PTO Revisions of the Examination Guidelines during the Clinton Administration: Exposing the Biotechnological Rips in the Legal Fabric

Aline Cresswell

2008 Rhodes Institute for Regional Studies

On March 14th, 2000, a joint proclamation from Tony Blair and Bill Clinton, with no power of law, struck world stock markets hard and swift. In response to years of turmoil surrounding patent difficulties associated with the Human Genome Project (HGP), the two leaders suggested, "raw fundamental data…including the human DNA sequence and its variations should be made freely available to scientists everywhere."[1] Though the statement also mentioned a need to recognize intellectual property protection of gene-products in order to stimulate biotechnological development, the public wrongly assumed speculative patent applications would be nullified. On March 15th, 2000, the stock market crashed: companies like Incyte Pharmaceuticals, holding some 353 gene patents at the time, lost some 20% of their stock value.[2] Market volatility was the consequence of years of debate among attorneys, scientists, CEO's , scholars, and more about what could be patented and under what circumstances. Under the Clinton Administration, the HGP greatly impacted the evaluations of patent law. The US Patent and Trademark Office (PTO) asked for public commentary and reviewed numerous court precedents aiming to establish viable examinations that would satisfy both researchers

[1] Bill Clinton and Tony Blair. "Joint Statement to Ensure that Discoveries from the Human Genome are used to Advance Human Health." March 14, 2000.
[2] Alex Berenson and Nicholas Wade. "A Call of Sharing of Research Causes Gene Stocks to Plunge." *The New York Times.* March 15, 2000.

and corporations. The PTO's struggle to establish clear definitions in lieu of new biotechnologies was evidenced in four separate revisions: *Revised Utility Guidelines (1995), Revised Interim Utility Examination Guidelines (1999), Revised Utility Examination Guidelines (2000), and Final Revised Utility Examination Guidelines (2001).* For the first time since its inception, the PTO came under scrutiny at the microscopic level, implored to change its well-established guidelines in order to reflect new and highly specific technology. Though the PTO successfully established legally viable definitions for biotechnological patents, the examinations and laws did not adequately represent the science it was aiming to protect.

Talk about the potential to decipher the human genetic code started in the mid 1980's. In March of 1986, scientists met in Los Alamos, New Mexico to conjecture about the feasibility of sequencing the human genome, just after the first automated sequencing began. The Department of Energy, DOE, agreed to fund the initiative, but called for improvements in sequencing and mapping technologies.[3] The DOE Human Genome Program officially commenced in 1987 to further develop technologies for sequencing and mapping the human genome. In 1988, the National Institute of Health (NIH) teamed up with DOE to progress this initiative. However, NIH adopted goals toward funding research and developing knowledge of disease genes.[4] Contrastingly, the DOE sought to improve technology and construct ordered chromosome maps. In tandem, the offices pushed the HGP forward. By February of 1990, the committees developed a five year

---

[3] U.S. Department of Energy: Office of Health and Environmental Research. "Sequencing the Human Genome." (Summary Report of the Santa Fe Workshop, Los Alamos National Laboratory, Los Alamos, NM, March 3-4, 1986.)

[4] HGMIS Staff, "U.S. Human Genome Effort: DOE/NIH Interactions". *Human Genome Quarterly*, Summer 1989, 1(2).

plan for the sequencing project and sent it to Capitol Hill. This plan proposed mapping and sequencing the human genome and other animal genomes, acquiring data, training researchers, developing and transferring technology, and addressing legal and social issues.[5] From 1991-1995, 1994-1998, and 1998-2003, the DOE/NIH partnership proposed a series of five-year plans that successfully completed the HGP. The history of funding the massive project verifies the difficulties of the PTO in properly addressing all parties involved.

The HGP officially received funding from Congressional appropriations in 1990, just before President Clinton's term. That year, the HGP received $59,527,000 to fund research.[6] In 1992, research funding nearly doubled reaching $104,756,000. Presidential support was paralleled by ever increasing appropriations for the HGP.

