Patents – the Starting Gun in the Race for the Human Genome

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Patents – the Starting Gun in the Race for the Human Genome

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Abstract

The race to sequence the human genome between the federal government's Human Genome Project and the private firm Celera Genomics is one of the most fascinating tales in the history of science. This paper explores the role that the prospect of obtaining patents on these DNA sequences played in stimulating that race. It then examines different policy rationales for and against DNA sequence patents. In doing so, two competing goals rise to the surface – incentivizing the creation of downstream products versus maintaining an open and cordial research environment. Finally, the paper explores how the current law deals with these objectives and suggests a number of possible changes to strike a better balance.

On March 14, 2000, President Bill Clinton and Prime Minister Tony Blair issued the following statement about attaching property rights to the "fruits" of the Human Genome Project:

> To realize the full promise of this research, raw fundamental data on the human genome, including the human DNA sequence and its variations, should be made freely available to scientists everywhere. Unencumbered access to this information will promote discoveries that will reduce the burden of disease, improve health around the world, and enhance the quality of life for all humankind. Intellectual property protection for gene-based inventions will also play an important role in stimulating the development of important new health care products. We applaud the decision by scientists working on the Human Genome Project to release raw fundamental information about the human DNA sequence and its variants rapidly into the public domain, and we commend other scientists around the world to adopt this policy.[1]

Although the statement deliberately highlighted the important role that patents would continue to play in bringing new products to market, its emphasis on making human DNA sequences "freely available to scientists everywhere" was mistaken as a call for the elimination of all gene patents. This misinterpretation sent the biotech sector plummeting, taking the rest of the NASDAQ with it. One company in particular, Celera Genomics, lost over $2 billion in market value; and, as we will see much later in this paper, many feel that this was more political gamesmanship than accident.[2]

Celera Genomics was founded by a scientist who has been either loved or hated, but never ignored. His name is Craig J. Venter, and he decided that Celera would sequence the human genome on its own. The race that developed between Venter's private company and the publicly-funded Human Genome Project, led by the equally (if not more) distinguished Francis Collins, is one of the most fascinating and significant stories in the history of science. It has its fingers right on the pulse of one of the most pressing ethical, political, economic, and legal issues of our day – the patenting of human DNA. Although DNA patenting is a fairly recent phenomenon, it has generated a significant amount of controversy. From religious leaders to

[2] James Shreeve, The Genome War: How Craig Venter Tried to Capture the Code of Life and Save the World 322 (2004).

biotechnological industrialists, there are a wide range of opinions as to whether such patents are appropriate.

Legally, DNA patents have been recognized, and this is in keeping with the general push towards the commercialization of basic research science that began with the passage of the Bayh-Dole Act of 1980.[3] *Briefly, the Bayh-Dole Act* was an effort to promote the commercial development of new technologies in the private sector by permitting the patenting of inventions made with the use of federal funds. Although both patent applications and private investment in biotechnology have increased since the passage of the Bayh-Dole Act, some commentators have suggested that "a proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development."[4] Furthermore, scientists (unaccustomed to the ways of the marketplace) have complained that basic science is losing its open, cordial, and cooperative atmosphere. Taken to the extreme, one might ask if society is better served by scientists concerned with peer-reviewed publications or stock options. Although I do not pretend to know the answer, it occurred to me that the race to capture the human genome involved two such different groups of scientists.

This paper will explore that race and the role that the patent law played in each group's rationale for running it. Specifically, §1 will discuss the events of "the race" that developed between the two different initiatives. §2 will provide background as to the general rationale for intellectual property protection and its role in the field of biotechnology. §3 will then examine different policy arguments for and against the patenting of DNA sequences. Finally, §4 will track the adjustments in the doctrines of patentability and infringement over time as a way of examining which policy objectives have dominated. Finally, two possible changes in the law will

[3] 35 U.S.C. §§ 200 et seq., P.L. 96-517, § 6(a), 94 Stat. 3019 (1980).

[4] Michael A. Heller & Rebecca S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science 698-701 (1998).

be suggested as a way to strike a better balance between the interests of the two opposing groups.

§1 – The Race for the Human Genome

A. The Public Initiative – The Human Genome Project

Although the National Institutes of Health (NIH) would eventually come to dominate the project, the idea to sequence the entire human genome was first put forward by the Department of Energy (DOE) at a meeting of the nation's top geneticists at Cold Spring Harbor Laboratory in 1986. The idea did not find a warm reception. Since the sequencing methods in 1986 were so slow, the scientists did not think the time was ripe to abandon their current strategy of searching for individual genes.

However, everything changed when James Watson committed to the project in 1988.[5] $Watsonagreedtobedirectoroftheof the Human Genome I$

Instead of sequencing immediately, the HGP used the first five years to map the genome, i.e. to discover particular genetic landmarks and note their location relative to each other. This "map first, sequence later" strategy also provided makers of sequencing technology with time to advance the state of the

[5] Shreeve, *supra*, at 40-42.

[6] To learn more about the NHGRI generally, or its Ethical, Legal and Social Implications program specifically, see `www.genome.gov`.

art.[7] $However, by 1996, Francis Collins, who had replaced Watson as director of the NHGRI, could not afford to wait any longer for a faster breed of sequencers$

In addition to the American genome centers, John Sulston's lab at the Sanger Centre (Cambridge, England) received a large grant from the Wellcome Trust and was slated to sequence a sixth of the human genome. The Wellcome Trust is a charity created by Sir Henry Wellcome, the founder of a successful pharmaceutical company, the Wellcome Foundation (today GlaxoSmithKline). On Sir Henry's death, all of his shares were placed in the trust, and the trustees were directed to use the income to benefit human health. The Wellcome Trust became the wealthiest medical research charity in the world following the company's introduction of AZT in 1992.[9]

The Wellcome Trust played a critical role in establishing the HGP's political credo of free, public, and immediate access to its genomic sequence. By 1995, many academics working on the HGP were anxious to start the sequencing phase of the project. As we'll see below, their anxiety was due to the fact that a number of private genomic ventures had launched a "gold rush" on the human genome. These companies were filing patent applications by the thousands for gene fragments called expressed sequence tags (ESTs). Ironically, it was the NIH (with Craig Venter listed as the inventor) that first filed an application for such an invention. Although the NIH eventually abandoned its controversial application, Pandora's Box had already been opened. Private companies such as Incyte Genomics picked up the idea of patenting ESTs and ran with it all the way to the bank.

[7] Shreeve, *supra*, at 44.

[8] *Id.* at 45.

[9] John Sulston and Georgina Ferry, The Common Thread, 91 (2002).

Desiring a consensus among the international sequencing community with regard to the issue of data release, the Wellcome Trust sponsored a meeting in Bermuda during February 1996.[10] *Most scientists in the academic community shared the opinion*

> By doing this, we would not only help science to progress; we would make the sequences in themselves unpatentable. Patenting opportunities would be open only to those who went on to do the real work of discovering what the sequences did and developing commercial products based on that understanding... But all this, while truly a calculation that we made, makes the policy sound too purely pragmatic, or at least too short-term. The fact is that we'd come to realize that the genomic sequence we were producing and dealing with is more than a commodity. It is the essence of biological heritage, the instruction book for living things... The only reasonable way of dealing with the human genome sequence is to say that it belongs to us all – it is the common heritage of humankind.[11]

Although Sulston's rallying cry was contagious, there was nevertheless a political obstacle for the American genome centers – the Bayh-Dole Act.

Since the American genome centers were receiving federal funds from NIH and DOE, they were technically required to secure patent rights on all commercially valuable discoveries before putting them into the public domain. However, Francis Collins and the other American leaders of the HGP agreed that the underlying human DNA sequence was too important to be controlled by one entity.

The scientists hammered out what has since become known as the "Bermuda Accord." They agreed that all DNA sequences longer than 2000 base pairs must be placed in GenBank (the public database administered by the NIH) within 24 hours of their discovery. The effect of the Bermuda Accord was that it would be impossible to patent these raw DNA sequences. Although technically in breach of the Bayh-Dole Act, Collins made it clear that no funding would be distributed to any lab that did not specifically state its intention to abide by the Bermuda Accord.[12]

[10] *Id.* at 143.

[12] Shreeve, *supra*, at 46.

The HGP community viewed the Bermuda meetings as a great success. The scientists had been able to compare notes on various sequencing issues and formulate a plan of attack for dividing and conquering the human genome sequence. They reaffirmed their intention to produce a sequence of the highest possible quality. Finally, the leaders of the HGP had struck a blow to private interests by adopting a data release policy of immediate public disclosure.

During the Bermuda meetings, one person who voiced opposition to Sulston's data release policy was Craig Venter, director of The Institute for Genomic Research (TIGR). Although distrusted by many academics due to his relationships with a private company, Venter and his lab had been selected as one of the six American genome centers to begin actual sequencing of human DNA in 1996. However, a mere two years later, Venter would become the HGP's ultimate pariah.

