8-2011

Intellectual Property and Policy Issues in Biotechnology

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To the Graduate Council:

I am submitting herewith a thesis written by Amy Iver Yancey entitled "Intellectual Property and Policy Issues in Biotechnology." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Plant Sciences.

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Intellectual Property and Policy Issues in Biotechnology

A Thesis Presented for the Master of Science Degree

The University of Tennessee, Knoxville

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August 2011

This work is dedicated to my daughter, Warren Arledge Jenkins.

For all your patience and your total acceptance of the time I spent working instead of playing. I love you Wren Bird.

Abstract

Intellectual property, particularly patents, plays a major role in innovation and discovery in biotechnology. Likewise, since the passage of the Bayh-Dole Act in 1981, patents have become an increasingly important factor in U.S. university-driven basic research, especially in the life sciences where patented technologies have transformed agriculture. Specifically, this paper looks at the potential impacts of these trends on university driven research, the university researcher, the pharmaceutical industry, and the farm sector with an emphasis on recent and pending court cases and legislation. This paper examines policy and adoptions issues in biotechnology and biomedicine in depth and touches on important developments in the tech sectors as a back drop for pending legislation and recent court rulings. How policy is adopted, implemented and interpreted have profound impacts on food production, medical ethics, ecology, U.S. and international farm and innovation sectors and the competiveness of the U.S. in the global economy.

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Introduction

Patents have become an important part of the university research process. Since the passage of the Bayh-Dole Act, large universities that receive federal funding for research have been required to actively seek patents on new technologies and license those technologies to the private sector. The purpose of the legislation was to help ensure that those discoveries funded by federal dollars made it into the hands of the public and were not destined to remain obscure or even abandoned.

The relatively recent pursuit of patents and income-generating licensing fees has created tensions for public universities in particular because their discoveries are partially underwritten by state dollar investment as well. Additionally, the trend to patent both by public universities and privates firms has placed a strain on the United States Patent and Trademark office, creating a backlog of patent applications and generating patent thickets in biotechnology, semiconductors and other arenas. Not surprisingly, strong patent protection from the courts has resulted in large damages awards, further muddying the waters and creating a cottage industry for firms that do not invent, yet profit from patent litigation.

Several groups have risen in the past decade to look at the special problems arising from intellectual property, particularly as it relates to food and medicine development. The U.S. Congress has been attempting to reform patent laws to address many of these issues, and the court system has been responding as well. This thesis looks at some very specific problems arising from these tensions, including: the likelihood of infringement suits against university researchers; the possible consequences of patent reform on the pharmaceutical industry; the rise and potential fall of glyphosate (arguably

the most widely-adopted patented agricultural product in history); and finally a guide to help early career professor understand the patent system with an eye to helping them make informed decisions about how to navigate the increasingly complex research landscape.

Chapter 1 Patents: Are university researchers at risk?

(This chapter was published in Nature Biotechnology (2007) 25: 1225–8 with the following authors: Amy Yancey and C. Neal Stewart, Jr.)

Amy Yancey was the principal author of the manuscript.

Abstract

Researchers at public universities face many challenges from anticommons effects in agricultural-and other biotechnologies. By and large academic researchers have ignored patents on key technologies as a strategy to maneuver around patent thickets and FTO issues, but they may be more at risk than they realize. There seems to be no legal impediment from patent holder prosecution of professors, students, postdocs and other researchers who are regular infringers.

Patent purpose and history

Hippodamus is credited with first suggesting that states should reward innovators for introducing useful products to society in Aristotle's *Politics* [1]. The basic idea is grounded in the tenants of utilitarianism, "reward the creator of a useful thing, and society will gain more useful things." Aristotle had reservations, even at that early date, about the tension between serving public good and rewarding individuals. Patents have played a significant role in Western civilization and the notions of progress since the late 1400s. In the United States, patents have been an important part in innovation and

science, but how could people in the 19th century and earlier envisioned biotechnology and today's research climate?

Anything under the sun

The statute language has changed little since 1793. "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore [2]." However, patent policy is still evolving through the interpretation of the courts and the United States Patent and Trademark Office (USPTO) and through legislation. Modern interpretations of the patent statute have changed to more precisely define utility, disclosure, enablement, novelty, nonobviousness and even the technical statutory bars, but the single most important change for biotechnology came from the landmark *Diamond v. Chakrabarty* decision on patentable subject matter. The Supreme Court decision allowed for patents on living microorganisms with the majority deciding that Congress intended patentable subject matter to "include anything under the sun that is made by man [3]." The *Chakrabarty* ruling has important implications for utility patents on plants and the evolution of agricultural biotechnology. Plants were originally only eligible for protection under the Plant Patent Act of 1930 or the Plant Variety Protection Act of 1970, but now utility patents are regularly granted on plants and related processes. A cursory search of plant-related utility patents shows that patents filed under the USPTO's plant classification have increased steadily from five in 1981 to 777 in 2006. Anecdotally at least, this would seem to suggest that granting utility patents on plants has indeed spurred innovation in that field.

Promoting progress or encouraging infringement?

Despite the apparent increase in plant utility patents in the past 25 years, private agricultural biotechnology research and development seemed, unexpectedly, to peak in the mid- to late-1990s [4]. This apparent discrepancy results from a number of complex issues, including industry consolidation through the formation of life sciences conglomerates. It has been suggested that one underlying reason seems to come from patent thickets and anticommons effects that arise from the patenting of basic research processes in agricultural biotechnology—essentially creating a situation conducive to market failure where innovation is invariably blocked because of the cost of bringing downstream technologies to market [5,6,7]. While a recent report from the Science and Intellectual Property in the Public Interest (SIPPI) project concludes that innovation blocking is not occurring, the matter is far from settled in the biotechnology sector [8]. The survey relies on the self-reporting of researchers, asking them how licensing of protected technologies were acquired and the effects of IP difficulties on research in their laboratories. It does not measure any effect on downstream technologies. Furthermore, an earlier report to the National Academy of Sciences suggests that at least part of the reason university research has not been impacted is because of regular infringement of patents by university researchers, which is neither a sustainable nor desirable solution [9].

Patent thickets occur from the patenting of enabling or platform technologies in certain fields such as biotechnology, semiconductors and software and result in difficulties in navigating the patent landscape [5]. Patents may be overly broad, blocking, or be held by rival companies who wish to exclude competitors from the market. Also,

while patents and patent applications are disclosed, license agreements are often not. Add to the mix defensive patenting, a complex and difficult USPTO classification system, and a lack of information available on the license status of certain technologies, and it becomes difficult to know what privately-developed technologies are available for use by researchers. Furthermore, because patents rights are negative rights, bestowing only the right and obligation to exclude others from making, using, selling, or importing the invention, patent holders are not required to utilize the invention—only to defend it—potentially resulting in the underutilization of important tools for addressing public welfare factors in food and fiber production, the casualties of which may be humanitarian and environmental benefits. Commonly referred to as the 'tragedy of the anticommons', the effect was first described by Michael Heller and then applied to research issues by Heller and Rebecca Eisenberg in 1998 [6]. The tragedy arises when rational individuals, acting separately, underutilize a scarce resource to the detriment of all. As applied to patents, the anticommons effect is the result of too many firms having the right to exclude others from a scarce resource to the detriment of the public good (contrasted with the tragedy of the commons where a common resource is over-utilized). Essentially, scientific advance is blocked if the cost of licensing-enabling technologies exceeds the potential value of a product when public researchers are barred from accessing proprietary technologies. And since 76 percent of agricultural biotechnology patents are held by private firms, public researchers have been and will continue to be denied official access to important technologies [7]. Worse, simply determining where a researcher has freedom-to-operate (FTO) is becoming more difficult—with important implications for

infringement, particular since patent infringement happens routinely in every university with biotechnology research.

Examples of thickets and anticommons at work in agricultural biotechnology include broad patents on the two most reliable and utilized plant transformation techniques. Monsanto's patent on the process of transforming plants through the use of *Agrobacterium tumefaciens* is claimed so broadly it could exclude all plant transformation processes that use any engineered bacteria to transfer foreign DNA into plant genomes. The other method, biolistics-mediated transformation, was developed by Cornell University, but licensed exclusively to DuPont, who has blocked competitors from accessing the technology [7, 1]. Similar issues for other enabling technologies exist. Monsanto also holds the patent on the neomycin phosphotransferase (*nptII*) gene, one of the most commonly used selectable markers, which confers antibiotic resistance in transformed plant material. The patent, though set to expire in 2008, has claims written so broadly as to cover all methods of conferring antibiotic resistance even though recent discoveries have produced less controversial methods that rely on plant versus bacterial mechanisms, which raise concerns among critics who fear exacerbation of antibiotic resistance issues REF [11].