Fiscal Year[7]	Funding (in Thousands of Dollars)
1993	106,095
1994	127,017
1995	153,789
1996	169,286
1997	188,909
1998	218,340
1999	279,030
2000	335,129
2001	381,971

By 1998, Al Gore visited Genentech, one of the largest research sites devoted solely to biotechnology, to announce the "new commitment to research and innovation by

[5]"Understanding Our Genetic Inheritance: The United States Human Genome Project: The First Five Years: Fiscal Years 1991-1995." Report to Capitol Hill, February 1990, http://www.genome.gov/10001477.

[6] National Human Genome Research Institute. "Funding History." February 4, 2008. http://www.genome.gov/Pages/About/Budget/FundingHistory90-09.pdf

[7] National Human Genome Research Institute. "Funding History." February 4, 2008. http://www.genome.gov/Pages/About/Budget/FundingHistory90-09.pdf

releasing the details of the new $31 billion 21st Century Research Fund for America".[8] Both Gore and Clinton stamped the presidential seal of approval on the growth of biotechnology, imploring Congress to do the same. The request was an unprecedented increase in funding by 32% in the research and development sector. In fact, when the HGP was completed, Clinton said it was "the most important, most wondrous map ever produced by humankind."[9]

Governmental involvement was beneficial to a fault. Though the Clinton Administration actively pushed for the HGP discoveries to be universally accessible, he asserted "the National Science and Technology Council in securing private sector involvement in its activities."[10] Clinton's private sector partnership suggested desires to expand the scope not only of biotechnology, but of commercial expansion of the GNP through privatization.[11] Clinton's administration was politically charged to boost the HGP, erstwhile creating the conundrum of keeping the new biotechnology industry afloat. Private sectors required capital, achieved best through patent speculation. The public-private sector cooperation promised to put the administration and the PTO between a rock and a hard place in respecting the wishes of academics for unfettered use of the profits of the HGP while providing companies with the commercial sanctions they needed to survive.

---

[8] Al Gore. Genentech Research Announcement: Genentech, South San Francisco: January 29, 1998.

[9] Peter A. Lawler. *American Political Rhetoric: A Reader.* (Roman and Littlefield, 2005). Page 233. http://books.google.com/books?id=YzUhr8CnYekC&pg=PR12&lpg=PR12&dq=American+Political+Rhetoric:+A+Reader&source=web&ots=qq_Geg-CTb&sig=ItNbZK-s2CuSWh7hPekNkWvUb7E&hl=en&sa=X&oi=book_result&resnum=1&ct=result#PPA2,M1 (Accessed July 8, 2008)

[10] Bill Clinton. Executive Order 12882: "President's Committee of Advisors on Science and Technology". November 23, 1993.

[11] National Science and Technology Council Meeting. "1994 Planned Initiatives." Roosevelt Room of the White House. June 29, 1994 (11:30-12:30).

The HGP provided the raw, fundamental sequence of human genomic DNA, but the mechanisms to understand the code provided inherent difficulties for both scientists and patent examiners. The information gleaned from the sequence is endless. Genomic data may be used to discover new proteins, genetically linked diseases, evolutionary traits, control mechanisms, and more. The HGP has already helped to characterize the genetic characteristics of Parkinson's disease, sickle cell anemia, and others. However, proper characterization of the nucleic sequences is hardly ever clear. DNA functions to encode proteins through codons. Codons, a set of three nucleotides, translate into amino acids, which then become proteins. Codons and the mechanisms by which they function introduce difficulty for patent examiners for two reasons. First, codons are redundant: e.g., the combination of CAA or CAG both translate into Histidine. Second, codons are read in frames to produce a specified protein, but these same codons may be read in alternate frameshifts to produce different proteins; one gene has the potential to encode many proteins depending on the mechanism it is read. Also, DNA and RNA are edited before final protein production. By a series of excisions of exons (non-coding segments of genes) and splicing of introns (protein coding segments), proteins are created. Protein production is determined by a series of spliceosomes which pick and choose certain segments to cut out of the genetic language. Depending on the choice, a certain and often very different protein results. These are just some examples of inherent mechanisms which control protein production. These mechanisms challenge patent law the variation inherent in the gene is not always accounted for in the patent description of utility.

