risk-adjusted profit. It is uncertain how many years research, development, and clinical trials will take.

Because there is so much room for unpredictable results and errors in the research design, it is difficult for investors to estimate the proper price for the drug without knowing how many years the monopoly will last. Measurement of patent life from the filing date may hurt the investors and cause significant financial harm if the drug only has a few years of exclusivity. Additionally, as John Thomas says, even with the measurement of patent life from the filing date, "the patentee gains no enforceable rights merely by filing a patent application" (2005: 282). It still has to be approved, but while it is pending, the contents of the patent application are publicly accessible information (18 months after the filing date of the application). Cooter and Ulen argue that inventors "risk more than lawyers' fees" when they apply for a patent (2011:119). In case the patent is denied, another competitor can take the idea and develop his own patent without violating the patent laws. Even if the application is approved, competitors can see the details and "engineer around the patent" (2011: 119). Thus, patentees are expected to be more cautious and spend more time developing their product before publicizing their ideas. As a direct result, taking more precautions causes delays and thus impedes innovation.

According to patent attorney Maurice Ross, "most applicants must wait eighteen months or more for a first "office action," and it is not unusual for applicants to wait three years or more before the Patent Office completes examination and issues and/or finally rejects a patent application" (2012). Prolonged wait and uncertainty about the approval of the patent can play a significant role in an investor's willingness to invest in a particular research. The change from first-to-file taken together with application review procedures places financial burden on inventors and small businesses (Ross, 2012). Often, they are not able to effectively defend their patents from large corporations, thus discouraging small-scale innovators.

This literature provides context to my research and outlines the major arguments for and against the URAA of 1994. The arguments in the literature I've examined so far are without a doubt eloquently phrased and well-researched. However, when discussing possible outcomes of the Act, scholars tend to rely mostly on theory and provisions of the legislation. Although scholar's arguments are valuable, especially in software and electronics, there seems to be a missing link in their works in terms of connecting these arguments to the realities of the pharmaceutical field. I plan to find that missing link by conducting interviews and surveys of the main actors of research and protection of intellectual property that were directly affected by the provisions of the Uruguay Round Agreements Act of 1994. Their knowledge and experience in the field of innovation and patent law will complement the currently existing research and can lead to more comprehensive conclusions about the effects of the Act on the innovation community. I am interested in seeing whether the changes discouraged or encouraged innovators and investors.

Methodology

Below I describe the design and methodology of my project. Then, I will identify why the methods I've chosen are appropriate and feasible. Once the methodology is described, I will present a list of questions I used during the interviews. Next, I will move on to discussing my sample and explain how I secured it. Because my project involves human subjects, I will also review the requirements of the Institutional Review Board of UC Berkeley. Following the IRB review will be an acknowledgement of limitations to my research that are currently apparent or anticipated in the future. I will then provide a list of anticipated challenges and describe how I overcame them.

Design

The design of my work will appear in a form of longitudinal research, as I will be ordering data in time. Essentially, I am intending to track the changes in strategies of investors and attorneys starting from 1994 until 2013. According to Russel K. Schutt, "[b]y measuring the value of cases on an independent variable and a dependent variable at different times, the researcher can determine whether variation in the independent variable precedes variation in the dependent variable" (2012: 177). Looking at the larger picture, the independent variable in my thesis is the URAA of 1994, and the dependent variable is any changes in innovation observed after the passage of the law. My research partially consists of an analysis of patent law that had existed prior to the enactment of the URAA of 1994 and after it was implemented. Additionally, I introduce scholars' opinions found in secondary sources. To test a few theories, I suggest several scenarios in which drug development is affected by the FDA ant PTO processing delays. In each scenario, I add or subtract years of effective patent protection to observe how they affect the overall drug value and as a result, the company value. Because many companies are sold to or are acquired by larger pharmaceutical corporations once successful and promising drugs are developed, it is worthy to calculate company worth using the net present value formula.

Furthermore, I will include a cohort study of the stakeholders. To clarify, the contextual definition provided by Schutt identifies stakeholders as "individuals and groups who have some basis of concern with the program" (2012: 361). Cohorts are described as "people who all have experienced a similar event or a common starting point" (Schutt 2012: 181). In this research, the cohort will consist of investors and attorneys who worked in their respective fields at least two years prior to the enactment of URAA of 1994 and at least two years after it is passage. Cohort study is one of the most appropriate and feasible method to answer the question about investors'

role in shaping innovation because information gathered from interviewing patent lawyers and investors will give me the necessary practical perspective that scholars had not sufficiently considered in their research projects. This method is subject to limitations.

Methods

My ultimate goal is to present an explanatory research that will a) attempt to identify the causes of the URAA of 1994 by consulting secondary sources, patent attorneys, and investors b) track the effects of the law on the innovation rates using mathematical methods (NPV formula to calculate a company's worth), and c) describe the practical roles of investors (subject to limitations), and draw the connection between, as Professor Musheno put it, "the law on the books and the law in action". First, I will analyze the policy change within the patent law field. After a brief summary and explanation of the relevant changes that the URAA of 1994 brought about, I will discuss how the issue was addressed in the scholarly legal, business, and policy literature to this date. Once I have laid the foundation for my research project by providing a summary of the changes brought about by URAA of 1994, I will introduce and analyze data collected through secondary sources, such as scholarly articles in journals or books, looking for arguments that were made about the factors that led to the passage of the Act. I will then ponder about its consequences.