Another important example of thicket problems is illustrated in the much-cited Golden Rice project. The provitamin A-enhanced rice was developed for humanitarian purposes to combat blindness and malnutrition in developing nations. Developing the rice required access to over 40 U.S. patented technologies [12]. Since there is no commercial value in creating humanitarian crops, it would have been economically infeasible to produce had companies not waived their license fees for the project.

While it is disturbing to consider anticommons effects on agricultural research, the repercussions are equally distressing in biomedical research, where similar problems arise. For instance, the genes *BRCA1* and *BRCA2* have recently been associated with hereditary breast cancer. A diagnostic procedure for identifying the genes was licensed exclusively to Myriad Genetics, who went so far as to block testing by a University of Pennsylvania researcher [13, 6]. The fast-paced software and semiconductor industries also face similar difficulties. Solutions in those arenas may prove helpful to addressing innovation-stifling problems in agricultural biotechnology.

Why should researchers care about patent policy?

On principle

In the US, the land-grant university (LGU) system was established in 1862 through the Morrill Act and later expanded through several acts to include mandates for research and cooperative extension. At the core of the values of the LGU system is the idea that public investment in education, research and outreach results in public benefits. Much of the basic research that has led to current patents on research tools were created by or in collaboration with publicly-funded university research or, at the very least, on the shoulders of over 100 years of public investment and developmental policy in agricultural research. Anecdotal evidence demonstrates that patents on those tools can be and are being used to block further research on downstream technologies that could save lives and serve the public well-being. Furthermore, important humanitarian and fair trade issues arise. Golden Rice is only one example of how patent thickets can pose difficulties in bringing improved nutrition to developing countries. In addition, numerous ethical

concerns arise when private companies have the capacity to exploit traditional knowledge of peoples in the developing world for profit, especially if they exclude those peoples from a share of proceeds or access to the benefits of additional discoveries derived from that knowledge. Perhaps the most complex ethical consideration arises over the blurring of our definition of products of nature versus products of man. The Supreme Court's failure to grant certiorari in the recent *Metabolife* case, which grants a patent on a basic scientific relationship, seems to suggest that FTO issues will only become increasing difficult for public researchers in the quest who seek to understand basic natural relationships for the public good [14].

Having our cake and patenting it, too

The Bayh-Dole Act of 1980 urges research institutions, including universities, to own inventions from federally-supported research and to license those technologies to the private sector [15]. Institutions are required to adopt formal patent polices for employees, seek patent protection on new technologies, and encourage the development of those new technologies [16]. Bayh-Dole adds to layers of complexity to the problems posed for public university researchers. There have been several significant instances in which a technology developed at the university level was licensed exclusively to a private company to the exclusion even of the researchers who invented it. And as universities continue to encourage and sometimes push scientists to produce transferable technology and reap income from license agreements and start-up successes, it becomes, arguably, less defensible for those researchers to infringe with impunity. Furthermore, it's unclear whether or not public researchers are accountable for infringement even if they do not

commercialize any technology as a result of research efforts. Could university professors performing basic research be successfully sued for infringing patents?

Many university scientists tend to ignore patents [9]. In today's climate where technologies are at the crux of science, it is unforeseeable that professors could successfully perform any meaningful research without infringing patents. But they do so at their own peril. While patent statute contains a clearly-stated research exemption, the 2002 court decision in *Madey v. Duke* limits the scope of the research exemption to experiments done "solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry [17]." Madey was not a company, but instead a disgruntled ex-faculty member, but the case has important implications for universities and their researchers. The court found that the precedent did "not immunize any conduct that is in keeping with the alleged infringer's legitimate business, regardless of commercial implications." Essentially, major research universities often conduct research projects without commercial application, but that research still advances the institution's educational mission to "increase the status of the institution and lure lucrative research grants, students and faculty." It is hardly for amusement.

Future consequences?

In private universities, the answer is made clear by *Madey v. Duke*. They can be sued for making, using, selling, or importing patented technologies, even if they have no intention of commercializing the fruits of the research. For public universities, Eleventh Amendment sovereign immunity rules apply in intellectual property cases; for now anyway. The four dissenting Supreme Court justices in the narrowly decided *Florida*

Prepaid case raised concerns over state institutions benefiting from intellectual property without being required to honor it [18]. This puts public universities in the proverbial tight spot between Bayh-Dole (on the Congressional side) and the potential loss of immunity (on the Judicial side). At the time, the ruling in favor of immunity prompted Congress to propose new legislation to close what they saw as a loophole in IP protection issues [19]. For now, sovereign immunity stands.

Also yet to be decided is the question of whether or not individual university researchers can be held liable for infringement. There certainly exists no clear precedent suggesting that they cannot be. Let us consider here recent cases in which the music industry has pursued university students for downloading copyrighted material since they cannot pursue immune public universities for failing to curtail the downloading—this is contrasted with the now infamous Napster case where the record industry effectively shut down Napster in 2001 instead of pursuing individual violators. Just because a researcher has not been sued does not mean he or she will not be in the near future. And if a researcher has stake in a commercial start-up company that is spun-out of university research, she or he may be in for a rude surprise. In fact, infringement need not be direct. Indirect infringement might be brought against a third party for helping Party A infringe Party B's patent. And willful infringement—usually avoided by private firms by conducting thorough FTO searches—can incur treble damages.

Good for the goose…

When and where might industry nip? The May 2007 Iowa State University Research Foundation suit against Monsanto alleges Monsanto willfully infringed on their low-

linolenic acid soybean and seeks treble damages [20]. Ultimately, as universities and researchers continue to actively pursue patent protection for inventions under Bayh-Dole, the line between business and public welfare becomes increasingly fuzzy and may in fact provide the impetus for private firms to aggressively protect their patents, especially as universities commercialize tools through license agreements or develop downstream products of commercial interest.

Emerging solutions

While the public forum seems the obvious place for reform, important barriers exist that may make solutions slow in coming, if they come at all. Recent Federal Circuit Court decisions seem to suggest a trend toward stronger protection for patents and other IP. The World Trade Organization's Trade Related Aspects of Intellectual Property Rights agreement (TRIPS) echoes the United States' emphasis on desiring stronger IP protection for all member countries. Congress has been slow to reform, even on procedural issues such as implementing a U.S. first-to-file system, but both the House and Senate have patent reform legislation bills to consider this year. Much of the special interest pressure comes from a private sector that is not uniform in opinion on resolving patent problems (patentlyo.com), but tends to lean toward stronger IP protection. On the regulatory side, the USPTO is understandably pro-patent. Still, recent innovations may help prevent overly-broad or nonobvious patents from being issued as the USPTO prepares to launch the first ever trial on a peer-to-patent process using a wiki where experts can comment on patent applications (www.uspto.gov). It also remains to be seen what effect the unanimous April Supreme Court ruling on *KSR International, Co. vs. Teleflex, Inc.* will

have in reducing the number of broad and obvious patents. The decision promises to allow more flexibility in applying the 'teaching, suggestion or motivation test' and consequently should allow examiners and courts more flexibility in determining that a patent is obvious to one skilled in the art [21, 22].

The market is responding as well. Several private companies are providing services designed to help steer clients to information and access to patented technology, some free. PatentMonkey.com offers free database searching and charges fees for more extensive services. LegalForce just recently launched an online marketplace that may prove useful in licensing, buying, selling and trading patented technologies. Several non-profits are also specializing in helping underserved communities in the developing world. Both LightYears, IP and Public Interest Intellectual Property Advisors offer volunteer expertise to help countries develop and protect IP. The Coalition for Patent Fairness is an advocacy group working to reform innovation-stifling practices and address patent litigation issues.