B. Craig Venter – Darth Vader of Genomics

Craig Venter's part in this story begins with his work at the National Institute of Neurological Disorders and Stroke, a part of the NIH. Although he was supposed to be studying brain cell-surface receptors, Venter recognized that genomics was the wave of the future. In 1987, he contacted Michael Hunkapiller of Applied Biosystems, a division of Perkin Elmer.[13] $Hunkapiller had designed a new automated DNA sequencer, and Venter signed on to have his lab observe as a tes$

Venter's method involved the sequencing of complementary DNA (cDNA). cDNA is obtained by apply-

[13] *Id.* at 78.

ing a special enzyme (called reverse transcriptase) to messenger RNA (mRNA) that has been extracted from tissue. Without getting into too much biology, obtaining this cDNA is the equivalent of isolating just the protein-coding regions of genes (the part of our DNA that is most likely to be useful for understanding diseases). Venter's idea was to use the new machines to sequence just enough of the cDNA (approximately 150-400 bases) to identify the gene as unique from the others expressed in the same tissue.[14] *Venter called these short stretches of gene sequence "expressed sequence tags" (ESTs). Besides identifying the existence of the new gene, Venter realiz*

Venter began by sequencing cDNA from brain tissue and started to churn out tons of new ESTs. By the summer of 1990, Venter's lab had found 2000 ESTs, "essentially doubling the number of known human genes."[15] *Venter was so excited that he wrote to James Watson in hopes of receiving HGP funding to locate more genes. When Watson decided not to abandon th*

Science article, he described how his cDNA method was "a bargain in comparison to the genome project."[16] *While this tactic surely a*

On June 20, 1991, Venter, on behalf of the NIH, filed a patent application which claimed over 300 human DNA sequences in the form of ESTs.[17] *To say that the application was controversial would be an understatement. Although the claims appeared to be limited to t*

At a Senate meeting the following month, James Watson let Venter and the NIH know what he thought of their application. After Venter testified that the NIH planned to file patent applications for 1000 ESTs per month, Watson dismissed the patent application as "sheer lunacy" and remarked that Venter's automated se-

[14] Sulston, *supra*, at 105.

[15] Shreeve, *supra*, at 82.

[16] *Id.* at 83.

[17] Who Owns Life? 76 (David Magnus et al. eds., Prometheus Books 2002).

[18] *Id.*

quencing machines "could be run by monkeys."[19] *He continued: "What is important is interpreting the sequence... If these random bits of sequences*

On the flip side, there was a legitimate argument for the actions of the NIH and Venter. In fact, although Venter was vilified for its filing, he was initially opposed to the patent application. Reid Adler, the head of NIH's Technology Transfer Office, approached Venter and told him that the NIH was obligated under the Bayh-Dole Act to try to patent the ESTs.[21] *Furthermore, Adler explained that biotech firms had begun to express concern about Venter's sequences being deposite* (something that we'll return to in §4). According to this rationale, it would be better for American business if the NIH first patented the ESTs and then licensed the rights to the sequences. Adler also noted that the NIH could provide free licenses to academics.[22] *Venter was eventually convinced and filed the application.*

As demonstrated above, James Watson could not live under the same roof with anybody who supported the patenting of ESTs. Because Bernadine Healy, then director of the NIH, refused to back down from her support of the Venter application, Watson resigned as head of the NHGRI in April 1992.[23] *The NIH eventually abandoned its patent application on t*

While Watson and the HGP were not interested in embracing his cDNA method for discovering new genes, Venter soon realized that many private ventures were. In fact, a venture capitalist named Wallace Steinberg

[19] Shreeve, *supra*, at 85.

[20] Who Owns Life?, *supra*, at 79.

[21] Shreeve, *supra*, at 84.

[22] *Id.*

[23] Who Owns Life?, *supra*, at 81.

[24] *Id.* at 87.

soon made him an offer he couldn't refuse.[25] *Venter would be allowed to run his own nonprofit institute and would receive* $70 *million, over the course o*

Venter brought the majority of his lab with him to TIGR. There they continued to sequence human cDNAs and discover new ESTs. According to the agreement, Venter's fresh sequences were first deposited into a database. HGS would then have six months to study them and decide whether to file any patents (HGS had the option of extending the period another twelve months for any sequence it found valuable).[28] *After that time, Venter was free to publish his discoveries in the academic journals, and researchers were free to use the sequences provided that they ya*

When HGS sold an exclusive license to its "early access" to SmithKline Beecham for $125 million, Venter instantly made millions. As happy as this surely made him, Venter was soon publicly lamenting about the fact that Haseltine was routinely applying the twelve-month extension to new sequences. As a consequence, very little sequence data from TIGR was entering the public domain.

The HGP community wasn't buying Venter's sob story. One key player in the HGP remarked: "When he went off with Bill Haseltine, Craig was seen as evil. The world looked on TIGR as an absolute den of corruption."[30] *Perhaps John Sulston said it best*:

[25] Shreeve, *supra*, at 86.

[26] Who Owns Life, *supra*, at 82.

[27] Shreeve, *supra*, at 87.

[28] *Id.* at 86.

[29] Sulston, *supra*, at 108.

[30] Shreeve, *supra*, at 88.

> I saw [Venter's] deal with Human Genome Sciences as compromising Craig's academic integrity. I felt he wanted to have it both ways: to achieve recognition and acclaim from his peers for his scientific work, but also to accommodate the needs of his business partners for secrecy, and to enjoy the resulting profits.[31]

Sulston's description causes me to think of Venter as the "Darth Vader of genomics." Like Vader, there seems to be some good in him. For example, frustrated with Haseltine, Venter turned his attention to the sequencing of entire microbial genomes. This move away from the lucrative human ESTs came at the peak time of the private-sector gold rush and infuriated Haseltine.[32]

The relationship between Venter and Haseltine continued to deteriorate over the next couple of years until the partnership between TIGR and HGS was finally dissolved in 1997.[33] During that time, Venter's repeated release of microbial DNA sequences into the public domain against Haseltine's wishes partially restored his tarnished reputation in the academic community. As noted above, TIGR was even selected as one of the six genomic centers to receive funds for human sequencing. Yet, Venter would soon enter into another Faustian-like bargain.

What makes scientists like Craig Venter act so differently than those like James Watson? Perhaps it's just a difference in attitude toward the commercialization of science. James Watson and many of the other leaders of the HGP fall into the older camp of "science purists." They believe in the free and open exchange of scientific knowledge. In their minds, only applications of science should be commercialized. On the other hand, Craig Venter is a clear product of the "Bayh-Dole generation" (if not the Bayh-Dole Act incarnate). This new breed of "commercial scientists" subscribes to the belief that science moves forward most efficiently when tied to the capital markets.

[32] Shreeve, *supra*, at 107.

[33] *Id.* at 112.

C. The Indirect Threat to the HGP

Even well-regarded scientists within the HGP community were seduced by the Sirens' song of the venture capitalists in the early 1990s. For example, Eric Lander, the director of the Whitehead Institute at M.I.T., co-founded Millenium Pharmaceuticals in Cambridge, MA.[34] $Conflict of interest problems aside, these scientists did not pose much of a threat to the l$

By the mid-1990s, the real threat to the HGP's credo of "free access for all" was the explosion of private gene-hunting firms that aimed to lock-up the sequence for themselves. Regardless of Venter's intentions, his NIH patent application and subsequent relationship with HGS launched a gold rush on the human genome. For example, Incyte Genomics (originally Incyte Pharmaceuticals) was formed in 1991 to find genes using Venter's cDNA method. When HGS signed its exclusive agreement with SmithKline Beecham, the other pharmaceutical houses flocked to Incyte's database to get their share of ESTs. Incyte's revenues soared as it collected nonexclusive licensing fees from these companies.[35]

Besides collecting database access fees, these gene-hunting companies were also filing patent applications. By the time the NIH abandoned its infamous EST patent application in 1994, HGS had filed patent applications for nearly 10,000 ESTs. Incyte had filed applications for over 40,000 ESTs and planned to file for over 100,000

[34] Sulston, *supra*, at 110.

[35] *Gene Patents and Other Genomic Inventions: Hearing Before the Subcommittee on Courts and Intellectual Property of the House Committee on the Judiciary*, 106^{th} Congress 121 (2000).

ESTs each year going forward.[36] $Although the HGP had begun in 1990, its decision to "map first, sequence later" meant that by 1994 only 1\% of the genome$

Ironically, the HGP's "white knight" took the form of the pharmaceutical company Merck.[38] $Like the HGP, pharmaceutical giants also op$

The HGP leaders applauded Merck's efforts. However, John Sulston of the Sanger Centre and Bob Waterston of Washington University wanted to go even further. They were worried that with so many ESTs being sequenced on the private side, Congress would begin to question the purpose of the public program.[40] $Sulston and Waterston understood the great value in having not only the genes themselves, but also the "junk DNA" regions that contained the valuabl$

The increased funding was not much of a stumbling block since Francis Collins knew he would have to ask Congress for more funds regardless of when the sequence phase actually began. However, the suggestion of generating a working draft, which in effect meant a reduction in accuracy, was met with great resistance. From the beginning, the HGP leaders had promised a sequence that would stand the test of time. They were not about to retract that promise. Finally, the proposal to limit the sequencing to three genomic centers was wildly unpopular. The twenty or so labs that had spent the last five years mapping the genome understandably felt entitled to also sequence their respective segments.[42]

[36] Who Owns Life?, *supra*, at 88.

[37] *Id.* at 118.

[38] *Id.*

[39] Shreeve, *supra*, at 88.

[40] Sulston, *supra*, at 119.

[41] *Id.* at 128.

[42] *Id.* at 127.

In the end, Francis Collins decided to stay the course and rejected the Sulston/Waterston proposal. Other leaders, such as Eric Lander of the Whitehead Institute, convinced Collins that a new breed of sequencers that would allow the HGP to maintain its high accuracy standard was just around the corner. However, the Sulston and Waterston labs had demonstrated that they were eager for battle and were rewarded accordingly. Sulston actually received his requested increase in funding from the Wellcome Trust, and Waterston's lab at Washington University received the largest grant when Collins finally decided in 1996 that the sequencing phase could wait no longer. In hindsight, the HGP probably should have adopted the Sulston/Waterston platform since, as we shall see below, it was later forced to switch to a "working-draft" strategy upon the arrival of Venter's private-sector competitor for the human genome sequence.[43]

D. The Direct Assault – Celera Genomics

As with the 1991 NIH patent application, the idea to privately sequence the human genome did not originate with Craig Venter. It was born at a Perkin Elmer (PE) business meeting. PE's Applied Biosystems, the division lead by Michael Hunkapiller, had a virtual monopoly on the automated sequencer market. Yet, PE's CEO, Tony White, was not content to simply sell the pickaxes to the gold-mining companies like Incyte. White wanted a piece of the action, and he had a secret weapon. [44]

[43] *Id.* at 138.