One other glaring difficulty in patenting genetic sequences is the use of homology as a definer of utility. Most families of proteins contain homologous regions. These are

evolutionarily conserved regions which are vital to some functioning of the protein. For example, BCL-2 class proteins, known for their role in programmed cell death, contain regions of homology characterized as BH1-BH4. However, some BCL-2 class proteins, despite characterized homology, function very differently to either inhibit or stimulate cell death. Essentially, a homology functions to provide one with an educated guess in protein functioning, rather than a definite characterization. This proposition to claim utility to a patent has been hotly contested.

Patent law was not well equipped to deal with the new discoveries of the biotechnological sector. US patent law has been inherently directed toward the release of information to the public. Patent law, from its inception, has aimed to "promote the progress of Science and useful Arts, by securing for limited time to Authors and Inventors the exclusive right to their Writings and Discoveries".[12] That granted right allows the owner to profit from governmental protection for a standard period of twenty years. One of the requirements of US Patent Law is full disclosure, "enabling another trained in the art to replicate it", (that item to be patented). [13] There are some difficulties in applying this framework to biological inventions for they are difficult to fully characterize and often require years of further research after discovery to do so. The expediency of patent protection may be sacrificed in the name of specificity, and vice versa. Typically, the science is sacrificed.

Many attempt to make the distinction between discovery and invention and its applicability to patent law. However, the PTO asserts both are covered under the law as long as they are compositions of matter, made by man, and not naturally occurring.

[12] US Const. art. I, 8, cl. 8
[13] 35 USC 112 (1988)

Naturally occurring products include the human genome in so much as it exists within its human form and system. Once a gene from the genome is isolated and purified, by the PTO's definition, it is a man-made composition and therefore patentable. There are many instances of applying such logic to biological materials including proteins, chemicals, genes, partial gene segments, expressed sequence tags, and single nucleotide polymorphisms. The patent office must ensure not only the protection of the biological material, but also the process.

Patents of process protect biotechnological techniques. These patents encompass the recipes for isolating proteins, purifying DNA, inoculating *E. coli*, etc.[14] The beauty and curse of these patents is the researcher's ability to utilize other non-patented methods to achieve the same ends. Thus, patented processes can be totally avoided in commercial ventures. Oppositely, it benefits academic communities who are not working for profit, known also as the research exception. Those researchers may freely use the published patent information to conduct experiments more reliably and efficiently.

Patents provide benefits to the academic community because it provides the possibility to work with isolated proteins and chemicals of known and disclosed properties and structures. However, for the private sector, the 20 year period of ownership of such patents may cause companies to focus on other proteins that have not yet been patented. This may slow progress. For instance, if a patent is issued for isolated p53, a known tumor suppressor, other companies may stop work on cancer discoveries associated with p53 because of a requirement to form licensing agreements with the patent holder. These licensing agreements often require exorbitant payments, only adding

[14] *Policy Finder*: H-140.944 "Patenting the Human Genome: CEJA Rep. 2, I-97" © 1995-1999 American Medical Association

to the already astronomical cost of research. [15],[16] Thus, just one company or person may work with isolated p53 until the patent expires, slowing the field of progress in avoidance of patent penalties and detracting from the initial goal of patents.

On July 15, 1993, the Senate passed the Biotechnology Patent Protection Act.[17] This act namely defined the term 'biotechnological process' as patentable as the following:

> any method of making or using living organisms, or parts thereof, for the purpose of making or modifying products. Such term includes recombinant DNA, recombinant RNA, cell fusion including hybridoma techniques, and other processes involving site specific manipulation of genetic material. [18]

Under the legislation, said 'biotechnological process' could be claimed as a non-obvious fulfillment of the patent application. The specificity of using living organisms *for the purpose of making or modifying products* was the key term, suggesting living organisms in and of themselves were not patentable. This was consistent with the non-patentable claims to objects as they exist in nature. However, it seemed unclear as to whether or not a patent was legally protected if it claimed the living organism itself was somehow altered and thus itself becomes the "made or modified product." Perhaps the process was patentable, but not the product.