The best solutions may be yet to come. One relatively recent, but promising, development is the formation of open-source movements to pool patents, provide improved databases and search capacities, and develop "workarounds". The movement, inspired by the software open-source movement, was begun by Richard Jefferson with the founding of CAMBIA. While critics point out the obvious—that unlike software development, biotechnology is not likely to be practiced in the garage [23]—open movements may be gaining ground. CAMBIA, which is "change" in Spanish, has several initiatives for fostering open-source solutions for issues in food security, health, and natural resource management in disadvantaged communities and developing countries

(www.cambia.org). One of the organization's primary goals is to develop and encourage development of enabling technologies through BioForge. Participants are free to use these technologies under open-license agreements that allow them to be used without fee so long as subsequent advances are made freely available. CAMBIA has already made strides toward producing efficient workarounds, including the Transbacter method for biological transformation of plants without using *Agrobacterium*. CAMBIA also has tools for enhancing open collaboration among scientists including Patent Lens, which uses database capacities to make the patent landscape more transparent, and BiOS, a system designed to help foster collaboration by scientists in an open community.

The Public Intellectual Property Resource for Agriculture (PIPRA) is another organization taking cues from open-source in the hope of improving access to agricultural intellectual property. PIPRA's goal is to "make agricultural technologies more easily available for development and distribution of subsistence crops for humanitarian purposes in the developing world and specialty crops in the developed world" (www.pipra.org). Headquartered at the University of California, Davis, PIPRA has worked to create special licensing language for humanitarian use and has also developed a searchable database of agricultural patents with over 6600 international patents in it. They are working on a plant transformation vector with maximal FTO and have just released an IP handbook that should help public researchers navigate the considerably murky waters of patent protection (www.IPhandbook.com). Based in part on the work PIPRA has done, some major research institutions such as the University of California have moved to include exceptions for public research in their license agreements and member institutions are following suit.

Conclusions

The original proponents of patent protection could not have foreseen a world where the very building blocks of life could be patented or farmers could be prevented from saving seeds from year to year, but our courts, regulators and political leaders are certainly aware of it now. Despite this fact, public policy solutions are slow in materializing and problems may get worse before they improve. It may prove that no silver bullet exists, but that with open-source solutions, pressure from open science advocates like Richard Jefferson, and open licensing from universities, anticommons effects can hopefully be avoided or minimized. In the interim, it seems prudent to conduct research on awareness of FTO issues by public university researchers, increase empirical evidence of the innovation-blocking effects of anticommons and patent thickets, and evaluate the effectiveness of those organizations seeking to increase collaboration among public institutions and create workarounds.

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Chapter 2 Patent Reform in the United States: What's at stake for pharmaceutical innovation?

(This chapter was published in Expert Opinion on Therapeutic Patents (2010) 20 (5): 603-8 with the following authors: Amy Yancey and C. Neal Stewart, Jr.)

Amy Yancey was the principal author of the manuscript.

Abstract

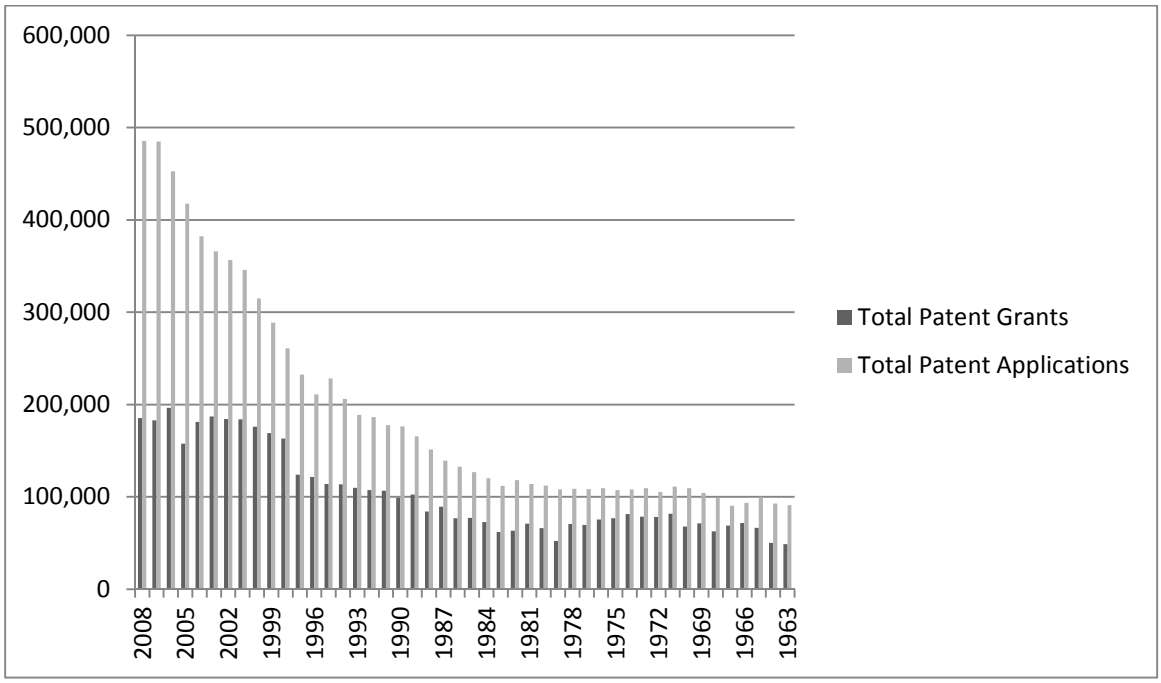
The current patent landscape in the United States has not undergone major legislative reform since 1952. The U.S. Senate version of the most recently proposed patent reform legislation proposes a number of rule changes that could impact the pharmaceutical industry. Among the bill's major provisions are moving to a first-to-file system, changes to post-grant review and reexamination procedures, and damages reform. Various industries with a stake in patent policy have responded to the proposed changes, but the stakes are particularly high for pharmaceutical industry which must invest a significant amount of time and money in the research and development (R&D) process in exchange for already abbreviated patent lifetimes due to the lengthy clinical trial process.

Introduction

In the United States, the idea that inventors should gain exclusive rights to their innovations was written into the Constitution and passed into law in 1790 [1, 2]. The

purpose of granting exclusive rights to inventors is to help foster innovation for the benefit of the public good. In the U.S., patent rights are a tradeoff—the inventor shows the world how the invention works in exchange for the right to exclude others from making, using or selling the patented technology for a limited period of time. In the U.S., this limited period of time is typically the longer of 20 years from filing or 17 years from the date of issue [3]. The belief that patents spur innovation is widely accepted, but not without controversy. In fact, over the past hundred years, support for strong IP protection has cycled substantially [4]. Over the past 30 years, patent rights have enjoyed considerable growth as indicated in Figure 1.

Figure 1. Patent grants and applications in the U.S. since 1963.



The Bayh-Dole Act, passed in 1980, requires universities and others using federal funding to seek patents on their inventions and to license those technologies when

possible to industry [5]. That same year, the Supreme Court decision in *Diamond v. Charkrabarty* expanded the definition of patentable subject matter to include "anything under the sun that is made by man [6]." And in 1981, Congress created the Court of Appeals for the Federal Circuit specifically to hear patent cases. With combined changes to the patent landscape came the predictable and intended boom in the race to patent [7]. The proliferation of patents has resulted in a number of conflicting issues for different fields including an overwhelmed patent office with a backlog of 718,835 applications (as of December 2009), patent thickets in the biotechnology and semiconductor fields, and the rise of non-manufacturing entities (NMEs), also called non-practicing entities (NPEs), in the high-tech sector [8, 9, 10]. These issues have begun to create barriers to innovation with long lead times on application reviews from the United States Patent and Trademark Office (USPTO) and evidence of anticommons effects in certain industries [11]. The outcry has been significant enough in the past five years to prompt Congress to attempt to significantly reform patent law for the first time in over 50 years, beginning with proposed legislation in 2005 [12].

Not all industries are equal

The pharmaceutical industry has much at stake in U.S. patent law reform. The pharmaceutical sector faces a unique set of challenges that combines large initial R&D expenditures, long lead times from patent application to product release, pressure from non-innovator firms (generic industry), and shortened patent protection due to the lengthy clinical trial process [13]. Pharmaceutical impacts are uniquely important. The industry is especially dependent on high research costs on the front end, and arguably relies on

'blockbuster drugs' to recoup those costs [14]. Central to the issue among analysts is the fear that if firms believe they cannot recoup their investment through strong patent protection, they will spend less time researching and creating new and safe therapies—with important implications for human health. And though far from the only factor to determine the ability of the pharmaceuticals to recoup their investments, it is a critical one [15].