Next I will run the NPV calculations for several scenarios to see how added or subtracted years of effective patent protection affect a company's value. Subsequently, I will move on to filling in the blanks by introducing a detailed summary of the hands-on experience that I extract from attorneys and investors. This part of my research will consist of analyzing data received from interviews with the stakeholders. By interviewing attorneys and venture capital representatives, I plan to ask questions that I did not find answers to after having conducted my

literature review. For instance, Tripp and Stockley argue that [the average pendency of] "chemical applications is 19.7 months", which results "in an average patent term of 18 years and five months from issue, under the new 20 year term" (1995: 315). However, Dr. Josh Bloom insists that it is "effectively about 11 years after accounting for development time (2012). However, it is important to understand that the two authors are referencing two different things – Tripp and Stockley talk about the actual patent pendency time with the PTO, whereas Dr. Bloom includes the time it takes to conduct the clinical trials for the drug and obtain FDA approval. One of the challenges this research project is facing is subjectivity of the findings, since each person will have different experiences with the patent system. Keeping the limitations in mind, the information obtained from investors and patent lawyers should shed some light on the disagreement over the patent life (subject to limitations). Currently, USPTO reports a 29.8 (as of June 2013) months traditional total pendency (USPTO, Visualization Center). However, this data is not specific to pharmaceutical patents – it also involves a large number of other utility patents that usually get approved faster because they do not involve an FDA approval and clinical trials associated with it.

Interviews

I conducted interviews with two groups of professionals: attorneys and venture capital representatives (investors). The attorneys I interviewed either practiced patent law at least 2 years before and at least 2 years after the enactment of URAA of 1994, or had appropriate knowledge about the law if they hadn't practiced patent law before 1994.

In my interviews with the attorneys I found out how the URAA of 1994 affected innovation. Mainly, I intended to learn how the attorneys see the change in their routine work by asking them the questions listed below.

Questions for attorneys:

1. How did the changes brought by the Uruguay Round Agreements Act of 1994 affect your legal practice and investment strategies of your clients?
2. Have any other events occurred at the same time as the URAA of 1994 was passed that may have affected innovation rates?
3. Why was this Act necessary to implement?
4. Has the patent application process become simpler or more complicated after the URAA of 1994 came into effect?
5. Is patent application process more costly for your clients?
6. Has the wait time for patent approval changed since the enactment of URAA of 1994? If so, how?
7. Why was there a drastic decrease in the number of patent applications in the year of 1996 compared to the previous and next years?
8. In your professional opinion, how did the URAA of 1994 affect the desire of venture capital firms to invest in pharmaceutical research?

Additionally, to learn how the law affected investors, I have conducted interviews with venture capital representatives. My goal was to learn how investors adjusted to the new rules and whether they changed their investment strategies.

Questions for investors:

1. Did the changes resulting from Uruguay Round Agreements Act (URAA) of 1994 change the investment strategy of your firm?

   If so, in what way?

2. Why was this Act necessary to implement?
3. Have any other events occurred at the same time as the URAA of 1994 was passed that may have affected innovation rates?
4. What is your formula for investment return calculation? Has this formula changed over time?
5. Do you invest in pharmaceutical innovation if your prediction indicates investment at a loss? If so, why?
6. How many investments has your firm made into the field of pharmaceutical innovation?
7. What is the current royalty rate that is predominant? (the rate helps determine how much profit the investors will make)
8. On average, how many years does it take to receive full return of your investment?
9. Excluding the time consumed by clinical trials and Food and Drug Administration (FDA) approval, how long is the average life of a patent?
10. Do you often file for an extension?
11. What are some other methods that your firm uses to extend monopoly in the market?
12. How often are extensions granted and on what conditions?
13. What is the average number of years for which the extensions are granted? (currently extensions can be granted for up to 5 years for pharmaceutical innovations, and only compensate 50% of the total delay caused by the FDA).

Sample

The convenience sample consists of attorneys who practice in the state of California, located in the San Francisco Bay Area. My thesis advisor is a practicing intellectual property attorney and a partner at the Wilson Sonsini Goodrich and Rosati law firm with offices in several major cities in the United States, Asia, and Europe. Although I could attempt to conduct interviews with attorneys who work at other US offices for the purposes of comparison, I am choosing to concentrate my attention within the borders of California. Due to the size and limitations of the project, including other regions would render my results inconclusive. Furthermore, I am not planning on drawing broad generalizations about the country based on the results of my research.

Institutional Review Board

Having discussed the project with Professor Musheno and read the instructions on the Berkeley IRB website, I came to the conclusion that due to its scope and non-invasiveness my research does not require an IRB review. Nevertheless, I asked each participant to sign an informed consent form that authorizes me to use information I receive from him or her during our interview and subsequent follow-up emails or phone conversations. I have provided each participant with a copy, as required by the IRB.