In consequence, in dealing with international patent infringement, the same act defined what was known as a 'biotechnological material.':

---

[15] Report of the Council on Ethical and Judicial Affairs of the American Medical Association. December 1997.
[16] The American College of Medical Genetics "Position Statement on Gene Patents and Accessibility of Gene Testing" August 2, 1999. www.gaseb.org/genetics/acmg/pol-34.htm

[17] S. 298. "To amend title 35, United States Code, with respect to patents on certain processes. (Engrossed as Agreed to or Passed by Senate). 103d Congress: 1st Session.
[18] S. 298. "To amend title 35, United States Code, with respect to patents on certain processes. (Engrossed as Agreed to or Passed by Senate). 103d Congress: 1st Session.

> any material (including a host cell, DNA sequence, or vector) that is used in a biotechnological process as defined…[19]

Not only was the process protected, but also the materials involved. This stipulation arose because both process and product patents were needed to protect inventors from fraudulent importations from abroad. For example, if the process but not the product was patented, one needed only to export the process to another country and import the resulting product.

The implications of this act were more far reaching than intended. If one gained rights to the 'non-obvious biotechnological process' and the 'biotechnological material', then one may obtain rights to something that is necessary to become a commercial utility, but may not be sufficient for this purpose. Simply put, a protein may be isolated in a non-obvious and therefore patentable way, and the biological material too may be patented, but it is still simply an isolated protein. Some proteins could be administered as therapeutic chemicals, but others, like actin, may not serve any medicinal or practical purpose. In consequence, pharmaceutical or genetic therapies may be slowed as private sector companies must establish licensing rights before accessing rights to these common use proteins, which themselves are not therapeutic, but can be used to make other products. Thus the scope of the act may have dangerously broadened the patent field, and the PTO had no choice but to accept the new legislation in order to protect claimants.

Patent law should have been about progress, not inhibition. However, the promise of patent gold posed venture capitalists against non-profit laboratories and other venture capitalists. Moreover, the patent process was not always transparent. Every item applying for patent protection needed to meet certain requirements as described by the PTO. The

[19] S. 298. "To amend title 35, United States Code, with respect to patents on certain processes. (Engrossed as Agreed to or Passed by Senate). 103d Congress: 1st Session.

three pronged requirements of an acceptable patent are novelty, non-obviousness, and utility. Novelty describes a product that has not been previously described in publication in this country or any other, nor has it been previously patented. Non-obviousness requires the item is not self-evident to anyone working in the field at the time. Utility is some use that is both specific and substantial. During the 1990's the most challenging prong to define was utility. To address this, the PTO called for comments and suggestions from the public on its Revised Utility Examination Guidelines.[20] After evaluating suggestions, in 1999, the PTO revised the guidelines for examining utility: defining a specific and substantial utility as something "useful for any particular practical purpose," that was made credible by an assertion of someone in the same field who agreed the invention is both specific and substantial in utility.[21] Given the acute lack of characterization of biological materials, the PTO's inception of this new guideline might have dropped some case load, but the broad definition provided no real solutions, especially for the scientific community. Moreover, how these terms are defined has been a story of contention for the duration of the 1990's: a drama performed through the constant revisions of patent examination and oppressively specific court cases.