Pharmaceutical firms have already seen erosions in the effective life of their patents. It takes an average of seven years to complete clinical trials, essentially limiting patent protection to 11.5 years [16]. The Hatch-Waxman Act further complicates the therapeutic landscape. Passed in 1984, it was created to bring generic, and consequently cheaper, drugs to market faster by creating a research exemption that further reduces the effective life of patented therapies [17]. Additionally, the 2007 *KSR v. Teleflex* decision could impact the controversial practice of "evergreening" patented medicines by making minor improvements in their effectiveness more difficult to patent [18, 19].

The Proposed Reform

In March 2009, U.S. Senators Hatch and Leahy introduced the Patent Reform Act of 2009 [20]. The bill (S. 515) is the fourth recent attempt to enact the first significant changes to U.S. patent law since 1952. The bill, as drafted, pits the interests of the high tech sectors against those of biotechnology and pharmaceutical innovators [21, 22]. High tech firms fear high litigation costs and being tied up in lengthy litigation with NMEs (often called patent trolls). They also often find technologies are obsolete by the time

patents issue [23]. Conversely, pharmaceutical firms want longer, stronger patent protection to protect their substantial investments [24]. Initially, reform was primarily intended to reconcile U.S. and international patent systems, but the current bill is drafted to change the U.S. to a first-to-file system, make it easier to challenge patentability and validity outside the courts, and reduce and clarify damages awards [25]. While the bill did not pass in 2009, it is sure to resurface, particularly due to the strong support for many of the proposed changes from multiple public and private sectors, including the American Association of Universities and high tech firms.

Overview of the major provisions of the bill

First-to-file

The U.S. system is unique among developed countries in that the statute supports a first-to-invent system, allowing inventors to "swear behind" the point of conception in interference proceedings where two similar patent applications are being prosecuted through the USPTO. Basically, this means that the applicant who can prove he or she first conceived of invention is granted priority over other applicants. The proposed legislation changes the rule. The first party to file an application on a new invention has priority over other applicants, doing away with the need for interference proceedings entirely [26]. The bill would eliminate the year-long grace period for disclosure of the innovation unless the disclosure was made by the inventor. The proposed legislation reconciles U.S. procedure with the European and Japanese models. The change does not have particular implications for pharmaceutical patents specifically, but should spur inventors in all sectors to file for application as soon as possible.

Post-grant review, reexamination and pre-issuance submissions

The Senate bill also proposes changes to post-grant review of issued patents, allowing any party to challenge a new patent within 12 months of issuance, based on any grounds for invalidity (except best mode). Previously post-grant review was based only on evidence of prior art. Reexaminations are also expanded, based on published prior art or prior public sale or use in the U.S. The bill proposes limits to the number of challenges a third party can make. Parties are estopped from requesting inter partes reexamination requests after a district court has already ruled on validity. The new legislation also allows third parties to submit prior art and publications with comment on patent applications during examination. These rule changes in particular will make patentability and validity easier to challenge.

Damages

The most contentious provision in the bill proposes changes to limit damage awards to consideration of "specific contributions over prior art [27]." Courts must decide if the valuation of a patented invention falls under one of three categories. "Entire market value" is when the infringing device or product is based predominantly on a single patent. "Marketplace licensing" is when damages determinations are based on a royalty for licensing a similar substitute. It is important to note here that if the similar substitute is in the public domain, this formulation could reduce damages to zero. "Value calculation" bases damages only on the portion of the economic value derived from what the invention contributes over the prior art.

Venue reform

Among the specific proposed changes in S. 515 is the requirement that suits be brought in states where the plaintiff has a physical place of business, is incorporated, or has an established facility. The legislation would prevent filers from incorporating in certain regions solely for the purpose of bringing suit in preferred, plaintiff-friendly courts such as the Eastern District of Texas.

Willful infringement

The bill also codifies tougher criteria for willful infringement (which incurs treble damages) in keeping with recent court decision *In re Seagate Technology, LLC* [28]. The bill creates a criterion of "objective recklessness" to incur treble damages. The infringer must have received written notice of the infringement, intentionally copied the patented technology or previously been found to be infringing. Also, if the infringer acted in "good faith" demonstrating that they believed the patent was invalid, unenforceable or not infringed, they are exempted from willful infringement.

What's at stake? University and industry response

The most recent version of the legislation garners strong support from universities and high tech firms. Universities have responded positively to the fact that lawmakers are incorporating the recommendations by the National Academies of the Sciences [29]. There is strong sentiment among academics who study patent policy that anticommons effects are starting to adversely affect innovation, particularly in the biotech and high tech

sectors. They cite increasing evidence that the landscape is becoming too difficult to navigate and that the USPTO is overwhelmed and issuing patents that fail to meet the criteria for patentability [30]. Table 1 shows the backlog of applications in the USPTO by technology sector.

Table 1. Patent backlog by technology sector.

Applications Awaiting First Office Action by Examiner	Applications	Number of Examiners
Total	**718,835**	**6,143**
Tech Center 1600 - Biotechnology & Organic Chemistry	60,836	532
Tech Center 1700 - Chemical and Materials Engineering	87,136	730
Tech Center 2100 - Computer Architecture, Software & Information Security	60,882	629
Tech Center 2400 - Network, Multiplexing, Cable & Security	39,669	698
Tech Center 2600 - Communications	127,956	875
Tech Center 2800 - Semiconductor, Electrical, Optical Systems & Components	123,122	1,056
Tech Center 3600 - Transportation, Construction, Agriculture & Electronic Commerce	83,535	766
Tech Center 3700 - Mechanical Engineering, Manufacturing & Products	116,522	744
Tech Center 4100 - Patent Training Academy	3,606	113

High tech firms view themselves as defendants. They are happy to avoid treble damages, plaintiff-friendly courts, and the mire of patent thickets. Their support stands in sharp contrast to the pharmaceutical and biotechnology industries, who largely see themselves as plaintiffs forced to enforce their right to exclude [31, 32]. These sectors have long lead times, particularly pharmaceutical companies. Industry analysts are concerned that reduced damages will reduce or nullify the deterrent to infringe by competitors. The Pharmaceutical Research and Manufacturers of America (PhRMA) states in its official response to S. 515 that "by lowering the penalties for those found by a court to have infringed another's patent, the bill would reduce the value of the patents that are the lifeblood of America's innovative business sectors, which depend on intellectual property protection [33]." The biotech industry has also come out with strong objections to proposed changes to damages calculations in the bill [34].

Expert Opinion

Patent rights have grown substantially over the past 30 years, and with the strengthening of those rights has come expansion. With the passing of the Bayh-Dole, the *Chakrabarty* decision, and creation of the Federal Circuit, patent applications, patent grants, and patent litigation have all grown at a rapid pace. This same period has seen a boom in pharmaceutical research, biotechnology, and high tech industries. Only the recent economic downturn stopped a 13 year trend in increased patent applications [35]. This period of growth has led to unintended consequences—a bogged down USPTO and a proliferation in some sectors where pro-patent effects stunt innovation and prevent

products from coming to market. Lawmakers are seeking to address those issues with one-size fits all legislation, but finding consensus among different industries is critical. In fact, a new book by Dan Burk and Mark Lemley, *The Patent Crisis and How the Courts Can Solve It*, argues that the courts are the best place for some reforms in light of the varying needs of different industries [36]. The proposed legislation as a whole, particularly considering the changes to damages calculations, weakens patent rights in an environment where recent court decisions have already eroded patent protections for the pharmaceutical sector. There can be little doubt that if the proposed legislation passes as is, pharmaceutical companies will find both that their patent holdings less valuable and more difficult to defend. . New legislation is critically needed. Law makers will continue to be pressed to address some of the very real and serious problems facing the U.S. innovation sector sooner rather than later. But Congress must not rush to pass legislation that favors high tech over pharmaceutical and biotechnology industry concerns, particularly as it relates to damages reform. There is still much work to do to avoid unintended consequences that could reduce the number of new and potentially life-saving therapies coming to market. Legislators should continue to work with industry and university stake holders across all major technological sectors to ensure that any legislation passed does not forsake innovation in one field for another.