[44] Shreeve, *supra*, at 60-61.

Hunkapiller's development team was close to finishing a new brand of sequencer that would render the current generation archaic. When a scientist at the PE business meeting joked that a couple hundred of Hunkapiller's new machines could sequence the human genome in three years, White instantly saw his opening.[45] *Whereas the other genomic companies were selling mere access to ESTs, his new company would provide access to the whole genome – – regulatory region*

Craig Venter.

Once Venter fully appreciated the speed of Hunkapiller's new sequencers, he became very excited about the opportunity. Yet, having so recently freed himself from the clutches of Bill Haseltine and HGS, Venter was reluctant. He agreed to head up the company on the understanding that the raw sequence would be freely available to the public. White assured him that "the company would seek patents on only a few hundred medically important genes."[46] *They decided to name the company Celera Genomics Corporation, based upon the Latin word for speed. PE would finance Celera to the tu*

Venter immediately began a series of shrewd tactical maneuvers. Even before informing Francis Collins and his other HGP collaborators, Venter contacted a reporter from the New York Times to lay out his vision for the company and suggested, in not so many words, that the public HGP should shift its focus in order to avoid redundancy.[48] *Venter explained to journalists and congressmen alike that "Celera's mission is to become the definitive source of genomic and medical infor*

Venter justified giving away the raw DNA sequence as an opportunity for something bigger. In answering his skeptics, he would explain:

[45] *Id.* at 64.

[46] *Id.* at 117.

[47] Sulston, *supra*, at 151.

[48] *Id.* at 154.

[49] Shreeve, *supra*, at 172.

[50] Sulston, *supra*, at 149.

> We're not a biotech. We're an information company, like LexisNexis. If you had the time, you could find the same information they have on your own. So why do they have two million subscribers? Because they've already done the legwork for you, so you can find what you want in seconds rather than hours. We're going to do the same for genomic information, on a global scale.[51]

Although the basic human sequence would be free, the other information in Celera's database would not. Venter realized that the real value in sequencing the human genome would be the discovery of how genetic variability predisposes a person to disease. Venter envisioned a future where not only biotech and pharmaceutical companies would log on to Celera's database, but also family doctors and laypeople interested in individualized medicine.[52] *PE and Tony White were betting $300 million on this vision, although they were hedging it with hundreds of patent applications.*

Intimately familiar with Venter's schizophrenic past, the leaders of the HGP again weren't buying any Venter's rhetoric. They couldn't help but think of Venter's initial opposition to the Bermuda Accord. Moreover even if Venter was sincere about wanting to give the genome away for free, the HGP leaders suspected that he would eventually "find himself shackled by the interests of his shareholders."[53] *At the annual Cold Spring Harbor symposium, James Watso*

The HGP community was right to worry. With $300 million and a fleet of sequencers that hadn't even hit the market, Venter seemed capable of completing the genome by 2001 and leaving the public program in the dust. The one big question mark in Celera's plan was its planned use of the "whole genome shotgun" method. Again, to avoid getting bogged down in the biology, it suffices to say that although Venter had used this method to successfully sequence microbial genomes at TIGR, most scientists in the HGP community

[52] *Id.* at 170.

[53] *Id.* at 124.

[54] Sulston, *supra*, at 151.

felt that it could not be used to assemble the human genome. Venter recognized this risk and decided to sequence the fruit fly, *Drosophila melanogaster*, as a pilot project.[55]

Although the idea of losing the race to Celera was bad enough, Collins realized that there wouldn't be any race at all if the Republican Congress determined that the private-sector could handle the job.[56]$Obviouslysensingthisopportunityhimself,$

Whereas a few years earlier the idea of assigning the sequencing to only a few labs was politically unpopular, it was now seen as a necessity. Collins not only limited the sequencing to his three most productive genome centers, but he also radically increased their funding (the DOE and Wellcome Trust matched this increase for their respective labs as well).[59]$Collinsalsomadethecontroversialdecisiontoabandonthe"finishasyougo"strategywhichgeneratedthehighestquality$

> We are in mortal danger of going out of existence. Think what's going to happen, early next summer. Celera could have ninety percent of their genome done. If we continue trying to finish as we go along, we'll have a third of ours. We can shout ourselves blue in the face that our one-third is a hundred times better quality than their ninety percent, but it won't make any difference. Folks won't understand the difference. They'll just be looking at who won a race.[61]

Collins simply felt that the HGP no longer had a choice.

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[55] Shreeve, *supra*, at 52.

[56] Sulston, *supra*, at 161.

[57] Shreeve, *supra*, at 185.

[58] *Id.*

[59] *Id.* at 187.

[60] *Id.* at 191.

Collins responded politically as well. At a budget meeting before Congressman Porter's subcommittee, Collins was asked point blank why the federal government should continue to fund the public program in light of Venter's claims.[62] Collins was ready with a two-part response. First, he explained why the whole-genome shotgun method was unlikely to succeed. Unlike the public program which was proceeding chromosome by chromosome, Celera was randomly sequencing human DNA in the hope that it could later assemble all of the pieces. Yet, due to the vast number of repeated sequences in the human genome, the HGP community had great doubts that it would work.

Although there was no doubt that Celera's method would generate a huge amount of DNA sequence, the patentability of that data was Collins's second concern. He explained to Congress:

> Many in the scientific community are concerned about a circumstance where large amounts of this critical information might, in some way, be constrained from utilization by everybody who wants to use it. It is such basic information, and the notion that it would, in some way, be moving out of a public domain enterprise into a single private company has raised some cautions in the minds of many of my advisors.[63]

Within a matter of weeks, the public program had received its money.

Ironically, the first thing the HGP did with its new funds was purchase hundreds of PE's new sequencers (causing people to speculate that this had been the purpose of creating Celera in the first place).[64] *Meanwhile, Venter continued to battle in th*

[62] Shreeve, *supra*, at 192.
[64] *Id.* at 194.

[65] Shreeve, *supra*, at 199.

[66] *Id.* at 205.

Although publicly a picture of confidence, Venter knew his business plan had taken some serious knocks. As much as he hated to admit it, the HGP's ramp-up had killed Celera's revenues. No sensible drug company was willing to sign a long term contract to Celera's database before seeing the quality of the HGP's working draft.[67] *To make matters worse, in April 1999, the Wellcome Trust and ten pharmaceutical companies had formed a non profit consortium to locate single nucle*

None of this was lost on Robert Millman, Celera's chief patent attorney. He began to lobby PE's management for a more aggressive stance on Celera's intellectual property. The USPTO had recently issued the first patent on an expressed sequence tag (EST) to Incyte.[69] *Although invalidation in the federal courts remained possible, Millman advised filing patent appli*

E. Mudslinging and Pizza Diplomacy

With the HGP and Celera paranoid of each other and churning out DNA sequence at unprecedented rates, the race quickly turned into a battle of press releases and mud-slinging. In September 1999, the NHGRI and Wellcome Trust reaffirmed that the public program was on track to deliver "the first draft of the genetic blueprint

[67] *Id.* at 265.

[68] Shreeve, *supra*, at 213.

[69] *Id.* at 229.

[70] *Id.* at 232.

[71] *Id.* at 235.

of humankind" by the spring of 2000.[72] In January, Venter held his own briefing and announced that his company had completed 90% of the genome.[73]

Things got worse for Celera and the NASDAQ on March 14, 2000. President Clinton and Prime Minister Blair had issued a joint statement declaring that "the raw, fundamental data of the human genome, including the human DNA sequence and its variations, should be made freely available to scientists everywhere."[76] The statement had been written by a staff member of the NHGRI and, although it explicitly supported "gene-based inventions," it was being misrep

To make an already long story slightly shorter, the mud-slinging between the two camps continued to worsen, with the language getting nastier and nastier. With paranoia at an all time high, each group lived in constant fear that the other would make a preemptive announcement of completion. The major problem with the endless rounds of press releases was that they had locked both groups into unrealistic time frames. The NIH found itself in a bind. If Celera declared victory first, its reputation would suffer in the eyes of Congress. Yet, if Collins and the HGP went public with a shoddy version of the human genome, the repercussions might be even worse.[79] Intense political pressure developed to get both groups to the negotiating table. After a number of failed collaboration attempts, the man who succe

[72] Shreeve, *supra*, at 290.

[73] *Id.* at 312.

[74] *Id.* at 304.

[75] *Id.* at 303.

[76] Shreeve, *supra*, at 321.

[77] *Id.* at 322.

[78] *Id.* at 323.

[79] Shreeve, *supra*, at 332.

After both leaders articulated their demands, it again became apparent that collaboration would not be possible. However, Patrinos noticed that both men expressed frustration with the sense of feeling rushed to finish. He suggested that instead of collaborating, the two groups could simply announce the completion of their respective genomes at the same time.[80] *Both Collins and Venter were intrigued by the idea and agreed to come back the following week. After a couple o* over pizza at Patrinos's house, the two generals of the genome war had declared a truce. Collins and Venter agreed that both groups would write their own paper and that publication should occur in the September 2000 edition of *Science*. As usual, the point of contention was public access to the data. Although Venter refused to deposit his sequence into GenBank for security reasons, he agreed to make it viewable for free on Celera's website.[81] *Both Venter and Collins agreed to refrain from many further disparaging remarks about the other's work. Finally, the two men agreed to stand side by side*

The public announcement and celebration at the White House went smoothly. The two camps had one more squabble over the specifics of Celera's data release, which eventually lead to the HGP publishing its genome in *Nature* as opposed to *Science* (but still on the same day).[83] While scientists on each side of the fence continued to argue about whose data was "better," from the public's perspective, the race ended as a tie that day in the White House.