Many cases were brought to the Federal Circuit and the Supreme Court before, during, and after the PTO examination revisions. The landmark case of *Diamond v. Chakrabarty*, established "anything under the sun that is made by man" may be established as patentable as long as it satisfied the other written criteria.[22] In *In re Soni,* 54 F. 3d 746, 34 USPQ2d (Fed. Circuit 1995), an improperly characterized chemical yielded unexpected results. The Circuit suggested the need for the "well-settled

[20] Federal Register. "December 21, 1999 Notices." Volume 64. No. 244.
[21] Federal Register. "December 21, 1999 Notices." Volume 64. No. 244.
[22] *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

requirement of objective proof" of utility, which was not stated at the time of patent filing. However, In *In re Brana*, 51 F. 3d 1560, 34 USPQ2d 1436 (Fed. Circ. 1995), the Federal Circuit "reversed the Board and held that there is a very low threshold for establishing utility." Where was the top and bottom to the utility definition? The courts asserted, as they had in *Brenner v. Manson,* any specific and substantial reasoning was acceptable for patent.[23] It seemed the basis of utility was in the known properties of the biological compound proven by testing and credibility, not unknown factors, but to what extent? By 2000, the PTO emphasized the need for only one stated utility, not a scope. Science was being set up for sacrifice at the hands of legally viable patent guidelines and practices.

Defining utility was not only a question of specificity, but also credibility. In *In re Ziegler*, Ziegler, a German, attempted to file for foreign patent laws. However, the patent was denied on the basis that Ziegler had not fulfilled the utility requirement. Ziegler asserted polypropylene could be "pressed into flexible film" and was therefore "plastic-like." [24] In reference to biological patents, the suggestion of the courts may be simply that it is not enough to have similar characteristics to other defined and patented items, especially considering polypropylenes are so varied in composition they may maintain many variable functions. For example, a patent for a gene would probably not be granted for a utility described as 'kinase-like.' When the determination of utility is based on homologies, rather than individual characteristics, one must assert the group in question possesses nearly 100% fidelity to the utility in question. Variation in the group introduces doubt as to the viability of the utility claim based on homology. In accepting proposed

[23] *Brenner v. Manson.* 383 US 519 (1966)
[24] *In re Ziegler,* 992 F. 2d 1197, 26 USPQ2d 1600 (Fed Cir. 1993).

homologies as the *only* means of establishing utility one not only accepts fuzzy science but a legal can of worms.

Many difficulties including controversial patent claims relayed the need to revise patent examination guidelines. Craig Venter, former director of the NIH, applied for many patents on expressed sequence tags (ESTs) and cDNA during and after his term. However, as a member of a government organization, there was public outcry against his actions.[25] Later, Venter broke off from the government, formed Celera Genomics, and began competition with the HGP in a race to complete sequencing. His threats to patent the whole human genome sequence, had he completed the task before the government, ushered in the public perception of a notorious Darth Venter.[26] Though he withdrew the applications while director, he nonetheless raised concern about the validity of patenting ESTs. During 1994, the PTO called for comments from the public on this very issue. By 1995, just before publishing a draft of the final Utility Examination Guidelines, they clarified the patentability of ESTs based on this commentary. Primarily, most of the scientific community considered the use of ESTs to be a scientific tool, not a product of itself when the gene it targets was unknown. [27] In response, the PTO cited Brenner V. Manson, stipulating the necessity of "disclosure of 'specific utility,' and of 'substantial utility'…where specific benefit exists in currently available form." [28] A patentable product needed a utility that was well defined and available in the present, not the future.

---

[25] Paul Riley. "Comments: Patenting Dr. Venter's Genetic Findings: Is the national institutes of health creating hurdles or clearing the path for biotechnology's voyage into the twenty-first century?" *J. Con. H. L. & Policy* 10:309 (1994).

[26] David Papineau. "Speed Reading the Book of Life." February 15, 2005. http://query.nytimes.com/gst/fullpage.html?res=9405E7D7133BF936A25751C0A9629C8B63&sec=&spon=&pagewanted=all (Accessed July 22, 2008).

[27] Federal Register. "December 21, 1999." Vol. 64, No. 244.