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Chapter 3 Saving glyphosate: A multi-pronged approach to managing glyphosate resistance in weeds

Abstract

The first confirmed glyphosate-resistant horseweed was discovered in the United States in 2001 in Tennessee and Mississippi. Since that time, eight major crop weeds have been added to the list across the country. Glyphosate and gylphosate-resistant crops represent the single most important and rapidly-adopted innovation in modern agriculture. Glyphosate is uniquely important among herbicides. It is economical for farmers, safe in the environment, effective against a broad spectrum of weeds, and facilitates conservation agriculture. It has facilitated mass production of major crops and saved farmers billions of dollars, literally helping the U.S. and other agricultural production countries feed the world. With over 90 percent of soybean, 68 percent of corn, and 70 percent of cotton in the US containing transgenic resistance to glyphosate, the loss or even reduced effectiveness of glyphosate for the control of weeds will have potentially devastating impacts on farm income and the environment. Scientists and corporations are exploring and recommending a variety of solutions, but without significant efforts to raise both farmer awareness of and adoption of recommendations aimed at stewarding glyphosate, it may prove difficult to save this crucial herbicide for long-term use.

Introduction

Glyphosate resistant (GR) crops have been the most rapidly adopted new crop trait in the history of world agriculture [1]. With that rapid adoption has come the pervasive and almost exclusive use of glyphosate as a weed control mechanism. According to the United States Department of Agriculture's Economic Research Service (USDA-ERS), over 136 million acres were planted with GR crops in 2009 in the U.S. Glyphosate is also used extensively for burn down of weeds before planting non-GR crops, sprayed along roadways, and used extensively to control residential and sports turf weeds. With the rise of glyphosate use has come the unintended selection of resistant weeds. Glyphosate resistant weeds pose a serious threat to world food production, U.S. agriculture and the environment. No other herbicide offers the same unique qualities that make glyphosate so desirable, and none are poised to replace it in the foreseeable future. University researchers and life sciences companies have long been looking for solutions in the laboratory and in the field and sounding the alarm. There are multiple recommendations for mitigating resistance, but farmers are largely unaware of both the threat and the methods for slowing the spread of resistance in crop weeds. Furthermore the economic and convenience advantages of glyphosate may deter even well-versed farmers from adopting stewardship recommendations and/or new, more expensive technologies until they experience weed pressure first hand. By then it may be too late.

Glyphosate and resistant crop technology

Glyphosate is a revolutionary and unique chemical herbicide first commercialized in the mid-1970s and best known under the brand name Roundup® by Monsanto. Glyphosate's

special status among herbicides comes primarily from its mode, or mechanism, of action. Glyphosate inhibits an important plant enzyme, 5-enylpryuvylshikimate-3-phosphate synthase (EPSPS), blocking the production of important amino acids, phenylpropanids, tannins and lignins [2]. Because EPSPS is found only in plants and certain bacteria, and because glyphosate binds tightly in the soil, breaking down into natural material over time, it has extremely low toxicity and an excellent environmental profile [3, 4]. These traits, combined with break-through glyphosate-resistant (GR) crop technologies, ease of use, low price and positive impact on farm income have made glyphosate and associated crop technologies the most important agricultural chemical of the past 100 years with its impact on world food production likened to the discovery of penicillin [5].

A major scientific break-through occurred in 1983 with the successful isolation of the CP4 strain of *Agrobacterium tumefaciens* which was highly tolerant of glyphosate and led to the successful insertion of the *cp4 epsps* gene [6]. In 1996, Monsanto released the first commercial transgenic crop with the GR event. The Roundup® Ready soybean allowed growers to treat crops post-emergently with glyphosate, providing convenience, promoting no-till practices and positively impacting farm income [7]. Soon after, many transgenic varieties were rapidly adopted in the U.S. As of 2009, over 91 percent of all soybean is glyphosate-resistant. Other GR crops quickly followed. Now over 68 percent of corn and 71 percent of cotton are glyphosate-resistant. GR canola and sugarbeet have also been commercialized and adopted. Newer transgenic crop varieties have been introduced with higher levels of resistance have been stacked with other transgenic traits like insect resistance [6].

The rapid adoption of GR technologies has been a boon to major U.S. crops and has subsequently been adopted in other countries, particularly in the Americas. The wide-spread use of glyphosate has had major economic and environmental benefits [7]. Furthermore, the widespread adoption of glyphosate as a post-emergent herbicide has resulted in energy savings and soil conservation from the adoption of no-till agriculture. And glyphosate is far more environmentally-friendly than other broad-spectrum herbicides. Glyphosate resistant technologies have transformed agriculture and food production in a world where exploding human population continually stretches food resources. Any threat to the effectiveness of glyphosate is a threat to U.S. agricultural production, the environment and world food production.

Clear and present – Glyphosate resistant weeds

Glyphosate-resistant horseweed was first observed in Mississippi and Tennessee in 2001. Horseweed escapes were reported in soybean fields that were treated at the recommended rates both preplant and post-emergent. Laboratory testing of seeds collected from the escapes showed 8-fold to 12-fold resistance over susceptible biotypes [8]. Since those early studies, Palmer amaranth, common ragweed, fleabane, waterhemp, giant ragweed, Italian ryegrass, rigid ryegrass, and Johnsongrass have all emerged in the U.S. with glyphosate resistance [9]. In March 2010, the first confirmed resistant giant ragweed was reported in Canada [10]. The problem will continue to intensify if sustainable practices are not rapidly adopted.

Glyphosate has been used around the world for over 35 years, but with the unprecedented adoption of GR crops since 1996 came the dramatically different use

pattern resulting in reduced weed-control diversity and strong and persistent use of glyphosate. With the adoption of successful GR crops, use of other herbicides diminished. Glyphosate is not only much more effective and environmentally safe, it is comparatively much more economical than other herbicides because it can be cheaply produced as a generic [11]. Also, crop rotation between GR soybean and GR corn also means that many fields are being treated twice a year, every year [12]. Also, glyphosate has facilitated conservation no-till farming practices, another key way to control for weeds. This increased (and sometimes constant) selection pressure has led to the emergence of weeds that persist even at recommended rates of application.

Both industry and academic researchers have poured a significant amount of time and resources in to solutions to slow or stem the spread of glyphosate resistance in weeds. There are numerous academic papers dedicated to the study of the issue. There is a major industry working group, the Herbicide Resistance Action Committee (HRAC), dedicated to the problem [15]. Ian Heap also operates a survey site (www.weedscience.com) monitoring the spread of specific weeds with funding and support from HRAC, the North American Herbicide Resistance Action Committee (NAHRAC), and the Weed Science Society of America (WSSA) . Monsanto operates a weed resistance website (www.weedresistancemanagement.com) with farmer recommendations and Monsanto and Pioneer have already developed crops with stacked transgenic resistance to other mechanisms [6]. Solutions for stewarding glyphosate fall into three main overlapping categories: more research into weed genomics and modes of resistance, crops with new GR mechanisms and stacked resistance, and diversification of weed management practices at the farm level.

More basic genomic research needs to be done at the university level to better understand non-target resistance to herbicides, especially glyphosate. Only a few resistance genes have been cloned and characterized in weeds [13]. Major modes of glyphosate resistance in weeds include alteration of EPSPS, which decreases the ability of glyphosate to bind to the enzyme, and the unanticipated reduced translocation of glyphosate to the roots and growing points of the plant [12, 13]. Reduced translocation is not a common mechanism for herbicide resistance, and a better understanding of this mechanism in resistant biotypes might lead to discovery of novel strategies for improving translocation. [13]

Several newly discovered technologies are currently being developed and/or commercialized that could both help mitigate GR weed problems and facilitate diversification of herbicide use. New glyphosate-resistance mechanisms have recently been discovered, including a newly discovered class of EPSPS enzymes with much higher resistance in corn, allowing for spraying at up to eight times the recommended field rate [6]. Another strategy, gene stacking varieties for resistance to multiple herbicides, should help facilitate diversification. Among the promising new stacks are glyphosate with ALS resistance. Other events that show promise for stacking with glyphosate resistance, or in some cases that are already in development, include: glufosinate, accase, auxin and dicamba resistance; HPPD-, and PPO-inhibiting herbicide resistance; and P450 metabolic resistance [6, 14]. In particular, glufosinate, which has no known resistant weeds, could be very effective, as could HPPD inhibitors which also has no known resistant weeds and soil residual activity comparable to glyphosate [6].