§2. Introduction to the Patent System and Its Role in Biotechnology

The story of the race to capture the genome is a fascinating mix of science, business, and politics. Since

[80] *Id.* at 342.

[81] *Id.* at 345.

[82] *Id.* at 350.

[83] Sulston, *supra*, at 234-35.

I'm preparing to leave HLS for a career in patent law, I was particularly struck by the role that patents (or the threat of them from the public program's perspective) played in stimulating the race. The more I read, the more I liked analogizing patent protection to the race's starting gun. Yet, the deeper question I want to explore further is whether the firing of that gun resulted in a "clean race." In other words, does the patent system work properly to protect both innovation and the public domain in the context of biotechnology generally and DNA sequence inventions specifically? If not, could any changes be made to strike a better balance?

Although the scientists from the HGP "triumphed" in the sense that the bare-bones sequence, i.e. the complete genetic blueprint to build a human, was made available to the public, it's clear that this sequence information is just the beginning of the road. Private entities in the pharmaceutical and biotechnology industries now want to utilize this information to create life-saving drugs and therapeutics. However, the costs of R&D and FDA approval are monumental. This great capital expenditure can only be undertaken with the assurance of patent protection. As Bruce Lehman, the former commissioner of the PTO explained, "there are few subjects of greater importance to the development of biotechnology than the issuance of patents."[84] Before we can explore the question of how smoothly the patent system is currently working in the context of genetic inventions, an introduction to (A) the justifications for the patent system, (B) biotechnology as intellectual property, and (C) DNA as patentable subject matter will be helpful.

[84]Bruce Lehman, Major Biotechnology Issues for the U.S. Patent and Trademark Office, 33 Cal. W. L. Rev. 49, 50 (1996).

A. Justifications for the Patent System

The best-known and most widely accepted justification for the patent system is utilitarian in nature. Patents are necessary to incentivize the creation and public dissemination of new technology and knowledge. Without the government-granted monopoly right, an inventor would not be able to recoup her research and development costs since her competitors could "pirate" her idea and sell the invention for a lower cost. The creation of these new technologies, which often make life easier, is generally understood to be a good thing. However, there are certainly trade-offs that come with the patent system. Perhaps the biggest is what's known in the language of law and economics as "deadweight loss."

Deadweight loss can be understood by imagining a world without patents (or alternatively by examining what happens to the price of a technology after its patent expires). Since competitors would be allowed to enter the market, the price of the invention would drop to just above its marginal cost (i.e. the actual cost of building the product). With a drop in price, more people would be able to purchase and benefit from the invention. However, as described above, the absence of patent protection would prevent the creation of new technology in the first place since inventors would not be able to recoup their costs. So, by allowing the patentee to charge the monopoly price, society necessarily must swallow the "deadweight loss" experienced by people who are denied the benefit of the invention because they have been priced out of the market. This loss isn't such a big deal when we are talking about fourth-graders who can't afford the latest and greatest skateboard wheels; but it is very much "real" in the context of HIV drugs. Regardless of the specific type of technology, the point is that the utilitarian theory of patent rights accepts this disutility (which lasts for the length of the patent term) because it assumes that society is coming out ahead overall by having incentivized the creation of the technology in the first place.

Patent rights may also be defended using deontological arguments. These arguments justify the existence of patents through a basic right to one's own intellectual property. Although not as popular as the utilitarian justification, two in particular merit description. The first is John Locke's notion of natural property rights.[85] *According to Locke, a person acquires property through mixing his labor with an un-owned resource. By extension, an invention properly belongs to it*

The second helpful deontological justification can be called "personality theory" and has been articulated best by Margaret Jane Radin[86] *and Jeremy Waldron.*[87] According to this theory, property rights are morally justified because they enable a person to develop a "life plan" and fully express oneself. Although this theory is normally used to justify the existence of private property rights, I will refer to it below in support of possible limitations on the private ownership of certain types of genes.

[85] David B. Resnik, Owning the Genome: A Moral Analysis of DNA Patenting 35-36 (2004).

[86] Margaret J. Radin, Property and Personhood, 34 Stan. L. Rev. 1002-08 (1982).

[87] Jeremy Waldron, The Right to Private Property, Ch. 8 (1988).

B. The History of Biotechnology as Intellectual Property

The ability to obtain product-patent protection for biological materials has its roots in the 1980 Supreme Court holding in *Diamond v. Chakrabraty*.[88] In 1972, Ananda Chakrabarty applied for a patent on a new bacterium that he had created (through breeding – not, as popularly believed, through recombinant DNA technology) that was able to degrade crude oil more efficiently than any natural strain. He thought that these bacteria could be used to assist the clean-up following an oil spill.

His application was rejected by the Patent and Trademark Office (PTO) because, at that time, living organisms such as bacteria and animals were considered unpatentable "products of nature" under 35 U.S.C. § 101.[89] Examining the legislative history of § 101, the Supreme Court noted that a 1952 Congressional Report explained that "anything under the sun that is made by man" should be patentable subject matter.[90] The Court adopted this broad construction and held Chakrabarty's bacterium to be patentable subject matter since "[h]is discovery is not nature's handiwork, but his own."[91] Following *Chakrabarty*, the fact that an invention is a living organism is irrelevant under 35 U.S.C. § 101.

In its opinion, the Supreme Court rejected the PTO's argument that since genetic technology was unfore-

[88] *Diamond v. Chakrabarty*, 447 U.S. 303, 65 L. Ed. 2d 144, 100 S. Ct. 2204, 206 U.S.P.Q. (BNA) 193 (1980).

[89] 35 U.S.C. § 101 states: "Whoever invents or discovers any useful process, machine, manufacture, or composition of matter or any new and useful improvements thereof, may obtain a patent therefore subject to the conditions and requirements of this title." This provision provides the statutory basis for both the patentable subject matter and utility requirements.

[90] *Chakrabarty*, 447 U.S. at 309. The Court explained further: "This is not to suggest that § 101 has no limits or that it embraces every discovery. The laws of nature, physical phenomena, and abstract ideas have been held not patentable."

[91] *Id.* at 310.

seeable at the time of § 101's enactment, the patentability of genetic inventions should be a decision left to Congress. The Court acknowledged that Congress would obviously have the power to alter the limits of patentability; but, citing *Marbury v. Madison*, noted it was the Court's job to interpret the version of § 101 currently in effect. Commenting on the *amicus* briefs submitted in support of the PTO's position, the Court remarked:

> The briefs present a gruesome parade of horribles. Scientists, among them Nobel laureates, are quoted suggesting that genetic research may pose a serious threat to the human race, or, at the very least, that the dangers are far too substantial to permit such research to proceed apace at this time. We are told that genetic research and related technological developments may spread pollution and disease, that it may result in a loss of genetic diversity, and that its practice may tend to depreciate the value of human life.[92]

Pleading incompetence, the Court responded by first stating that these arguments were matters of high policy appropriately left to the legislative process. Secondly, the Court stated that their decision as to patentability would not put an end to genetic research, but may simply "determine whether research efforts are accelerated by the hope of reward or slowed by the want of incentives."[93]

To say that the *Chakrabarty* decision simply "accelerated" biotechnological research efforts would be a huge understatement. Private biomedical research and development (R&D) rose from $2 billion per year in 1980 to $50 billion per year in 2000.[94] This huge rise in venture capital funding can be explained by the new protection afforded by the biotechnology patents pouring out of the PTO. Post-*Chakrabarty*, the PTO has issued utility patents on all sorts of biological materials including plants, multi-cellular organisms as

[93] *Id.* at 317.

[94] Resnik, *supra*, at 3. Note that this was also the year of the passage of the Bayh-Dole Act. It seems that *Chakrabarty* and Bayh-Dole have acted synergistically.

"advanced" as rhesus monkeys, human stem cells, proteins, and, as we shall see in the next, DNA.[95]

C. The Current Status of DNA as Statutory Subject Matter

Moral arguments aside, the legal question as to the patentability of genetic inventions has been resolved in the Court of Appeals for the Federal Circuit (the exclusive appellate court for questions of law specific to patents) in favor of patentability. Although all of the requirements under the Patent Act (statutory subject matter, utility, novelty, written description, enablement, and nonobviousness) must be met before the issuance of any patent, the prohibition against "products of nature" as statutory subject matter under 35 U.S.C. § 101 is the first hurdle for any application that claims a DNA sequence invention.[96]

The Federal Circuit explained in the 1991 case of *Amgen, Inc. v. Chugai Pharmaceutical Co.* that applications for gene patents may only claim purified and isolated DNA sequences since only they qualify as products of human ingenuity under *Chakrabarty.* [97] In that case, the Court affirmed the validity of Amgen's patent which claimed: "a *purified and isolated* DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin" (emphasis added).[98] The Court emphasized the point by noting that "[i]t is important to recognize that neither Fritsch nor Lin [the two inventors fighting for priority in the case]

[95] The PTO has stated that "a claim directed to or including within its scope a human being will not be considered to be patentable subject matter under 35 U.S.C. § 101." *Ex Parte Allen*, 2 U.S.P.Q. 2d (BNA) 1425, *aff'd*, 846 F.2d 77 (1998). The commissioner stated that such a claim is prohibited by the Thirteenth Amendment of the Constitution. *See* Commissioner of Patents and Trademarks, Policy Statement on Patentability of Animals, 1077 Off. Gaz. Pat Office 24 (Apr. 7, 1987).