[28] 383 US 519, 534-35, 148 USPQ 689, 695 (1966)

Thus, the EST, having no directed or targeted known gene and no utility as available in the present, would not have been patentable. However, the issue was not solved, for the utility requirement was notoriously loose. Experiencing firsthand the difficulties of slowed research and exorbitant licensing fees, the American Medical Association lamented to the PTO:

> The utility requirement has never posed a significant barrier to obtaining a patent; any proposed use generally is considered sufficient for purposes of the application,

noting the PTO was more likely to issue questioned utility patents than reject them.[29] The patent itself found favoritism, not the science nor the medical sector. Again, politically and economically, the PTO granted as many marginally viable patents as possible because it provided twenty years of revenue from the invention into the GNP. It also boosted the image of the US's fast growing R&D sector; trumping the international competition.

In response, the PTO cited *In re Deuel*, to quell some conundrums. In essence, claim on the isolated gene of heparin binding growth factor (HBGF), was denied by the PTO based on the determination the claim in question could be obviously known by prior art. When Deuel appealed the rejection, he challenged what was considered non-obvious in lieu of prior art. The courts reversed the PTO's rejection granting the *redundancy* of the genetic sequences made the claim non-obvious stating

> The fact that one can conceive a general process in advance for preparing an undefined compound does not mean that a claimed specific compound was precisely envisioned and therefore obvious.[30]

[29] Report of the Council on Ethical and Judicial Affairs of the American Medical Association. "Patenting the Human Genome." December 1997. http://www.ama-assn.org/ama1/pub/upload/mm/369/ceja_2i97.pdf

[30] *In re Deuel*, 51 f. 3d 1552, 34 USPQ2d 1210 (Fed. Cir. 1995).

The reasoning was sound. A proposed EST would be necessary, but not sufficient to targeting the desired protein. The court seemed to imply a proposed process does not necessarily achieve a proposed outcome and was therefore non-obvious. The danger in this ruling, however, was the verification that ESTs could potentially be patented. Thus Darth Venter, in all of his evil wisdom, may have easily gained the rights to hundreds of ESTs, reaping the profits of licensing agreements. The decision, though both legally and scientifically viable, does not address that certainty may not always be gleaned from ESTs. It seems ironic the *lack of characterization* aids in the establishment of non-obvious. This plays at odds with determining utility in some scientifically sound form for if a sequence is inherently non-obvious due to redundancy, then there are frequently multiple utilities at work, not just the one required in order to file patent.

These were not the only court cases of the 1990's. The smattering of cases covered everything from the viability of *in vitro* testing to the translatability of data from animals to humans and everything in between. The drudgery of specificity in case-by-case examination forced the PTO to adjust its examination guidelines in order to better equip examiners with legally viable analysis. Not only the courts, but also the public, interest groups, and the bureaucracy played leading roles in influencing the PTO during the revisionary process.

The Human Genome Project was largely a bipartisan commitment to furthering the promises biotechnology promised to fulfill. However, the legal concerns entangled with burgeoning research and development polarized interest groups. Many in academic and bureaucratic fields, such as the Human Genome Organisation (HUGO), and international fellowship aimed at completing sequencing, pushed to ensure the HGP and

the genetic sequence was counted a discovery of nature, unpatentable, and unencumbered for public use. The Bermuda Rules helped to establish etiquette on the immediate publishing of sequence discoveries by demanding newly discovered sequencing information be published within 24 hours of discovery.[31] Established by HUGO and participating publicly funded laboratories, these rules not only ensured the goal of unfettered access to genetic information would be achieved but also helped combat speculative patent competition in the race to sequence the genome. On the opposite side of the spectrum, biotechnological companies hoped they could patent 'anything under the sun made by man[32] be it nucleic acids, chemicals, proteins, or genes. The benefit of patent protection for these companies was of course, endless rights to innumerable products with the potential to be commercial developed to yield millions of dollars. Since biotechnological research had such an incredible capital overhead, only speculation on granted patent and tax-payer dollars could potentially fund the project.

The government remained in the vague middle of two opposing sides. The PTO, however, working as a separate bureaucratic entity, had the task of determining how to politically please all sides. Interest groups and lobbyists played a large role in persuading the PTO to change regulations and policies. But the process of adapting scientific practice into universal legal patent would prove to be difficult, if not impossible.