Facilitating adoption of diverse weed-management practices

While scientists have been tracking glyphosate-resistant weeds in earnest since 1997 and companies have been actively working to mitigate effects and develop new technologies, the farm sector has surprisingly little awareness of the magnitude of the problem. A major 2009 survey of farmer awareness, showed that only 30 percent of farmers thought GR weeds were a serious threat and that most did not understand that recurrent use of the same herbicide was the primary mechanism for the development of resistant populations [1]. Most farmers believe that a new herbicide will be developed before GR weeds become a major problem. Since the 1960s, the number of compounds that needed to be screened to yield a single product has grown exponentially. Likewise, most of the known herbicide modes of action (MOA) involve enzyme inhibition. A few disrupt other processes such as cell division or auxin response, but no new MOA has been discovered since sulcotrione was introduced in 1991 [13]. No herbicides with new modes of action are currently on the horizon. The authors of the aforementioned survey also noted that information has been disjointed and confusing to farmers who are more likely to get information from the farm press than other sources that may only present part of the story or fail to make strong recommendations, finally recommending that a consistent message relaying the seriousness of the problem and recommendations for farmers come from universities, farmers groups, corporations and governments. A new National Academy of the Sciences (NAS) study on transgenic crops concludes that weed problems will become increasingly problematic as a result of herbicide and glyphosate resistance. The NAS study similarly recommends a concerted effort from all sectors and stakeholders [16].

Another major concern that needs to be studied is the willingness of farmers to adopt new technologies and glyphosate-conservation practices even if they are aware of the magnitude of the problem. A substantial amount of research has been done on the willingness of farmers to adopt new technologies and conservation practices, and suggest farmers can be slow to act [17]. GR crops are convenient, familiar and economical. Until farmers actually experience serious weed competition on a personal level, it seems questionable that they will invest in the time, equipment and additional chemical and seed costs to institute sustainable practices, particularly since the least educated group consisted of small, part-time farmers, the group least likely to assume perceived risks of adopting new practices. By then, it may be too late to save glyphosate. Additional research needs to be undertaken to determine the extent of what farmers are willing invest in time and money to adopt sustainable practices. It seems likely that without special incentives, education will only be the first hurdle. Monsanto may be best poised to influence farmers to make changes in seed and chemical applications because of their market share, but with a recent anti-trust investigation from the Justice Department, their influence may soon wane [18].

Conclusions

Glyphosate use in conjunction with GR crops represents the most important advance in agriculture production, and with it comes the ability to keep pace with increased food demand from a rising world population. GR crops have had an overwhelmingly positive effect on farm income in the U.S. and glyphosate remains one of the safest and environmentally-friendly agronomic advances used in modern agricultural production.

The loss or even reduced effectiveness of glyphosate could have devastating impacts on U.S. agriculture and the world food production. Yet despite overwhelming and conclusive evidence that glyphosate-resistant weeds are a major threat, little has been done to send a consistent message to the farm sector. University and corporate researchers have been hard at work, monitoring the advance of GR weeds and identifying effective ways to slow their advance. Life sciences companies have several products in development that could replace or supplement existing GR crops. Continued research will point to novel ways to address resistant weeds and the development of newer technologies, but without education and resrouces, it seems unlikely that farmers, particularly small, part-time farmers, will adopt newer, more expensive practices or technologies to fight GR weed spread. A concerted effort to educate farmers needs to be undertaken as NAS suggests, but more will likely be needed. Incentives for adoption of new practices and technologies may need to be implemented to encourage farmers to investment time and money before they personally experience significant problems from GR weeds, at which point it may be too late.

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Chapter 4 Patent uncertainty: A primer for university researchers in the life sciences

Abstract

Recent pressure from industry, universities and research groups has resulted in increased pressure on the U.S. Congress to pass patent reform legislation. The U.S. Court of Appeals for the Federal Circuit (Federal Circuit) and the U.S. Supreme Court have recently decided several landmark cases that address specific issues impacting the technology sectors. These recent court rulings and proposed legislation have important consequences for the life sciences, and in particular, important implications for biotechnology. Recent articles have focused on particular cases or issues, but very little in recent literature provides a comprehensive overview of the patent system at large with an eye to the way recent and proposed changes effect the university researcher.

Introduction

Special consideration is given to the life sciences when it comes to intellectual property. Large investments of time and money make patent protection especially crucial as an incentive to the development of innovations [1]. Additionally, these sectors face patent thickets and problems from overly broad, overlapping and poorly-claimed patents [2, 3]. Ethical and humanitarian considerations further complicate the complex landscape of patents in biotechnology and biomedical sectors [3]. Changes to the patent system have several purposes: reconciling U.S. patent law and international patent policy; addressing extensive backlogs in the system and related problems such as poor patent quality; and

clarifying statutory rules for patent eligibility. Many of the changes specifically address problems, sometimes very polarized, in the technology sectors and have particular implications for biotechnology [1]. A thorough review of the literature reveals that there is little available that provides researchers with context for recent and proposed changes or a practical guide for what impacts, if any, the changes would likely have on a researcher's process for disclosing his or her invention. There is a need for both an overview of the role of patents in university research and an overview of what impacts recent and proposed changes will have on biotechnology as researchers make decisions about whether or not their discoveries are patentable and whether or not they should be patented.

What is a patent?

A patent is a type of intellectual property that covers "new and useful" inventions [4]. Intellectual property rights are considered negative rights because they exclude or limit others' use of those new ideas or inventions. Patent rights specifically exclude others from making, using or selling the invention [5]. An important caveat for researchers is that, unlike copyright protection, there is no "fair use" clause. In other words? The exclusion of rights extends to academic use and all but the narrowest of research exemptions [3].

Patents can be categorized as sanctioned, limited-duration monopolies, with the first formal system dating back to fifteenth-century Europe. Congress's power to extend intellectual property rights to inventors was drafted by the framers of the U.S. Constitution [6]. Justification for exclusive rights to certain types of 'products of the

mind' is added incentive for inventors to bring the invention to light for the benefit of society. For patents, the trade for the exclusion of other makers is both disclosure and enablement of the invention. In other words—the inventor must show the world how the invention works. Other statutory criteria for patent eligibility are subject matter, novelty, nonobviousness and utility. These criteria are codified into U.S. statutory law, but are dynamic and evolving as clarified through case law [6].

In addition to the lack of a functional research exemption, another important distinction university researchers should note is that unlike authorship, an inventor must have had a substantial hand in bringing the invention to light. Simply being hands-on does not make a lab technician or graduate student a co-inventor, and improperly attributing inventor status invalidates the patent [6]. Also, in university settings as in corporate settings, the inventor usually assigns rights to his or her employer's designee. Many universities have a separate technology transfer entity, often a foundation or corporation, to which ownership of the invention is assigned [7, 8].

Origins of U.S. Patent System

The basic tenets of modern patent law can be traced to fifteenth-century Vienna in which inventors were granted a ten-year right to exclusively offer their inventions [6]. The first documented case of granting exclusive rights to inventors dates back to the third century BC, in the ancient Greek city of Sybaris where chefs were granted exclusive rights to produce their culinary inventions for a year [9]. The formal granting of intellectual property rights was written into the U.S. Constitution and codified in the Patent Act of 1790 [5]. The law was refined in 1793 and has gone through occasional reform since

then. Protecting intellectual property on the international front is also gaining increasing importance. In 1994, the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) was drafted by the World Trade Organization (WTO) and defines IP regulation for WTO Members [10].

Constitutional and Statutory Law

The Constitution grants Congress the authority "To promote the Progress of Science and useful arts by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries" [11]. Important revisions to the 1793 law were passed in 1836 and 1952. The more recent Bayh-Dole Act of 1980, Federal Courts Improvement Act of 1982, which established the Federal Circuit, and the Hatch-Waxman Act of 1984, which created the generic drug system by allowing generics to go through an abbreviated drug application process, have also had significant impacts on overall U.S policy.

Statutory law stipulates the requirements for patentability: subject matter, novelty, nonobviousness, disclosure and utility. An invention must also meet the statutory bars, and an invention cannot be patented if any of the following have occurred more than a year prior to patent application: the invention is patented or described in a printed publication available anywhere in the world; the invention is in public use in the United States; or the invention is on sale in the United States [12].