[96] John J. Doll, The Patenting of DNA, 280 Science 689-90 (1998).

[97] See *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 U.S.P.Q. 2d (BNA) 1016 (Fed. Cir. 1991), *cert. denied*, 502 U.S. 856 (1991).

[98] U.S. Patent No. 4,703,008, October 27, 1987 (DNA sequences encoding erythropoietin).

invented EPO or the EPO gene."[99] *Because gene patents are limited to the* "purified and isolated" forms of specific DNA sequences (as distinct from the chromosomes in which they exist in nature), holders of such patents have no leverage over you or me since our genes are in their "natural state." In other words, an average Joe walking down the street can't infringe a gene patent simply because his body is operating normally.

As tempting as it is to say that this is mere semantics, there is a good policy rationale behind it. Furthermore, this problem is not unique to biotechnology. Many chemicals that exist in nature in an impure or mixed state can become new and useful when put into a purified form. For example, in 1958 the Fourth Circuit upheld the patentability of purified Vitamin B-12.[100] *One commentator has explained*:

> This is not simply a lawyer's trick, but a persuasive response to the intuition that patents should only issue for human inventions. It prevents the issuance of patents that take away from the public things that they were previously using (such as the DNA that resides in their cells), while allowing patents to issue on new human manipulations of nature. Those of us who simply use the DNA in our own cells, as our ancestors have been doing for generations, should not and need not worry about patent infringement liability. On the other hand, those of us who get injections of recombinant insulin or erythropoietin should in fairness expect to pay a premium to the inventors who made these technological interventions possible.[101]

In summary, although patent lawyers continue to argue over other requirements for patentability (which will be addressed below), the legal status of purified and isolated DNA sequences as statutory subject matter is secure within the federal courts.

§3. Policy Arguments For and Against DNA Patents

A. The Bayh-Dole Rationale in Support of DNA Patents

[99] *Amgen, Inc.*, 927 F.2d at 1206.

[100] Merck & Co. v. Olin Matheison Chem. Corp., 253 F.2d 156 (4th Cir. 1958).

The general utilitarian argument for patents can easily be applied to the field of biotechnology. As described above, the most-widely accepted justification for the patent system is two-fold. First, patents incentivize innovation by allowing inventors to recoup their costs (and often much more) in the form of monopoly profits. Second, by requiring full disclosure of the invention as part of the *quid pro quo* for the monopoly grant, the patent system places the fresh knowledge immediately into the pubic domain so that others may learn from it (as opposed to trade secret protection). Applying this "incentive rationale" to genetic research causes a couple of criticisms to quickly emerge.

An initial criticism is that geneticists don't need this kind of incentive. Indeed, the gut reaction is that people who go into the fields of biology or chemistry usually do so because they have a genuine love for the work, not because they are chasing dollar signs (granted this may be changing due to the increased presence of intellectual property law). The recognition they have traditionally sought has been in the form of awards or peer-review publications. However, this criticism misses the point that genetic research is extremely expensive. Although not all of these researchers are in it for stock options, the capital clearly must come from somewhere.

In other words, the prospect of patent protection creates an incentive for capital formation in high-tech industries like biotechnology (where discoveries by scientist-employees are assigned to the corporation-employer by contract). Biotechnology patents, of which DNA patents are a significant part, have allowed the industry to flourish. In 1999 alone, the industry spent $11 billion on R&D and accounted for 437,000 U.S. jobs.[102] *Theseeconomicbenefitsarecertainlytangibleherein Boston,aswellasmanyothercitiesinourcountry.Thefederalgovernmentalonecouldnotmatc*

[102] Resnik, *supra*, at 68.

I do not mean to belittle the role that the federal government plays in funding basic science research. In fact, the federal government's funding of basic science is so significant that it serves as the basis for a second major objection to DNA patents. Critics of gene patents argue that since the government often pays for the research leading to the discovery of these genes, the genes should belong to the government. In other words, it is unfair to make taxpayers pay monopoly prices to private companies when those companies didn't incur the expenses that resulted in the discovery. The answer to this criticism is not intuitive and requires an explanation of the rationale for the Bayh-Dole Act of 1980.[103]

Before the Bayh-Dole Act, it was very difficult to transfer discoveries that were made with federal funds to the private sector.[104] *The problem was not that basic science discoveries weren't being made, but rather that no downstream products or treatments were being de* As we learned in winter-term, pharmaceutical products must go through three rounds of extensive clinical trials before they may be prescribed to patients by doctors. The Pharmaceutical Research and Manufacturers of America claim that only 0.1% of compounds that demonstrate potential in animal testing reach clinical trials in humans.[105] *Once at the clinical trial stage, only one drug out of five receives FDA approval. The average cost of development for an approved drug is* $500,00

[103] 35 U.S.C. §§ 200 et seq., P.L. 96-517, § 6(a), 94 Stat. 3019 (1980). The Policy and Objective section states: "It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area."

[104] See Who Owns Life?, *supra*, at 45.

[105] Pharmaceutical Research Manufacturers of America, Why Do Prescription Drugs Cost So Much?, available at `http://www.phrma.org/publications/publications/brochure/questions/questions.pdf`

[106] *See id.*

chance against the big pharmaceutical houses. Lead time advantage would be nothing compared to the awesome marketing and distribution capabilities of these international conglomerates.

The passage of the Bayh-Dole Act allowed universities to patent their discoveries made with federal funds. Congress decided that the universities were in a better position to license these rights (often exclusively) to the appropriate players in the private sector. The result is that, by now, most research universities and nonprofits receiving federal funds have established a technology transfer office to obtain and license their patent rights (think Harvard Oncomouse). While many people, e.g. Jeremy Rifkin, continue to object to the Bayh-Dole Act as a form of "corporate welfare,"[107] $most in the biotechnology industry, including a number of in-house patent counsel with whom I have spoken w$

There can be little doubt that the Bayh-Dole Act, together with the *Chakrabarty* decision, facilitated the deluge of private capital into biotechnology. I believe that the rationale for the Bayh-Dole Act demonstrates why patent protection is necessary even if the discovery of a particular DNA sequence was discovered through the use of federal funding. The fact that some people will be overly burdened by higher prices until the patent expires is no doubt unfortunate. However, stepping back, I view this as a sacrifice that must be made so that society may continue to benefit from new products in the long run.[108]

Patents on DNA sequences have clearly produced economic and scientific benefits through the bolstering of the biotechnology industry. While there have been some tangible medical benefits (mostly in the form of

[107] Resnik, *supra*, at 70.

[108] This paper presumes the continued existence of the U.S. patent system. However, commentators have discussed an alternative reward-based system. The potential benefit of such a system is that, after the government pays the inventor her "reward," the technology would fall immediately into the public domain, thereby eliminating the deadweight loss. Although appealing, I think this system would be administratively unworkable. For more on the idea of a "rewards system," see Steven Shavell and Tanguy van Ypersele, "Rewards versus Intellectual Property Rights," 44 J. of Law & Economics 525 (2001).

diagnostics as opposed to treatments/cures), it must be admitted that medical science has not yet experienced the full potential of the genomic revolution. Yet this is precisely why I feel that gene patents are important enough to wrestle with some of the potentially adverse social messages discussed in the next few paragraphs. Gene patents will provide the security for investment in "proteomics" – the next step in acquiring the life-saving therapies of tomorrow.

As noted above, recognizing property rights in DNA sequences does not come without challenges. The biggest danger in deciding that genes are patentable is that we are therefore also saying that genes are marketable (since patents are usually obtained for commercial interests). Some find this "commodification" immoral in itself. Others, including myself, feel that it has the potential to harm society if allowed to run rampant. Explaining the commodification objection to gene patents is tricky for a couple of reasons. First, the word "gene" means different things to different groups of people. For example, a patent lawyer in court might say that a gene is a "mere chemical" since that is how the legal system has thus far treated it.[109] *On the other hand, a preacher at the pulpit might define a gene as "the sacred work of God's hand." Second, the concept of "commodification," best describe*

Why not? At the risk of butchering some basic metaphysics (not my forte), the danger in the commodification of genes is that we risk blurring the Kantian distinction between "the self and its properties as a subject, and the nonself as objects."[111] *Like Kant, I believe that all peoples hould be treated as "subjects" of equal worth and intrinsic value. By extension, I do not believe*

[109] See *Amgen, Inc.*, 927 F.2d at 1206 ("A gene is a chemical compound, albeit a complex one. . . ").

[110] See Who Owns Life?, *supra*, at 166.

[111] *Id.* at 168.

As a side-note, I view this argument as a sort of anti-"personality theory" argument. Normally, Radin's personality theory is used to support the establishment of property rights because those rights are necessary to freely express one's personhood. Here, the opposite might occur if we accept that gene patents will result in the valuation of human traits. In other words, the creation of patent rights in genes might limit a person's autonomy because he will either label himself or be labeled by others as inferior.

Although I do think commodification is a real threat that merits a watchful eye and/or future regulation, I don't buy this autonomy argument for two reasons. First, I think gene patenting would likely result in incomplete commodification. We must be careful not to overlook the fact that we can treat something as having both a market value and a nonmarket value. For example, although I might insure my own life for one million dollars, I would not believe that this was my "true worth." [112] $Similarly, the fair market value of my "height" gene might not be a true measure o$

B. Do We Have A "Tragedy of the Anticommons?"

Although I do not think the potential for adverse social consequences described above justifies prohibiting patents on DNA inventions (and therefore slowing down the delivery of new, life-saving treatments and products), other critics have questioned the premise that patents always facilitate the delivery of new health care products. Professors Michael Heller and Rebecca Eisenberg of the University of Michigan have articulated an argument whereby the increase in intellectual property rights due to the privatization of biomedical

[112] Resnik, *supra*, at 100.