Limitations

This research faces several limitations. The main one is the sample size (for the interview portion of my work), which in turn, leads to the necessity to employ convenience sampling rather than random. However, convenience sampling is an acceptable choice in this case because I am targeting a certain population (investors and attorneys). This sample is not representative of the

whole country, or even the state of California, but the conclusion will be properly adjusted to account for the limitations.

Another weakness relates to the policy research portion of my work. Due to the impossibility to control for other factors that could have caused increases or decreases in the number of utility patent applications filed per year, I will not be able to make a conclusive statement about whether it was the URAA of 1994 that caused the shifts. However, I will attempt to find out whether and how the legislation affected investors and attorneys in practice. Moreover, I will attempt to find out whether the current 20-year patent life from the date of filing is sufficient to promote innovation in the pharmaceutical industry. And lastly, I will probe the interviewees about any other major developments that have affected the field of pharmaceutical innovation to see if there were any external factors I have not considered yet.

Interview report

David Mack, Ph.D.

Dr. David Mack is President and CEO of PMV Pharmaceuticals. Prior to co-founding PMV Pharma with famed biologists Arnie Levine and Tom Shenk, David was a General Partner at Alta Partners from 2002-2013. His first investment was Angiosyn (acquired by Pfizer in 2005) where he was a Director and CEO. David currently serves on the board of directors of Aerie Pharmaceuticals, aTyr Pharma, Ceregene, Proacta Therapeutics, Sutro Biopharma, and PMV Pharma. Dr. Mack has co-authored more than 30 scientific articles and reviews, including papers published in Cell, Science, and Nature, and is an inventor on 25 issued US patents.

According to Dr. Mack, developing new drugs is extremely costly. Often it makes sense to kill potentially unsuccessful drug development early in the game because the amount of money that will be lost increases each day. He says, “if we take a novel small molecule drug as an example, a novel chemical entity (NCE), we would file composition of matter IP on it once we felt it had promise as drug in pre-clinical studies”. The 20-year IP clock begins with that first filing. From that point a series of detailed pre-clinical and manufacturing studies would be performed to create an investigational new drug (IND) application to be submitted to the Food and Drug Administration (FDA), which would allow for a first-in-man clinical trial (a Phase 1 safety trial). A smooth IND process would take anywhere from 12 to 18 months. At this point, there is about 18 years of patent life left on the molecule. To put things into perspective, Dr. Mack briefly goes over the timeline for clinical trials.

Phase 1 is a safety study (takes about 1-2 years), during which clinicians are trying to test the drug to determine the highest safe dose that can be administered to a patient. They increase the dose until one sees a serious adverse advent (SAE). Dr. Mack says “if you see a serious adverse event, you back off that dose”. There are situations when the SAE is so severe that the trial is halted, and the clinical development is completely shut down. The Phase 1 process establishes the drug’s maximum tolerated dose (MTD), and allows one to move onto a Phase 2 efficacy trial.

Depending on the indication, a Phase 2 could take about 18-24 months, and is needed to measure drug efficacy in patients. By the end of Phase 2, clinicians should know the optimal dose.

Phase 3 consists of a pivotal trial (in oncology for example on average, 2-3 years can be spent in phase 3). If successful, one then applies for a new drug application (NDA) with the

FDA. If the NDA is processed smoothly with the Agency, this process should take 12-18 months. By this point in time, one has spent $500million-$1billion dollars on the research and development of the drug.

In Dr. Mack's experience about 10 years of effective patent life is lost in the drug development process before even launching the drug. He says, "if you're lucky, only 10 years of exclusivity remains". Then, once every step of the development is complete and the drug is ready to be sold in the market, it usually takes about 5 years to reach peak sales. So, at the end, there are only 5-7 years left to robustly recoup the tremendous costs and make profit. Again, Dr. Mack cautions, "this is the best case scenario, assuming that there were not any significant issues during clinical trials and FDA approval". Any mistakes or miscalculations may delay drug development by months or even years thus reducing the effective patent life and discouraging investors.

In addition to filing a patent application on a new molecule composition, it is common practice to extend the label of existing drugs. For example, when the drug is already developed and approved, sometimes it can be repurposed and used to treat other conditions. The process begins at phase two (there is no need to start from the very beginning). However, the clock has been running on the current patent term. New methods of treating need to be discovered and tested. But extending the label of the drug will provide additional IP protection on the basis of methods of treating. For example: "IP on methods of treating RA rheumatic arthritis – in such cases, composition matter is easy to defend", says Dr. Mack.

However, new strategies to extend the term need to be developed in order to make profit. For instance, one could patent a manufacturing protocol (method of synthesizing the molecules could also be protected).

There are 3 key areas within which one can file for a patent.

1. Composition matter
2. Method of treating
3. Formulation

The ultimate goal of a small pharmaceutical company is to be acquired by a large company because it is nearly impossible for a small company to develop a sales and marketing organization, while the large pharmaceutical organizations can “plug in” a new drug with relative ease. Because composition matter patent (patenting a molecule) offers stronger IP protection than the other two areas, large companies value such patents more when it comes to acquisitions of smaller companies. So a small company needs to own IP rights on a valuable drug, which a large pharmaceutical company would be interested in acquiring. When large companies acquire small ones, intellectual property becomes key because it directly affects pricing. In the absence of a relevant patent, a generic drug company will simply reference the previous clinical data and begin sales.