The United States Patent and Trademark Office (USPTO)

The USPTO is the federal office charged with issuing patents. Approximately 6,000 examiners with expertise in subjects as diverse as chemistry, telecommunications,

mechanical engineering, nanotechnology and software engineering drive the issuance of patents [13]. Filers submit an application and pay a fee. An examiner is then assigned to review the invention in light of statutory requirements, USPTO rules, and court decisions. The examiner reviews all claimed functions of the invention and communicates back with the inventor(s) or his or her representatives. Often this is a process of writing and re-writing until the examiner is satisfied the claimed device meets all of the requirements of patentability [6]. This process is referred to as "prosecution", not to be confused with the criminal law definition.

The patent office also holds interference procedures for competing patents filed near the same time. The U.S. system is unique in the world in that the first inventor to conceive of the idea has the right to the invention but must prove the point of conception. The rest of the international community has simplified this process, granting priority to the first filer, and this is one source of tension that has led to a push to reform the U.S. system [1]. Patenting is often defined as a race in economic terms, and certainly a first to file system enhances the sense of urgency for inventors to file an application [14].

The Federal Court System

The U.S. court system hears allegations of infringement and has the final authority to determine if a patent is valid, or meets all of the criteria for patentability. U.S. District Courts hear infringement suits and makes declaratory judgment actions related to patents [5]. The Federal Circuit Court, established in 1982, is the primary court deciding questions of statutory law involving patent rights and regulations. It serves as appeal court for cases heard at the District Court level. The Federal Circuit, with its panel of

expert judges, has largely been left to decide the most important questions of patentability: defining subject matter and its scope, establishing a test for determining novelty and obviousness from prior art, and formally construing enablement and utility [5].

Federal Circuit decisions may be appealed to the U.S. Supreme Court, but since the creation of the Federal Circuit, the Supreme Court has not granted certiorari in many patent cases. Thus, Federal Circuit decisions have typically stood as the final word; however, lately, the Supreme Court has been hearing important cases with serious implications for patent seekers and holders. By and large, decisions by the Federal Circuit and the U.S. Supreme Court are applied across all fields of invention. But some cases, such as the landmark *Diamond v. Chakrabarty* and pending *Association for Molecular Pathology v. USPTO and Myriad Genetics, Inc*., have particular importance for the biotechnology sectors [15, 16].

Research Universities and Patents

The Bayh-Dole Act mandates that institutions conducting research with federal research dollars pursue patents on new technologies and license those technologies to private industry. Other nations have looked toward passing similar legislation in light of the success of university patenting, however, with success has come unintended consequences both for the innovation sector and for university researchers, putting the two at odds at times and contributing to patents on basic research tools that feed patent thickets [3, 17].

According to the Association of American Universities, 56% of basic research is conducted by universities [18]. Since Bayh-Dole passed, the number of patents granted to universities has climbed from 250 mostly agriculture-related patents per year to over 3,000 in fields that span from biotechnology to superconducting. U.S. universities collectively now earn almost $2 billion annually from license agreements, but there are only a few extremely profitable players, such as the University of California system, and many that struggle to break even [17].

To effectively pursue patents and license marketable technologies to private industry, universities have set up corporations or foundations that analyze new inventions, determine whether or not to seek a patent, and then handle the filing of the patent on behalf of the inventors [7, 8]. Referred to as "technology transfer offices," inventors assign their rights to the invention to the university, but then share a percentage of the revenue with the university. Often a university's website discloses much of the process and revenue sharing on their technology office's website.

The call for reform

A strong patent system results in more patents, and indeed the number of patents pending in the USPTO has more than doubled in the past ten years [19]. With the influx of applications has come both obvious and unanticipated problems including increased and expensive litigation, growing patent backlogs, the issuance of poor and controversial patents, the rise of non-manufacturing or non-practicing entities, and tension between generic and research drug manufacturers [19, 1]. Furthermore, the "one-size-fits-all" model doesn't allow for the very different climates within the life sciences sector versus

the tech sector. The issues affecting biotechnology and pharmaceutical research relate to high costs, long lead start up times, and whether the research is in an academic or clinical trial setting versus the fast-paced, rapidly evolving software market in which innovations can be obsolete in as little 18 months. In all industries, the cost of patent litigation has risen dramatically. The cost of defending a patent in court has risen steadily and can cost $650,000 to $4.5 million [20].

In technology sectors, the field is crowded, and many technologies are developed simultaneously by different firms. The cost of litigation and fear of rulings that invalidate important patents has led to unique problems for tech firms. Google recently bid $900 million for a suite of patents, reportedly to avoid patent litigation [21]. In fact, patent litigation has become a cottage industry for some. Called non-practicing, or non-manufacturing entities, these “patent trolls” are companies that search for opportunities to draft new patents without ever intending to market them. Instead they watch for large firms to invent similar tools with the intention of suing them for large infringement awards. This practice runs counter to the very purpose of the patent system, which is to bring new and useful inventions to market for the public good. The now infamous Blackberry and eBay cases demonstrate how much large practicing entities have at stake when they were nearly shut down by non-practicing entities in separate cases [22]. Likewise, the patent backlog has resulted in controversial patents issuing on inventions that many considered obvious like Amazon’s controversial patent on “one-click” check-outs because overwhelmed examiners may not be as diligent as they could be. Furthermore, the three year average length of time from application to patent often renders the technology obsolete, yet technology sectors are caught in a ‘prisoner’s

dilemma', forced to defensively patent new technologies despite the fact that doing so is not in the corporation's best interest because of the time, cost and sort life expectancy of tech patents [14, 6].

The life sciences face a different set of problems brought about by the boom in patents, many of which have been well covered in recent articles, including patent thickets, that present unique challenges in an industry in which there are multiple humanitarian consequences for food, vaccine and therapeutic technologies [23]. The potential for an anticommons effect, first described by Heller and Eisenberg in 1998, remains and the thought that a company can produce a life-saving technology, or hold the patent for an important agricultural breakthrough but not produce it, is fraught with ethical considerations [24].

The America Invents Act

In March 2011, the Senate passed the America Invents Act (S.23) in an attempt to modernize the patent system. It was the fourth such attempt since 2005. In late April, the House version of the bill (H.R.1249) passed the House Judiciary Committee and is expected to pass on the floor in June [25, 26]. The bill has broad, bipartisan support, the support of major industry groups such as BiO and Phrma, and has been actively supported by major university groups such the Association of American Universities (AAU) [1, 18]. Major changes to the law are intended to normalize the U.S. system with international systems, to reduce the patent backlog with the ultimate goal of having patents issue within a year of application, and to improve the quality of those patents that

do issue. Important provisions in the two bills are written with these goals in mind, the most significant of which are:

The first-to-file provision

Current U.S. law grants patent rights to the first to invent, not the first to file. Moving to a first-to-file system is retained in the current bill from earlier versions. It normalizes U.S. law with international standards and is intended to eliminate costly and time consuming interference proceedings as well as future litigation costs associated with proving the conception of the invention first. A one-year grace period for disclosure exists in the legislation, largely at the urging of universities, but a weakness of the bill is that it does not define disclosure [14, 25]. The grace period and definition of disclosure are of key importance to university researchers, who must balance the potential for a potentially patentable (and profitable) new invention with academic priorities for publishing and advancing their fields of research.

A small, but vocal group of detractors argue the U.S. system is stronger than other countries because it rewards the inventor instead of the first filer. Further, independent inventors believe firms would have an advantage under the proposed system, and some have claimed the new provision is unconstitutional [14].

Third party submission of prior art

The proposed law codifies third party submission of prior art to the USPTO by extending the period allowed for such submission to six months. By extending the submission period, it is hoped third parties will have more time to submit evidence that an invention is obvious [25].

Elimination of Fee Diversion

The proposed legislation makes several procedural changes for the way the USPTO operates, the most significant of which being the elimination of fee diversion practices. Congress currently redirects the fees collected by the USPTO to other Federal programs. Elimination of fee diversion will allow the USPTO to keep revenues and direct them to areas of need including hiring more examiners and creating satellite offices to address the patent backlog [25].

The Courts

The courts play a pivotal role in defining patent eligibility, enforcing issued patents, and determining validity on questionable patents [6]. The USPTO looks to court decisions to interpret statutory law and offer clarification of questions such as how to determine nonobviousness and what constitutes prior art. The most significant changes to patent law over the past five years have come from the courts. For the first thirty years since the creation of the Federal Circuit, the Supreme Court was largely silent on patent case law, presumably to allow the lower court the chance to establish a record of interpretation [5]. Since its creation, the Federal Circuit has heard more than 2,000 appeals. [14] The Supreme Court has broken its silence as of late and begun reviewing the Federal Courts decisions and providing guidance on several important issues. Decisions from both courts are helping to refine and redefine what is patentable in the United States.