[113] Who Owns Life?, *supra*, at 168.

research "may lead paradoxically to fewer useful products for improving human health."[114] Their argument is a spin-off of the "tragedy of the commons" metaphor in which a scarce resource is overused because the government allows too many individuals access to it. The flip-side is the "tragedy of the anticommons" in which the resource is underutilized because the government has granted too many people the right to exclude others from using it.

Heller and Eisenberg note that biomedical research has been moving from a "commons model" to a "privatization model:"

> Under the commons model, the federal government sponsored premarket or "upstream" research and encouraged broad dissemination of results in the public domain. Unpatented biomedical discoveries were freely incorporated in "downstream" products for diagnosing and treating disease. In 1980, in an effort to promote commercial development of new technologies, Congress began encouraging universities and other institutions to patent discoveries arising from federally supported research and development and to transfer their technology to the private sector. Supporters applaud the resulting increase in patent filings and private investment, whereas critics fear deterioration in the culture of upstream research.[115]

Clearly what is being distinguished here is the same difference in ideology between the two camps in the race for the human genome, i.e. the difference between the Bermuda Accord and the Celera business plan. James Watson, Francis Collins, and the rest of the HGP leaders were accustomed to the "commons model" of government sponsored research wherein all findings were put into the public domain. On the other hand, Craig Venter, Tony White, and Robert Millman have "gone with the flow" and embraced the Bayh-Dole model of product development.

[114] Michael A. Heller & Rebecca S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science 698-701.

Although Heller and Eisenberg acknowledge that "patents and other forms of intellectual property for upstream discoveries may fortify incentives to undertake risky research projects and could result in a more equitable distribution of profits across all stages of R&D," they seem consumed by the potential dangers of the Bayh-Dole or "privatization model."[116] *Commenting on how they believe filing patents is a* necessity today for researchers, Heller and Eisenberg note:

> Upstream patent rights, initially offered to help attract further private investment, are increasingly regarded as entitlements by those who do research with public funds. A researcher who may have felt entitled to coauthorship or a citation in an earlier era may now feel entitled to be a coinventor on a patent or to receive a royalty under a material transfer agreement. The result has been a spiral of overlapping patent claims in the hands of different owners, reaching ever further upstream in the course of biomedical research. Researchers and their institutions may resent restrictions on access to the patented discoveries of others, yet nobody wants to be the last one left dedicating findings to the public domain.[117]

According to their argument, the privatization of upstream biomedical research has the potential to create anticommons property. This is problematic because future research may be obstructed if it requires getting a license from too many patentees from earlier discoveries.

Heller and Eisenberg are careful to distinguish this underutilization from the normal underuse that naturally accompanies a patentee's ability to charge the monopoly price for her invention. In other words, the tragedy of the anticommons is not equivalent to the "deadweight loss" discussed at the start of this paper as an inherent part of the patent system. Instead:

> The tragedy of the anticommons refers to the more complex obstacles that arise when a user needs access to multiple patented inputs to create a single useful product. Each upstream patent allows its owner to set up a tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical invention.[118]

[116] *Id.*

Heller and Eisenberg believe that their anticommons "tollbooth" model strongly suggests against the issuing of patents on gene fragments.

They begin their case by calling attention to the significant change in DNA sequencing technology that occurred in the late 1980s/early 1990s (largely due to the work of Michael Hunkapiller at Perkin Elmer).[119] *Before the creation of this new* high-throughput DNA sequencing, DNA sequences found in patent claims generally consisted of cloned genes that were used to produce the protein of interest via recombinant DNA technology. For example, as we saw above, Amgen (in perhaps the most successful cloned-gene patent of all time) claimed "a purified and isolated DNA sequence encoding erythropoietin."[120] *Since it owns the* exclusive rights to the "purified and isolated" gene, only Amgen can put the gene into bacteria to make the protein. EPO has not only made incredible profits for Amgen, but has saved the lives of countless anemic patients worldwide. The point is that before the early 1990s, patents on genes "generally corresponded closely to foreseeable commercial products, such as therapeutic proteins or diagnostic tests for recognized genetic diseases."[121] *In other words, functions for these DNA sequences were already known at the time of their patent application filing.* The federal courts analogized these "cloned gene" DNA sequences to chemicals, and used the prior case law on chemical inventions to resolve patent law issues in the DNA sequence context.[122]

The strategy for filing DNA sequence patent applications radically changed after the adoption of high-throughput DNA sequencing. Ironically, the initiator of this change was none other than the NIH itself with

[119] Shreeve, *supra*, at 78.

[120] U.S. Patent No. 4,703,008, October 27, 1987 (DNA sequences encoding erythropoietin).

[121] Heller & Eisenberg, *supra*, at 699.

[122] See *Amgen, Inc.*, 927 F.2d at 1206 ("A gene is a chemical compound, albeit a complex one. . . ").

its controversial 1991 patent application on Craig Venter's expressed sequence tags (ESTs). To refresh the reader, an EST is a DNA sequence just long enough to demonstrate that it is a unique portion of the translated region of a gene. However, an EST tells nothing of either the location of the gene or the protein that it encodes.[123] revolution in automated sequencers, these new claimed sequences "look less like new chemical entities than they do like new scientific information," a problem that will be examined in the next subsection.

The potential danger of granting patents on gene fragments is that:

> Foreseeable commercial products, such as therapeutic proteins or genetic diagnostic tests, are more likely to require the use of multiple fragments. A proliferation of patents on individual fragments held by different owners seems inevitably to require costly future transactions to bundle licenses together before a firm can have an effective right to develop these products.[125]

Heller and Eisenberg are worried that downstream firms will be deterred from attempting to develop new products because of the increased transaction costs that accompany the acquisition of multiple licenses.

There are a number of responses to Heller and Eisenberg's "patent thicket" argument. The first is that we've essentially heard all of this before. John J. Doll, then director of the PTO's Biotechnology Examination Division, acknowledged (in the same issue of Science as the Heller and Eisenberg article) the many critics against gene patents. Yet, he explained that in the PTO's view:

[123] See Who Owns Life?, *supra*, at 76.

[124] Heller & Eisenberg, *supra*, at 699.

> New areas of technology do not create the need for a whole new specialized patent law. In many ways, the arguments currently being used for DNA sequence technology resemble those voiced 30 to 40 years ago when polymer chemistry was an emerging technology. At that time, people argued that if broad generic claims were granted on the building blocks of basic polymers, it would devastate the industry. In fact, no such disaster occurred.[126]

Any DNA sequence invention would still have to meet the individual patent law requirements, e.g. utility and nonobviousness; but, in Doll's opinion, if a gene fragment can do so, there is no reason why it should be denied dominant status. The situation should be no different than the following example:

> A patent might be granted for compound X, which is disclosed to have a specific use (such as a headache remedy). If other investigators find that X has a new and unexpected use, perhaps in combination with compound Y, for treatment of heart arrhythmias, they may have to obtain a license from the individual who first patented compound X in order to sell XY... In summary, once a product is patented, that patent extends to any use, even those that have not been disclosed in the patent. A future nonobvious method of using that product may be patentable, but the first patent would have been dominant.[127]

The problem with the Heller and Eisenberg argument is that it applies to any fundamental invention that leads to further invention.

Dr. Randall Scott, who in 2000 was president and chief scientific officer of Incyte Genomics, used the following example to rebut Heller and Eisenberg's argument:

> The invention of both the transistor and the integrated circuit enabled the microprocessor industry, which has seen innovations by and patents issued to countless inventors. While many of these inventions overlap, the industry has been able to work out cross-licensing arrangements that have enabled the delivery of unprecedented computing power to the general public. If one applied the reasoning of commentators like Professor Eisenberg, then patents on the transistor and integrated circuit should never have been granted. The difficulty with this reasoning, then, is that those inventions that are most fundamental, and are presumably most worthy of patent protection, would be denied protection on the basis that they are most likely to block further innovation by others.[128]

Scott would say that scientist/entrepreneurs like Venter and himself are involved in no Faustian bargain. Instead, he believes that Incyte's business model is accelerating the use of DNA sequence inventions by

pharmaceutical, biotechnological, and academic researchers.

Scott explained to Congress:

> At my company, Incyte, when we founded the company back in 1991, we were driven by the principle that science was long and arduous. Identifying a biological function and then painstakingly purifying the one molecule out of a commish of biological molecules was very hard work. In effect, we began operating on a different principle, that we could take cells and tissues of interesting biological meaning, such as prostrate cancer and normal prostrate tissue, and start to scan thousands of genes and look at the differences between those genes, [i.e.] which genes associated with different diseases.[129]

Incyte made the novel decision (at the time) to focus solely on this important stage of drug development. Whereas other companies were still fully vertically integrated, i.e. they performed all operations from target discovery down through clinical trials, Incyte invested more and more money into DNA sequencing and became better and better at generating results. Naturally, to protect its large investment, Incyte filed and obtained patent protection for its discoveries.

By 2000, Incyte had obtained nearly 500 gene patents (second only to the NIH). Considering those patents to be an "incredible trust," Incyte decided that they would only license those patents nonexclusively in both the research and diagnostics fields. Furthermore, the company established a policy of licensing the patents broadly, i.e. to anyone who asked.[130] $Scott feels that, by adopting these licensing strategies, Incyte has$ not only avoiding becoming a "tollbooth" on the road to discovery, but has instead created an "EZ Pass" lane:

[130] *Gene Patents and Other Genomic Inventions: Hearing Before the Subcommittee on Courts and Intellectual Property of the House Committee on the Judiciary*, 106^{th} Congress 121 (2000).