In addition, the strength of exclusivity and time of exclusivity matter. “If there is a weakness, it is used against you on determining overall value”, Dr. David Mack warns. The patent on composition matter is considered to be stronger because normally there should be no debate in composition matter. Timelines are also very important. As soon as the patent expires, companies experience extreme drops in revenues. A good example of a drug falling of a patent cliff is Lipitor. When it was under patent protection, Lipitor was making $12 billion a year (for Pfizer). However, as soon as it went off patent and generics penetrated the market, the profits plummeted to $750 million a year. That is 16 times less money that the company is now making.

Thus, patent is a highly valuable asset to have for a smaller company who wants to get acquired by a large pharmaceutical corporation.

When a major franchise is going off its patent cliff, there are different ways to deal with it. The most common approach is to combine the drug that is coming off patent with another drug and create an entirely new formulation. Another way of keeping IP rights longer is to file for an extension. There are a couple of other ways in which one can qualify for a patent extension: a) by tweaking the original formula or coming up with a novel formulation; b) by combining existing drugs.

As discussed above, clinical trials consist of 3 main phases that each new drug has to go through. The fourth phase takes place after the approval is granted, but can cost millions of dollars nevertheless. The cost of clinical trials varies from drug to drug. Some require only a few dozen of human subjects for phase 2 and 3, but others, like cardiovascular drugs, require 5,000-10,000-person trials. Dr. Mack claims that phase 3 can cost hundreds of millions of dollars. Because the process is so costly, everyone looks for ways to accelerate every step of it. Dr. Mack adds, “when the clock starts when I discover something versus when I file on it is a huge difference”. If the timeline for development of a certain drug, because of its indication (for example), is going to take 15 years and its exclusivity is going to last only 2-3 years – that does not attract investors. “When am I going to get to the market and how many years do I get for peak sales?” – is a question investors generally need answers to before they offer to invest their money. There is also a risk that patent does not get approved, or by the end of the reprocess, claims are extremely watered down. “It's all about timing”, Dr. Mack adds. “There is always the risk of the clock ticking and not knowing what is going to be allowed by the end of the day”, he concludes.

Richard Ogawa

Mr. Ogawa is a practicing patent attorney with over twenty years of experience who specializes in high technology. The industry, and thus his experience, is admittedly different from the field of biotechnology. Mr. Ogawa's experience brings in a different perspective on utility patents and allows a comparison to be drawn between the two fields and their patent-related issues.

Mr. Ogawa says "when law changes, it seems like there's a catalyst". One of the biggest triggers for the changes that came with the URAA of 1994 was the need to eliminate submarine patents. Mr. Ogawa, like other attorneys, agrees that Jerome Lemelson was that catalyst. Lemelson discovered a hole in the system and exploited it. Lemelson's name began coming up around 1992, mostly because he had filed some patents on electronic inventions that have been pending for 40 years, sometimes even 50. Because at that time, the patents were not published until they were approved, many companies ended up paying large amounts to Lemelson in royalty payments. Lemelson was mostly acting within the automotive and electronics industries, where the patent term was still different from other countries (17 years from issue date, rather than 20 years from filing). When asked if it was a change for the better, Richard says that "for high tech, there was not much of a difference". For software and some hardware, the patent application approval turnaround is 18-36 months. When it comes to software and hardware developments, it may take a thousand of patents for devices like iPhones. "Patents on improvements are different from those in the biotech industry", Mr. Ogawa says. In high tech, product cycles are quite quick, but in biotech molecules may not work if they are changed, thus delaying the approval process.

In general, the overall drug approval process for the biotech industry is much longer because it involves clinical trials and certain pre-approval stages. Richard says he still remembers that day – June 8, 1995 – when he was sitting near the patent office close to the biotech lawyers. There were frantic people in the office filing a lot of cases that day. As Richard says, his clients clearly didn't care as much as "biotech people" about the new changes in the law because it didn't affect them in a negative way compared to those in the biotech industry.

When filing for an improvement patent, it restarts the 20-year term, as long as the improvement patent is not a continuation. Inventors would have to tweak it considerably, and the patent needs to comply with the current patent law.

According to Mr. Ogawa, when URAA of 1994 took effect, biotech suffered most. In addition, new material science such as semiconductor, plastics, and the like were disadvantaged as well. The uncertainty about the effective patent protection term made it more difficult for investors to calculate returns on their multimillion-dollar investments, so estimates were used instead. When something gets funded, patent counsels are brought in right away to secure monopoly.

There is one big common similarity between the biotech and the high-tech fields – investors won't offer their money to finance research and development until they get their monopoly. Patents are taken very seriously in this field. In software business where capital investment is not as significant as in the pharmaceutical field, funding comes from large companies with big pockets who made discoveries. Investors who work in high tech didn't see much of a difference when the URAA took effect, but they didn't like the law either, according to Mr. Ogawa.