The 1996 Bermuda Rules established a self-enforced international policy to publish sequence information under the direction of HUGO. By 2000, the National Human Genome Research Institute implemented new policy stipulating "those who generate the primary data freely should have both the right and responsibility to publish

[31] HUGO. "Summary of Principles Agreed at the First International Strategy Meeting on Human Genome Sequencing." Bermuda. February 25-28, 1996.
[32] *Diamond v. Chakrabarty.* 447 U.S. 303 (1980).

the work in a peer-reviewed journal".[33] Researchers were often stripped of the bragging rights to their discoveries because of limitations placed on non-profit organizations and their ability to claim rights to patent (especially when using tax-payer dollars). Though these proclamations had no legitimacy as law, the academic community exhibited the desire to claim bragging rights, if nothing else. Does the application of a patent by a company, though discovered by an academic infringe on hypothetical bragging rights? Do published scientific discoveries translate into modified product patents? In essence, though scientists devoted the hours and resources to scientific progress, their commercial well-being as well as their 'pride in discovering' was null and void. Academics desired unfettered access to information and recognition. Both could have been potentially ignored.

The PTO also received direct commentary from professors and researchers. In voicing concern about the patentability of genes, Gemunu Gunaratne of the University of Houston wrote,

> To limit patentability and therefore utility requirements to applications brings maximum benefit to both academic researchers and industry in terms of insuring unfettered access to the cornerstone knowledge necessary to advance biomedical research and therapeutics.[34]

Similar outcries were made by Sailen Barik, University of S. Alabama, who claimed patenting was like "the Lynching of the Human Genome;" Jennifer Dziewala, Texas A&M University, who said "the core of human genetic knowledge cannot be considered for ownership;" and Dr. Steven A. Scherer, Baylor College of Medicine, who relayed

> I believe that at least human genomic sequence goes to the core of what it means to

[33] NHGRI Policy for Release and Database Deposition of Sequence Data. December 21, 2000. http://www.genome.gov/page.cfm?pageID=10000910
[34] Gemunu Gunaratne. Memorandum to PTO. March 22, 2000. http://www.uspto.gov/web/offices/com/sol/comments/utilguide/ghg.pdf

> be human and no individual or corporation should control or have ownership of something so basic.[35]

Scherer recruited individuals from California, Texas, and North Carolina to write some 30% of the total commentaries. Moreover, large groups like the American College of Medical Genetics, the American Physiological Society, the Association of American Medical Colleges, the National Academy of Sciences and others all issued statements of concern in patenting genetic sequences to the NIH. Clearly academics stood for unencumbered access to raw, genetic sequence, going so far as pursuing the request to make genes non-patentable. Once commercialism and capitalism is taken out of the patent question, it becomes clear the quickest and most direct course to proper characterization of the genome and the development of drugs to cure disease is through collaboration and information sharing, not secrecy and patent protection.

Perhaps the largest and most influential group of private sector lobbyists was the Biotechnology Industry Organization (BIO). Formed of nearly 900 separate biotechnological companies and researchers, they pushed for a wide spectrum of patentable biological materials. Their doctrine was "an unquestionable dependence on effective patent protection for [their] innovations."[36] Furthermore, BIO worked to push for genetic and partial genetic fragments to be fully patentable. In a statement to Q. Todd Dickinson, Charles Ludlam, a legislative council for the US Senate, amicus curiae of *Eli Lilly v. Barr Companies,* and active member of BIO detailed:

> There is no difference of opinion among the BIO membership regarding the desirability of making available patent protection for specific chemical compounds that are adequately characterized by their chemical structure or physical characteristics. This includes compounds identified by an amino acid or nucleotide sequence, (*e.g.*,

[35] Sailen Barik, Jennifer Dzielawa and Steven Scherer. "Public Comments on the United States Patent and Trademark Office "Revised Interim Utility Examination Guidelines" 64 FR 71440, Dec. 21, 1999, corrected 65 FR 3425, Jan. 21, 2000." March 22, 2000. http://www.uspto.gov/web/offices/com/sol/comments/utilguide/index.html

[36] Charles E. Ludlam. "Comment 55. Letter from BIO." March 22, 2000.