Patentable Subject Matter

Several recent and pending decisions have important implications for the biotechnology and pharmaceutical sectors. Perhaps the biggest are *Bilski v. Kappos*, and *Myriad Genetics*. In the 1980 landmark case *Diamond v. Chakrabarty*, in which the Supreme Court ruled that patentable subject matter extends to "anything under the sun made by the hand of man" and essentially ruled any invention that is not a product of nature or natural law was patentable, including living organisms [15]. Thus, ideas cannot be patented, but transformative processes including those on organisms can be patented. The *State Street Bank v. Signature Financial Group* decision extended patentable subject matter to include business models and allowed for software to be patentable as transformational steps [27]. The Supreme Court's decision in *Bilski* largely abandons *State Street*, making certain business models unpatentable, but upholding the important machine or transformation test for subject matter. However, the court clarifies that this is not the sole test patentable subject matter. The decision eliminates patents on business models and may have implications for software patents, but it paved the way for a new test for patentability in cases such as optimized vaccine schedules or diagnostic tests that measure natural phenomenon but require an inventive step [28].

The *Myriad* case, which is being closely watched by industry and academics alike, is currently being heard by the Federal Circuit after a lower court, with the urging of the Department of Justice, ruled that patents on isolated, purified genes amounted to a "lawyer's trick" and are ineligible as a product of nature. The patents on the breast cancer genes *BRCA1* and *BRCA2* have generated a host of ethical considerations, and the case has profound implications for all of the life sciences since the ruling would apply not

only to genes, but to proteins, cell lines, and antibodies [27]. Analysts expect the Federal Circuit to overturn the lower court's decisions, but most observers anticipate that the case will ultimately end up in the Supreme Court.

Obviousness

Probably the hardest test for a new invention to meet is the standard of nonobviousness. The 2007 Supreme Court ruling in *KSR Int'l Co. v. Teleflex Inc*. created a standard for the courts to make determinations about what someone of "ordinary skill in the art" would find obvious to do [29]. In other words, what prior art would another inventor in the same field look toward to solve a particular problem? Also, the *In re Kubin* ruling by the Federal Circuit in 2009 changed the obviousness rule significantly for biotechnology patents. The *Kubin* decision found that a known protein renders its related gene obvious since the protein suggested its function, and the methods for finding and isolating the gene are well-known [30].

Utility and Enablement

Biotechnology patents must also meet a more stringent rule of utility. In other disciplines, the standard is low enough to be presumed; however, biotechnology patents are not issued on expressed sequence tags (ESTs) because an EST cannot be used to determine the purpose and use of the gene it helps locate. The Federal Circuit's 2005 *In re Fisher* case found that patents on DNA fragments had to amount to more than a "hunting license" and demonstrate "specific and substantial utility." [32]. Likewise, the 2010 *Ariad v. Lilly* decision addressed the disclosure and enablement requirements, and reminiscent

of the *Fisher* decision, the court essentially found that an inventor cannot claim genus if only a few species are described solely because there are certain to be more species to be discovered [33].

What it means for university research

The courts and the proposed changes to patent laws show continued support for a strong and functioning patent system, important for the long-lead times facing biotech and pharmaceutical patents. Recent higher court decisions show continued support for biotechnology and pharmaceutical innovation, but with tougher and narrower standards for meeting the criteria of patentability. The courts appear to be deliberately working to tighten claim construction and demand precision in biotechnology in ways that address broad, over-reaching and obvious patents that harm all sectors. Far from settled, new legislation, if it passes the house and the two bills can be reconciled, will be heard and refined through the courts as researchers and their institutions work to find a balance between an academic mission with its emphasis on early publishing and the imperative to get new technologies into the private sector and bring those goods to market. For now, university researchers would do well to follow the *Myriad* case closely as well as watch developments and interpretations of the currently proposed reform legislation. Probably the most important point for inventors to watch is the year-long grace period for disclosure. Early disclosure to the university technology transfer office means that licensing experts can begin analyzing potentially important inventions even while the researcher begins to work on writing publishable results. Good resources for the interested researcher can be found at uspto.gov, autm.org, patentlyo.com, aau.org and his or her own institution's technology transfer Web site.

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Unintended Consequences: Final Conclusions and Considerations

When I embarked on an inquiry into the role of patents in agricultural biotechnology five years ago, it was with the assumption that humanitarian problems arising from the patenting of food technologies was perhaps the most important threat arising from the particular problems facing the U.S. patent system. Direct and deliberate focus revealed a host of more practical, definable issues resulting from backlogs in the USPTO: poor patents quality, the rise of predatory litigation, and the implications of private and public investment in research driven by the innovation sector. Solving those practical and procedural issues have great capacity for lasting ability to serve "the greater good" as it relates to food and medicine.

One of the biggest surprises in the past five years which helped focus my line of inquiry was the lack of emerging humanitarian issues on the agricultural side of biotechnology. Despite well-documented problems in the well-known Golden Rice case, few new instances of humanitarian crop development arose specifically because of patent thickets. This was due largely to the fact that the EU and Africa remain suspicious of transgenic crop production. It is unlikely that engineered humanitarian crops will have the opportunity to solve global or sub-Saharan hunger with extreme opposition to the import of these crops. Still, the potential for similar cases remains and as world population continues to grow toward a projected 2050 peak. Increased demand for food could erase or diminish the taboo on transgenics. Fortunately, two focused and dedicated non-profit groups have been looking extensively at humanitarian issues related to the patenting of crop biotechnologies. PIPRA and CAMBIA remain committed to studying

this issue and providing workaround solutions that eliminate barriers to improved food technologies.

The ethical considerations for the biomedical side of the coin; however, continue to expand with important implications for biotechnology. The looming "patent cliff" for big manufacturers (several drug companies' patents on blockbuster drugs are set to expire in the next two years), decreased research and development (R&D), and increased pressure for affordable medicines and vaccines will likely demand focused policy analysis and reform in the coming decade—particularly in light of population growth, increased globalization and in this country, the aging of the baby-boomers.
What becomes clearer through focused research is that the anticipated fears of environmental groups has been misapplied. The advent and widespread adoption of biotechnologies has not resulted in environmental disaster, but instead the unintended consequences and most-pressing ethical considerations become those of economics and policy.

The patent backlog threatens to undermine the very foundation of American research—the notion that we should invest new inquiry in undiscovered paths so that new discovery can serve the public good. Patents have helped drive private and public investments that improve, enhance and prolong life. Indeed the success of the U.S. patent system in some ways has ironically become its biggest problem. New research investment dollars from corporations and industry has demanded the 'guarantee' of protected, exclusive rights to intellectual property, yet the mire of unresolved patent applications in the USPTO has left many inventors in limbo, unable to market new products with confidence, especially in the tech sectors where their ideas may be obsolete

before they come to market. In the life sciences, failure to invest in or market known technologies might mean the difference in life-saving bird flu or HIV vaccines or new diagnostic tests for potentially fatal E.coli strains or worse. The *Myriad Genetics* case will have consequences both good and bad that reverberate for decades.

The main conclusion that must be drawn is that the courts cannot solve the array of problems facing the innovation in the U.S.—Congress knows it must step in, and the Obama administration has made a significant push to make certain legislation succeeds this time around. Still, with a Senate bill passed and the House version due for a vote this year, there are no guarantees that this Congress will be able to reconcile the two versions of the law and pass comprehensive reform. Even then, it could be years before the impacts of legislation and new court rulings play out in the innovation sectors. What has emerged over the past five years is a clear picture that innovation, one of the primary economic goods in an information market, is most threatened by its own boom. U.S. legislators must make important changes to free resources need to meet increasing demand. Still, it is ominous our legal and legislative system continues to lag behind human innovation and appears ill-equipped to handle the pace and gravity of technological advances. Not surprisingly, the pressure for reform has not come from the ethical and humanitarian considerations that arise from ownership of the building blocks of life, but from corporate and university interests with the very practical need to get meaningful patents on new discoveries. Now, more than ever, researchers and universities must stay informed and active in intellectual property policy and embrace their public mission to ensure that research is driven by ethical and humanitarian considerations in addition to economic ones.

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