Robert Blackburn

A former vice president & chief patent counsel of Chiron Corporation, Mr. Blackburn practiced during the time when the URAA took effect, and remembers the day the law changed… On June 8 1995, he had to re-file many applications before the deadline because after the deadline, new terms applied. Mr. Blackburn shares his experience: “Chiron’s patent portfolio did not have to do much with small molecule pharmaceuticals, the primary areas were in therapeutic proteins, diagnostics and vaccines”. Mr. Blackburn could not recall what the average timeline was, but knew that patent investigation timelines for diagnostics were generally shorter than those for pharmaceutical chemical entities (small molecules), and some vaccines took quite a bit longer (several years).

Mr. Blackburn was on the National Academy’s committee that was issued a report on patent reform, “A Patent System for the 21st Century.” Wes Cohen, an economist at Duke University who was also on the committee, was doing a study whether patenting research tools inhibited research. Interviews with patent department heads tended to indicate that research tool patents were a problem. Heads of research, on the other hand, felt differently and viewed innovative tools valuable additions to their research arsenal that were worth licensing. This was probably because research heads benefited from the use of tools, but patent departments were only consulted when a licensing problem arose.

Mr. Blackburn believes that the “need to have complete protection for technology” is evident. New medical therapies are often the result of several serial breakthroughs. The patent system is good at protecting the final step, for example the particular small molecule that ends up as the drug. The patent system, however, is very poor at protecting (i.e., providing incentives) for

the upstream innovations that made the final step (e.g., the drug) possible. Thus, the system does not provide incentives to invest in upstream technologies like research tools. In fact, venture capitalists (VCs) are simply not interested in such investments now. Thus, medical innovation is very much dependent on government-funded academic upstream research. Unfortunately not only is such research usually not very targeted at finding the fast route to market for a new product for patients in need, government funding is on the decline. Mr. Blackburn says, "patents are not valuable because they cover what you do, they are only valuable when they cover what your competitor would do but cannot do for the patent."

On June 8, 1995 Mr. Blackburn had to refile many continuations on his current patents. According to Mr. Blackburn, there was a "huge line" at the patent office, and everyone was trying to get their patent applications in before the end of the day to qualify under the old law. Mr. Blackburn says that there was not any perceptible change in their research and development strategies after that because, being a multinational company, they were living with that patent term in the rest of the world.

When Mr. Blackburn was chairman of the IP Committee, he was one of the people who lobbied Congress on behalf of Biotechnology Industrial organization over patent term extension. He says they were by large successful in getting what they wanted in terms of patent term extension. But the problem getting patents through was not the applicants' slow response, but the backlogs of the patent office. The PTO patent examiners were not necessarily slow, but they declined many applications that eventually in fact were patentable, and they were just trying to make up their minds about those pending applications. There was a culture then that if they allowed a patent, it was a potential mistake they could be held accountable for. But if they just kept rejecting it, no one would ever complain about that. However, this was mostly happening in

the biotech field. When asked whether it became more difficult to calculate respective profits for investors after the URAA took effect, Mr. Blackburn said “it had no impact”. The target market was understood and known before the project was even started. When inventors decided to go after a certain disease, they knew the patient population. People used the rule of thumb of how much market penetration they could get with product x or y. They had ways to calculate what the potential return was for development of a particular drug. Since the patent term was being measured from the date of filing, by 1995-97 people in biopharmaceutical field were thinking about holding back and waiting because the decision to file a patent was complex and involved significant risk (and possible monetary loss).

Mr. Blackburn says, “you would file for patent before you go outside the company for clinical trials… but the question is whether you would file on individual molecules that can only be tested in the lab before you’ve got solid clinical study”. Mr. Blackburn also shared his experience with the classic model:

> The classic model for small molecules was to file relatively early (first filing is on a chemical genus, which you try to file before you find out what the lead compound was in hopes that it was not actually in that group. Then you can have another filing that would have a later expiration date on a new compound. That is easier said than done, as it does not always work out that way. Everything that changed the patent term made later stage clinical level inventions, manufacturing inventions, more important. For example, filing a patent on optimized dosage came out of clinical trials – it could have been ten years after the original compound patent was filed. If that’s going to end up on your approved FDA label, that’s as good as a compound claim because the generic has to copy your label. And if they copy a label that has your label of dosing, then they are infringing and you

can sue. FDA makes them copy the label of the pioneer drug exactly. This happens after the original patent expires or someone has challenged its validity (Robert Blackburn, interview).

In agreement with legal scholars and his fellow attorneys, Mr. Blackburn also believes that submarine patents and Gerome Lemelson were largely the reason why the new patent law was implemented in the first place. Lemelson did foresee a lot of things that people ended up putting into practice later and filed secret patent applications, waited until the product became successful, and then "popped out" that patent. On the one hand, Lemelson was playing completely by the rules of the time; on the other hand, Mr. Blackburn adds, "can we really say it's unfair that someone who developed a product based on Lemelson's innovation share with him some small percentage of their profits?" Mr. Blackburn adds, "It's not like they were not making money. Was this guy ahead of his time, he certainly foresaw a lot of these optical control systems that ended up being used today." Lemelson often collected 10 millions of dollars per piece from large companies who made billions. When Mr. Blackburn dealt with him, Lemelson was quite reasonable, but he still held up some companies and caused them to lose money.