> By essentially making this technology available broadly, we think we have added tremendous value to industry and a tremendous value to society. We also believe that we're seeing a changing time in the pharmaceutical industry, just as we've seen in the computer industry. In the early days of the computer industry, every company did everything. They made their own chips. They made their own software. They had their own sales and distribution network, but effectively, as Intel and Microsoft and many companies came along, they began to fragment that industry. Pretty soon it was discovered that it was much more effective for one company to make chips and sell them to all manufacturers.
>
> You're beginning to see some of that same influence in the pharmaceutical industry, where in the past every company, every researcher, went all the way from A to Z, making the discovery, screening and developing the compound, developing that drug. Companies like ourselves no longer focus on the end product of manufacturing a drug and taking that to the clinic and to the market, but rather on the early discovery phase and providing that as a service to the entire industry. That's been the basis of our company. We now have 18 out of the top 20 pharmaceutical companies in the world already subscribed to our database. They have licenses to all the genes that we've identified. They have those nonexclusively, so they share with each other the capability to do research and to develop diagnostic and therapeutics off of that information.[131]

Although today Incyte plans to take its drug candidates through proof-of-concept Phase I or IIa clinical trials, it still relies on partnerships to advance through the final stages of clinical development.[132] *Regardless, most biotechnology firms still lic* these firms could not continue to fund further research (nor could they have acquired venture capital funding in the first place).

C. Monopoly vs. Competition Theorists

Randall Scott's position on avoiding duplicative waste is a relevant consideration to the ongoing debate between economists as to whether broad protection for upstream discoveries is helpful in the long run for generating mature downstream products. Here, we again find two new labels that could be placed on the

[132] See `http://www.incyte.com/drugs_incyte_approach.html`.

two different camps of the race for the human genome – monopoly versus competition theorists.

On one side of the line are the monopoly theorists. They argue in favor of broad upstream protection, believing that firms will be incentivized to pursue development since they will not have to partake in "wasteful patent races."[133] Furthermore, monopolies are believed to encourage greater risk-taking in terms of downstream development because of the assured rewa Scott (and his business plan for Incyte) clearly fall into this camp in that he feels that it would be wasteful for other firms to replicate Incyte's work.

Competition theorists, on the other hand, contend that races to develop new technologies are not wasteful (the fact that many of science's greatest discoveries were accidental, e.g. the discovery of penicillin, lends credence to this argument). Instead, they believe that greater competition will yield better products more quickly. These theorists also point out the fact that a monopolist firm has no incentive to improve a product that already dominates the market.[134]

According to professor Rai, broad monopoly protection is advantageous in the biopharmaceutical context due to the high cost of bringing drugs market.[135] This concern is very similar to the concern (articulated earlier in this paper) about awarding patent to in awarding patent protection under the Bayh-Dole Act was not to encourage this initial innovation, but rather to encourage firms to incur the great costs in developing and bringing a product to market. Furthermore, Rai

[133] Arti K. Rai, Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust, 16 Berkeley Tech. L.J. 813, 824 (2001).

[134] *See id.* at 825.

[135] *See id.* at 830.

notes that these broad rights will likely be held by smaller biotechnology firms.[136] *It's unlikely that these firms will fail to vigorously develo*

Although Rai favors broad upstream patents within the biopharmaceutical industry, he is aware of the potential dangers that come with layers upon layers of licensing. Rai cites an article by Eisenberg that documents licensing difficulties between downstream pharma houses and upstream patentees.[137] *Yet, the dangers articulated by Heller and Eisenberg ar*

As we will see next, the PTO and federal courts have attempted to prevent such harmful patents through the doctrines of patentability and infringement.

§4. The Law on Patentability and Infringement and Some Suggestions for Change

A. The Recent History of the Utility Requirement

Before an inventor can receive a patent, he must show that his invention is statutory subject matter,[138] *useful*,[139] *novel*,[140] *nonobvio*

already discussed above in §2. To review, the Federal Circuit in *Amgen* determined that DNA is a chemical

[136] *See id.* at 831.

[137] *See id.* at 832.

[138] 35 U.S.C. § 101 (2000).

[139] *Id.*

[140] 35 U.S.C. §102 (2000).

[141] 35 U.S.C. § 103 (2000).

[142] 35 U.S.C. § 112 (2000).

that, when purified and isolated, is statutory subject matter.

The next requirement, utility, has played a crucial role in the debate over the patentability of genes and gene fragments. Tracing the history of this requirement within the PTO throughout the course of the HGP provides great insight into why private companies like Celera, Incyte, and Human Genome Sciences got "into the game." Furthermore, we'll see that the PTO's latest utility guidelines, when combined with the § 102 novelty requirement, have the potential to preclude certain patents on DNA sequences elucidated during the HGP.

The utility requirement in patent law usually doesn't have much bite. In the first place, inventors (think mechanical inventions here) don't usually invent things that serve no purpose. Secondly, from an economic perspective, even if such a patent were to issue, it wouldn't be worth the paper it was printed on. However, the utility doctrine takes on a more important role in the chemical and biological arts.[143] *In Brenner v. Manson*, the Supreme Court held that chemical compounds are not useful per se.[144] *The Court rejected the plaintiff's argument that this compound (a*

> Such a patent may confer power to block off whole areas of scientific development, without compensating benefit to the public. The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point – where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.[145]

[143] See Donald S. Chisum, Principles of Patent Law 729 (2d ed. 2001).

[144] *Brenner v. Manson*, 383 U.S. 519, 531 (1966).

Going further, the Court held that mere chemical resemblance to a useful compound was insufficient to demonstrate utility.

Although the holding in *Brenner* seems clear enough, over time the Court of Appeals for the Federal Circuit softened the utility requirement. The PTO went along with this softening and stated in its 1995 Utility Guidelines that the applicant need only assert a utility which "would be considered credible by one of ordinary skill in the art."[146] In other words, the burden had now shifted to the PTO. Utility would be presumed unless the PTO could show that a person having ordinary skill in the art (PHOSITA) would consider the proffered utility insufficient. Scientists (following the lead of the earlier Venter/NIH application) began asserting that ESTs (i.e. gene fragments) were useful in that they could serve as probes to find the corresponding full-length genes. When the PTO announced in 1997 that this utility was acceptable, the gold rush referred to many times in the first section of this paper reached its climax. By 1999, Incyte alone had filed "applications covering 1.2 million partial gene fragments."[147] *The PTO was swamped and critics like Heller and Eisenberg were busy penning their polemics.*

Indeed, the PTO's stance on ESTs seemed to fly in the face of *Brenner*, and in 1999 it issued Revised Interim Utility Guidelines (the final version of which were promulgated in January 2001).[148] *Although these guidelines do not have the force and eff*

The new guidelines significantly raise the bar with regard to the utility requirement. Besides being "credible,"

[146] Notices, Department of Commerce, Patent and Trademark Office, Utility Examination Guidelines, 60 Fed. Reg. 36,263 (July 14, 1995).

[147] John Murray, Comment, Owning Genes: Disputes Involving DNA Sequence Patents, 75 Chi.- Kent. L. Rev. 231 (1999).

[148] Notices, Department of Commerce, Patent and Trademark Office, Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

[149] *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) (adopting the PTO's Guidelines for determining compliance with the written description requirement).

the utility proffered must now also be "substantial." In *Brenner*, the Supreme Court defined "substantial utility" as when a "specific benefit exists in currently available form."[150] *The* new guidelines explain that the use of an EST as a probe for finding the full-length DNA does not satisfy this test because it is not a "real world use." Therefore, without more, these sequences are no longer patentable.

B. The Novelty and Utility Requirements Together May Be Problematic

The novelty requirement in patent law is easy to grasp. In the plain words of Donald Chisum, author of perhaps the most widely used treatise on patent law: "It makes no sense to grant someone a patent on an invention that already exists."[151] *The novelty requirement is found in* §102 *of the statute. It states (in relevant part) that*:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others, or patented or described in a printed publication... before the invention thereof by the applicant for patent, or
>
> (b) the invention was patented or described in a printed publication... or in public use... *more than one year prior to the date of the application*... (emphasis added)[152]

§ 102(a) prevents someone from obtaining a patent when someone else had already made the claimed discovery. § 102(b), on the other hand, forces an inventor to file a patent application within one year of making the invention publicly known (notice here that the inventor herself destroys her ability to obtain a patent by waiting too long to file an application). In other words, under 102(b), once an invention has been in the public domain for more than a year, it may not be patented.

[150] *Brenner*, 383 U.S. at 531.

[151] Chisum, *supra*, at 335.

The § 102(b) novelty requirement and the PTO's stricter utility guidelines together form a roadblock for the future ability to patent DNA sequences which were made public via the HGP. As we will see below, the combination of these rules suggests that when scientists eventually do discover the biological function of the full-length genes (to which today's ESTs are simply a part), they will be limited to receiving only improvement patents. Because improvement patents, as opposed to patents claiming the compound itself (known as composition claims), are "not as easily enforced against patent infringers, they have the potential to discourage investment in new drugs and pharmaceuticals."[153]

The problem stems from the fact that scientists do not yet know the function for the vast majority of the DNA sequence that was elucidated during the HGP. As described above, since these sequences do not meet the specific and substantial utility tests under the altered PTO utility guidelines, i.e. they do not posses a "real world use," they may not be patented. Although researchers are working around the clock to discover the biological function of genes associated with disease, § 102(b) stands over them like the Grim Reaper:

> Subsections (a) and (b) of 102 prevent patents when the invention is known by others for more than a year, regardless of who invents the product. As scientists place the human genome in the public domain, it starts the clock for 102, which bars anyone from obtaining a patent a year after is publication. For many sequences, this one-year bar has passed already. The problem arises... because the 1999 Utility Requirements prevent patenting of DNA where the function of the sequence is unknown. If a scientist finds a real world, specific use, such as curing disease, and if this discovery occurs more than one year from the time the information entered the public domain, the scientists may not obtain a patent.[154]

Essentially, if scientists do not discover a real world use for the sequence and file a claim within one year

[153] Mary Breen Smith, Comment, An End to Gene Patents? The Human Genome Project Versus the United States Patent and Trademark Office 73 U. Colo. L. Rev. 747, 770 (2002).

from the time it was first deposited into a public database like GenBank, then they are barred from later receiving a composition type claim.