So how exactly does the URAA limit or eliminate submarine patents? Mr. Blackburn says that patent system should provide predictability and may even change the decision to invest. Now that the patent information is publicized before the patent is approved (18 months after the application is filed), is there risk of losing protection? There is a provision in the law that if you get a patent issued, you can potentially go back and collect some royalties. But if the patent is denied, there will be no protection – you can only go back and collect if the patent issues. Mr. Blackburn believes that the application process became more complicated because there is now a need to do more strategic planning and decisions upfront. Filing costs were not significantly

affected, fees may have changed, but the patent figures in general were not affected much. Mr. Blackburn does not think there is a direct cost to the companies. The real question, he says, is "will you have your protection." As an attorney, he was responsible for making sure his patents were issued by the time the drug is approved by the FDA, which on average took 10 years. So , he states, it's somewhat irrelevant whether or not a patent is issued at the time the drug was approved because for a "new chemical entity" (i.e., a new drug, not a new use nor an optimized formulation of an old drug) the FDA gives at least some period of time before a generic can file for approval of a copy.

Findings and Conclusions

Having completed the literature review and conducted interviews with the stakeholders in pharmaceutical, diagnostics, and high-tech industries, I realized that opinions of the scholars largely collide with those of the stakeholders, mainly on the issue of the effective patent life. To check how adding and subtracting effective patent years can affect the sales and company's worth, I ran a series of mathematical calculations to understand how additional years of patent protection could change the chances of a drug that costs $500,000,000 to be developed and marketed. All calculations begin in 2013 and vary based on the rules of the scenario (see Appendix I for excel spreadsheet calculations). The discount rate is set at 15% (.15) because it is the current predominant rate investors use to compute the pharmaceutical company's worth.

The NPV formula used to arrive to the calculations below is the following:

$$\mathrm{NPV}(i,N) = \sum_{t=0}^{N} \frac{R_t}{(1+i)^t}$$

In this formula, *i* stands for discount rate, *Rt* – net cash flow at time *t*, *N* is the total number of periods included in the calculation.

In the first scenario, patent term begins in 2013 and ends in 2032, providing the 20 years of total protection as outlined in the law. However, one can see that the effective patent life in Scenario I is only 10 years (because investors do not begin making money until 2023). This is the most typical scenario in the pharmaceutical field after FDA and PTO delays are accounted for. In this scenario, innovators only have 10 years of effective protection, which means that investors only have 10 years to recoup their costs and generate risk-adjusted profits. The total NPV turns out to be $620,281,423.94. Below are the calculations:

$$\mathbf{NPV} = \frac{0}{(1+0.15)^{0}} + \frac{0}{(1+0.15)^{1}} + \frac{0}{(1+0.15)^{2}} + \frac{0}{(1+0.15)^{3}} +$$

$$\frac{0}{(1+0.15)^{4}} + \frac{0}{(1+0.15)^{5}} + \frac{0}{(1+0.15)^{6}} + \frac{0}{(1+0.15)^{7}} + \frac{0}{(1+0.15)^{8}} +$$

$$\frac{0}{(1+0.15)^{9}} + \frac{500{,}000{,}000}{(1+0.15)^{10}} + \frac{500{,}000{,}000}{(1+0.15)^{11}} + \frac{500{,}000{,}000}{(1+0.15)^{12}} + \frac{500{,}000{,}000}{(1+0.15)^{13}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{14}} + \frac{500{,}000{,}000}{(1+0.15)^{15}} + \frac{500{,}000{,}000}{(1+0.15)^{16}} + \frac{500{,}000{,}000}{(1+0.15)^{17}} + \frac{500{,}000{,}000}{(1+0.15)^{18}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{19}} = \mathbf{\$620{,}281{,}423.94}$$

In the second scenario, investors make money beginning from 2023 as well. However, in this scenario I added 2 more years of protection at the end of the term to compensate for the delays caused by the FDA (assuming the delay was 4 years, and that only 50% of total delay caused by the FDA is compensated, the extra protection is only 2 years). So this patent is scheduled to expire in 2034 instead of 2032 (as in Scenario I). Investors have 12 years of effective patent protection, from 2023 to 2034, and the total NPV equals $669,947,057.10

$$\mathbf{NPV} = \frac{0}{(1+0.15)^{0}} + \frac{0}{(1+0.15)^{1}} + \frac{0}{(1+0.15)^{2}} + \frac{0}{(1+0.15)^{3}} + \frac{0}{(1+0.15)^{4}} +$$

$$\frac{0}{(1+0.15)^{5}} + \frac{0}{(1+0.15)^{6}} + \frac{0}{(1+0.15)^{7}} + \frac{0}{(1+0.15)^{8}} + \frac{0}{(1+0.15)^{9}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{10}} + \frac{500{,}000{,}000}{(1+0.15)^{11}} + \frac{500{,}000{,}000}{(1+0.15)^{12}} + \frac{500{,}000{,}000}{(1+0.15)^{13}} + \frac{500{,}000{,}000}{(1+0.15)^{14}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{15}} + \frac{500{,}000{,}000}{(1+0.15)^{16}} + \frac{500{,}000{,}000}{(1+0.15)^{17}} + \frac{500{,}000{,}000}{(1+0.15)^{18}} + \frac{500{,}000{,}000}{(1+0.15)^{19}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{20}} + \frac{500{,}000{,}000}{(1+0.15)^{21}} = \mathbf{\$669{,}947{,}057.10}$$

Third scenario looks into a situation in which the FDA delay is two years shorter. Thus, effective patent life begins in 2021 and ends in 2032, giving investors a total of 12 years to collect payments. However, even though in both Scenario 2 and 3 investors have 12 years of effective patent life (money-making period), the final numbers look different. The cash flow becomes discounted at a higher rate at the end of the term than in the beginning, showing that it is more beneficial for investors to get the extra two years of exclusivity early rather late. The total NPV for Scenario III is $886,004,983.02.

$$\mathbf{NPV} = \frac{0}{(1+0.15)^{0}} + \frac{0}{(1+0.15)^{1}} + \frac{0}{(1+0.15)^{2}} + \frac{0}{(1+0.15)^{3}} +$$

$$\frac{0}{(1+0.15)^{4}} + \frac{0}{(1+0.15)^{5}} + \frac{0}{(1+0.15)^{6}} + \frac{0}{(1+0.15)^{7}} + \frac{500{,}000{,}000}{(1+0.15)^{8}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{9}} + \frac{500{,}000{,}000}{(1+0.15)^{10}} + \frac{500{,}000{,}000}{(1+0.15)^{11}} + \frac{500{,}000{,}000}{(1+0.15)^{12}} + \frac{500{,}000{,}000}{(1+0.15)^{13}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{14}} + \frac{500{,}000{,}000}{(1+0.15)^{15}} + \frac{500{,}000{,}000}{(1+0.15)^{16}} + \frac{500{,}000{,}000}{(1+0.15)^{17}} + \frac{500{,}000{,}000}{(1+0.15)^{18}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{19}} = \mathbf{\$886{,}004{,}983.02}$$

Unlike the first three scenarios, Scenario IV provides a considerably long effective patent life. The assumption is that the FDA delay is reduced by two years, and the remaining delay is compensated at the regular 50% rate (inventors get 2 years of additional patent protection for the 4 years lost due to the FDA delay). The total NPV is $935,670,616.18, which is almost 34% more than the value computed in Scenario I. So, if this scenario is applied in reality, the chances of the drug drawing an investment is, conceptually, 34% higher, which may benefit the health care industry as well as the patients.

$$\mathbf{NPV} = \frac{0}{(1+0.15)^{0}} + \frac{0}{(1+0.15)^{1}} + \frac{0}{(1+0.15)^{2}} + \frac{0}{(1+0.15)^{3}} +$$

$$\frac{0}{(1+0.15)^{4}} + \frac{0}{(1+0.15)^{5}} + \frac{0}{(1+0.15)^{6}} + \frac{0}{(1+0.15)^{7}} + \frac{500{,}000{,}000}{(1+0.15)^{8}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{9}} + \frac{500{,}000{,}000}{(1+0.15)^{10}} + \frac{500{,}000{,}000}{(1+0.15)^{11}} + \frac{500{,}000{,}000}{(1+0.15)^{12}} + \frac{500{,}000{,}000}{(1+0.15)^{13}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{14}} + \frac{500{,}000{,}000}{(1+0.15)^{15}} + \frac{500{,}000{,}000}{(1+0.15)^{16}} + \frac{500{,}000{,}000}{(1+0.15)^{17}} + \frac{500{,}000{,}000}{(1+0.15)^{18}} +$$

$$\frac{500{,}000{,}000}{(1+0.15)^{19}} + \frac{500{,}000{,}000}{(1+0.15)^{20}} + \frac{500{,}000{,}000}{(1+0.15)^{21}} = \mathbf{\$935{,}670{,}616.18}$$

Based on the results we obtained by running NPV calculations, we can conclude that the company worth diminishes proportionally to the reduction in the effective patent term. The actual numbers vary from one drug to another, but the point can be made that the two extra years in the beginning of the money-making phase and two more years added to the end of the effective patent term could make a difference in an investor's decision. For example, in the case of a $500,000,000.00 drug, 34% of extra value is quite significant and could lead to funding and development of the drug. But if there isn't enough time to recoup the costs of research and

development, investors may refuse to finance it and the drug may never be developed, thus creating an impediment to innovation.

The formula that investors use to calculate potential profit from their investment has not changed – it remains to be the net present value calculation. Investors run estimates and use the result to support their decision whether to invest in a drug or not. One component that did change is the number of years that a patent is valid – instead of running the NPV calculations for 17 years, now investors are forced to rely on estimates. Some may say that uncertainty negatively affects financial decisions like this, but others could argue that in pharmaceutical innovation quite a lot of things are uncertain, and a deviation in effective patent life isn't detrimental (for instance, side effects can affect the timeline or even result in a drug being pulled off the trials). However, it is clear that stronger and longer IP protection benefits pharmaceutical industry and the consumers in the long run.