However, those later scientists would still be able to receive "method of use" claims, often referred to as an "improvement patents." An inventor of a DNA sequence invention would prefer a composition claim to a method of use claim for a number of reasons. First, composition claims give the broadest rights. Once an inventor receives a composition type claim to a DNA sequence, she may exclude all uses of that sequence for the duration of the patent term (even uses that are unknown at the time but will be created later). Method of use claims, on the other hand, grant more limited rights. Although the patentee is able to exclude others from using his new improvement, he might not even be able to practice the invention himself without getting a license from the holder of the composition claim. Second, because composition claims give the patentee the right to exclude anyone else from "making, using, or selling" the DNA sequence, the patentee may sue another manufacturer for literal infringement. In contrast, holders of method claims may find them harder to enforce:

> Infringers of a method claim are those who use the product, not the manufacturer of the product. For example, the manufacturer of the protein does not infringe the method patent. Rather, the end-user, such as the doctor prescribing its use to cure cancer, infringes. Plaintiffs find it much more difficult to sue many end-users than to sue one manufacturer.[155]

Because composition of matter claims are so preferable, there is worry that their unavailability will chill firms' willingness "to invest the huge sums necessary to bring these types of therapeutics to market."[156]

C. Two Possible Responses to Strike a Better Balance

[156] *Id.* at 778.

Thus far in this paper, we have seen the battle between upstream versus downstream patent rights played out in a number of different ways. We've seen how the entrance of the market into academia has influenced the culture of science and served as the starting gun for one of the biggest races in the history of science – the sequencing of the human genome. We've seen how legal commentators like Heller and Eisenberg feel that upstream patents could result in a patent thicket logjam, whereas industrialists like Randall Scott of Incyte believe that early patent protection is absolutely critical for capital formation and efficient development of downstream products. Finally, we've seen how an administrative agency, the PTO, has swayed back and forth in its regulations on the patentability of DNA sequence inventions.

In tracking the history of the PTO's utility requirements for genetic inventions, it's easy to see the battle between those in favor of the Bayh-Dole rationale and those against it. For example, from 1995 to 1999, when private firms were forming and ESTs were being churned out at an unprecedented rate, the PTO embraced the implicit notion that using an EST as a probe was a real world use. Although this seems undoubtedly true (as evidenced by the fact that Celera, Incyte, and Human Genome Sciences were making millions by providing access to these sequences), the PTO continued to wrestle with the question of whether these companies were worthy of receiving the broad set of rights that would accompany composition of matter claims on these DNA sequences. On one side of the coin (the side of the Bayh-Dole proponents), these patents would assure the financing necessary to fully explore the functions of the sequences and to develop useful downstream products. Yet, on the other side (the side of the "tragedy of the anticommons" and competition proponents), allowing these companies to exclusively control the future development of the human genetic code might not be in the best interests of society.

In 1999, the PTO (flooded with applications) reversed its course and, in instituting the new Utility Guidelines,

seemed to embrace many of the concerns of the leaders of the HGP and commentators like Heller and Eisenberg. In other words, since no patents on ESTs alone would issue under the new guidelines, researchers could feel free to experiment without fear of infringement liability. However, in my opinion, the current law still does not provide the optimum incentives since after only a year the utility and novelty requirements together prevent that a composition claim can ever issue on the DNA sequence. Strong patent protection (at some point) is simply too important for the eventual creation of health care products to risk switching all patents in this field to the weaker method of use type.

I believe that a combination of legal maneuvers could address the concerns of both sides of this argument, i.e. could move the two warring tribes of the race for the human genome that much closer to peace. The first step would be to have Congress "adopt a specific exception for DNA sequences from the HGP from the operation of [§] 102 of the Patent Act."[157] *Such an exception would remove the one year limitation and allow the PTO to issue composition type patent claims if* and when inventors discovered specific and substantial utilities for the claimed sequences. In terms of the policy rationales:

> Because DNA released by the HGP would remain generally non-patentable, scientists could work without fear of interfering with any patents, thus encouraging basic research. Yet, granting patents to such DNA when and if a commercial use is discovered would reward the inventor who discovers a new way to treat disease. This result is consistent with the United States patent system policy of demanding innovation from inventors before rewarding them with a government-sponsored monopoly. Because much hard work and innovation is still required to find new disease treatments even with knowledge of the human genome sequence, the proposed exception to [§] 102 would advance the purpose of the United States patent laws.[158]

Keeping the stricter utility standards but adding the exception to § 102 prevents the gold rush mentality while at the same time reinstitutes the Bayh-Dole rationale for patent protection.

[157] Smith, *supra*, at 782-83.

However, some within the scientific community (e.g. James Watson) would say that this is not enough. A second maneuver that might satisfy both "old school" scientists and profit-driven corporations alike would be expansion and codification of the judicially-created experimental use defense to patent infringement. Briefly, besides denying that his conduct falls outside of the scope of the plaintiff's patent or challenging the validity of it, a defendant may also claim a number of affirmative defenses. The experimental use defense, which permits use of a patented invention for "philosophical experiment," is one such affirmative defense.[159] *However, as the Federal Circuit has recently explained in the case of* *Madey v. Duke University*, the experimental use defense is extremely narrow.[160]

In *Madey*, the plaintiff, a former professor of Duke University, owned a number of patents on certain laser technology. After the relationship between Madey and Duke soured, Duke continued to use the patented technology, and Madey sued for infringement. The district court granted Duke's motion for summary judgment, reasoning that, under the experimental use exception, uses "solely for research, academic or experimental purposes" did not infringe.[161] *The Federal Circuit reversed on the grounds that Duke's use of the patented technology was in furtherance of its "legitimate bu* and "increasing the status of the institution and luring lucrative research grants, students, and faculty."[162] *After* *Madey*, the experimental use defense is limited to actions performed "for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry."[163]

[159] *Whittemore v. Cutter*, 29 F. Cas. 1120 (C.C. Mass. 1813).

[160] *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002).

[161] *Id.* at 1355.

[162] *Id.* at 1356, 1361-62.

[163] *Id.* at 1361 (quoting *Embrex, Inc. v. Service Engineering Corp.*, 216 F.3d 1343, 1349 (Fed. Cir. 2000)).

Besides the extremely narrow experimental use defense, the 1984 Hatch-Waxman Act provides a statutory "safe harbor" which allows firms to use a patented pharmaceutical for regulatory compliance in preparation for bringing a generic on the market after the patent term expires.[164] *This safe harbor allows manufacture, use, or sale of a patented invention*

In *Integra Lifesciences I, Ltd. v. Merck KGaA*, the Federal Circuit refused allow Merck to use proteins covered by Integra's patent in preclinical research involving tumor angiogenesis.[166] *The Court explained that the safe harbor did not "reach back*

In dissent, Judge Newman argued that the experimental use exception should have immunized Merck's activity. She explained:

> The purpose of a patent system is not only to provide a financial incentive to create new knowledge and bring it to public benefit through new products; it also serves to add to the body of published scientific/technologic knowledge. The requirement of disclosure of the details of patented inventions facilitates further knowledge and understanding of what was done by the patentee, and may lead to further technologic advance. The right to conduct research to achieve such knowledge need not, and should not, await expiration of the patent.[169]

In her opinion, to hold Merck and its academic collaborator liable for preclinical studies using the patented

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[164] 35 U.S.C. § 271(e)(1) (2000).

[165] *Id.*

[166] *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003).

[167] *Id.* at 865.

[168] *Id.* at 866.

technology would stifle early stage research and inhibit the discovery of new uses (which in turn could lead to improvement patents). Judge Newman recognized that the common law exception can't be unlimited as the original incentive to innovate must remain primary.[170] Yet, referring to the "fair use" doctrine in copyright, she believes that the facts of a particul allow "distinction between research and development."[171]

I believe that a codified experimental use defense for preclinical research is something that Congress should seriously examine. Although, as noted by Judge Newman, such a defense would involve a highly fact-specific inquiry, I do not believe that this determination is any harder than the myriad of others that federal courts must make during patent infringement lawsuits. The adoption of such a defense would alleviate many of the concerns of patent thickets and provide upstream researchers with peace of mind (think James Watson smiling). Furthermore, the defense would likely reduce the incentive to engage in defensive patenting – a tactic that is inefficient since its sole purpose is to prevent others from exploring uncharted waters. Finally, since the defense would be limited to preclinical research, patents would still protect all inventions with commercial value, and therefore would continue to bolster capital formation within the biotechnology industry.

In closing, I think these two possible changes in the law could help the two different "camps" to see eye to eye. Indeed, the goal of both groups is the same – they both want to see increased discovery in the realm of human genetics and creation of life-saving health care products. They just seem to be focused on different ends of the development spectrum. The Bayh-Dole industrialists (if you will) are concerned with obtaining the patents necessary to protect their significant development costs. On the other hand, the

[170] See *Integra*, 331 F.3d at 876.

[171] *Id.*

"put everything into the public domain" members of the scientific community are focused on maintaining a healthy system of basic science research. These two changes in the patent law would move us closer to a world where "everybody wins." They would lead to better products while maintaining open research. The human genome deserves such a result.