To conclude, I would like to use the results to suggest a potential improvement to keep innovation on the rise. As one can see, the best scenario for a company is to secure as many years of effective patent protection as they reasonably can. Defining a reasonable term is difficult, because for blockbuster drugs that make billions of dollars within just a few years, while average drugs may require 10 or more years of patent exclusivity. It is also inefficient to review each drug's patent term individually as it will only add to the current backlog at the PTO, however, Dr. Sukhatme agrees that "[i]n an ideal world the length of patent term would be tailored across different industries" (2013: 5). He adds that "[i]ndustries with very high fixed costs, slow obsolescence or long regulatory delays would feature longer patent terms than industries with lower fixed costs, fast obsolescence and no regulatory delays." (2013: 5).

One possible way to extend the overall effective patent term would be to extend the patent term by 100% of the FDA delay instead of the current 50%. It would not completely compensate for the delay since the value is discounted on average at 15% each year, but it is a realistic method and does not add any significant cost for the FDA. Also, as seen in Scenario IV, simply expediting the FDA approval process by 2 years (without the added 2 years at the end of the term) increases the amount by around 28%. Both inventors and the FDA will need to expedite the process on their respective ends to achieve such efficiency. As Mark Lemley stated in his article, the URAA also resulted in some benefits. Now that the patent clock is ticking from the day the application is filed, the inventors and their patent lawyers are incentivized to expedite their applications and not wait until the deadline or file even past the deadline by paying penalties (1994: 379). However, as Mr. Blackburn pointed out in his interview, the process is now more complicated since effective patent term has to be estimated and investors may be uneasy about investing in a low-profit yielding drug that is estimated to only have a few years of exclusivity at the end. Generics will overtake the market and the original inventor will not be adequately compensated, thus resulting in less innovation and higher social costs in the long run.

Per Dr. Mack's experience, after the clinical trials have been done and FDA approval and patent have been issued, there are 5-7 years left to recoup the costs of the drug development, provided there weren't any significant errors or side effects that delayed the approval. For an average drug, it may be too little time to receive a return, and thus investors may turn down such a proposition. It is peculiar that although Mr. Blackburn lobbied Congress over patent term extension, he seems to value patent extensions to a much lesser degree than other stakeholders. He stated in the interview that the URAA didn't impact calculation of profits for investors largely because the "market was understood and known before the project was even started".

One reason why Mr. Blackburn's opinion differs could be the fact that he worked in the field of diagnostics, therapeutic proteins, and vaccines. He pointed out that the timelines for these areas were "generally shorter than those for pharmaceutical chemical entities (small molecules)". It is safe to assume that if timelines in those areas were indeed considerably shorter, then the investors did not feel the same need to rely on extensions as compared to the stakeholders in the pharmaceutical chemical entities.

It is essential to find the equilibrium between the benefits and costs of pharmaceutical patents. Based on my findings, I suggest that pharmaceutical patents should be treated differently from other utility patents because they involve much higher research and development costs. As mentioned in my limitations, my research is of an exploratory character. I recommend that a more extensive and generalizable research be conducted in order to determine how efficiency can be achieved in the field of pharmaceutical innovation.

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Appendix I

Scenario I

Year	Sales
2013	$0
2014	$0
2015	$0
2016	$0
2017	$0
2018	$0
2019	$0
2020	$0
2021	$0
2022	$0
2023	$500,000,000
2024	$500,000,000
2025	$500,000,000
2026	$500,000,000
2027	$500,000,000
2028	$500,000,000
2029	$500,000,000
2030	$500,000,000
2031	$500,000,000
2032	$500,000,000
	$620,281,423.94

Discount Rate 0.15

Scenario III

Year	Sales
2013	$0
2014	$0
2015	$0
2016	$0
2017	$0
2018	$0
2019	$0
2020	$0
2021	$500,000,000
2022	$500,000,000
2023	$500,000,000
2024	$500,000,000
2025	$500,000,000
2026	$500,000,000
2027	$500,000,000
2028	$500,000,000
2029	$500,000,000
2030	$500,000,000
2031	$500,000,000
2032	$500,000,000
	$886,004,983.02

Discount Rate 0.15

Scenario II

Year	Sales
2013	$0
2014	$0
2015	$0
2016	$0
2017	$0
2018	$0
2019	$0
2020	$0
2021	$0
2022	$0
2023	$500,000,000
2024	$500,000,000
2025	$500,000,000
2026	$500,000,000
2027	$500,000,000
2028	$500,000,000
2029	$500,000,000
2030	$500,000,000
2031	$500,000,000
2032	$500,000,000
2033	$500,000,000
2034	$500,000,000
	$669,947,057.10

Discount Rate 0.15

Scenario IV

Year	Sales
2013	$0
2014	$0
2015	$0
2016	$0
2017	$0
2018	$0
2019	$0
2020	$0
2021	$500,000,000
2022	$500,000,000
2023	$500,000,000
2024	$500,000,000
2025	$500,000,000
2026	$500,000,000
2027	$500,000,000
2028	$500,000,000
2029	$500,000,000
2030	$500,000,000
2031	$500,000,000
2032	$500,000,000
2033	$500,000,000
2034	$500,000,000
	$935,670,616.18

Discount Rate 0.15