> polypeptides, proteins, nucleic acids) including compounds containing nucleotide sequences that correspond to complete human or animal genes, or to portions of such genes.[37],[38]

Interesting enough a BIO member not only influenced the PTO, but also the Senate, the possible implications of granting such a request may have equated to granting patents to vaguely classified compounds or genes that may or not have appeared multiple times within the genome encoding variable proteins. Moreover, the proposal suggests once these genes were identified, they may be made unavailable to competitors even though their sequences are relatively easy to find, their proteins may be easily isolated, and new and different products could result from their characterization. By isolating genes to one patent owner, the possible benefits for treating or manipulating that gene in a commercial way become dependent on a single mind or corporation, rather than a multitude. The very essence of science and genetics is in an uncountable amount of variables and outcomes; this request ignored the essence of biological material utility as multiple. However, the ability to patent what was desired would ensure not only protection rights on future products, but also invite speculation and investment into a new market with almost guaranteed success. More so, if investments increased, then scientific progress may also potentially have increased thus speeding up the processes to make product. Still, innovation might be less than if genes were accepted as public domain. BIO still pushed for patent favoritism in the name of capitalism, rather than science.

Some other players in the commentary sector were concerned citizens. Though ill-equipped to properly address concerns to the PTO on complicated issues of biotechnological and patent specificity, some citizens such as Gail Bundy, Toby

[37]Comment 55. Letter from BIO, Ludlam, Charles E. March 22, 2000.
[38] Biotechnology Law Report. "Eli Lilly & Co. v. Barr Laboratories, Inc. et all." October 1, 2001, 20(5): 769-798. doi:10.1089/073003101753212087.

Cockcroft typify how far reaching the patent issue spread. Cockcroft in his letter, displays the kind of fear that the public felt in granting the ability to patent genes by relating

> What if Issak Newton had patented the Laws of gravity. Would NASA have to pay a royalty every time it made a calculation in order to send the shuttle into space, or would a child have to pay every time he threw a ball. Obviously this is obsurd.[39]

Be it due to their lack of knowledge on the issue, the PTO hardly addressed these issues. However, these letters displayed the helplessness of the common public in addressing such issues of concern, despite the fact that the revisions might affect whether or not the public received improved health care and how much it would cost.

Despite overwhelming concerns the PTO was allowing overly broad scope claims to genes, gene fragments, and nucleotides, the PTO did little to change the guidelines. The PTO made just five major changes to the guidelines in 2001. The addition of 'credible' to the litmus test for utility was a satisfactory addition to add some stringency to the guidelines. Groups like Incyte Genomics, the International Center for Technology Assessment, the BioIndustry Association (BIA), and many others applauded the PTO for this move. However, the follow-up reaction encompassed fears of too little stringency and too much. For example, BIA expressed some concerns the level of proof required to establish utility would be as stringent as those levels demanded by regulatory authorities (like the FDA).[40] Oppositely, Genentech expressed concerns "a claim cast in an open

[39] Toby Cockcroft. "Comment 3 to PTO." March 22, 2000. http://www.uspto.gov/web/offices/com/sol/comments/utilguide/tcockcroft.pdf

[40] Andrew Sheard. BioIndustry Association. Comment 46 "Public Comments on the United States Patent and Trademark Office "Revised Interim Utility Examination Guidelines" 64 FR 71440, Dec. 21, 1999, corrected 65 FR 3425, Jan. 21, 2000. http://www.uspto.gov/web/offices/com/sol/comments/utilguide/bia.pdf

format may literally encompass billions of potential sequences."[41] The polarizing guideline was the emphasis put on the need for only *one* well-established utility in order to satisfy the requirement. Though this may be legally viable, from a scientific perspective, this is near ludicrous. Biological compounds often serve multiple functions in multiple systems. It is nearly impossible to characterize *every* function of a given protein or gene. When allowing the patenting of genes based on a single utility, the PTO did not consider a given gene could inherently code for two different characteristics. For example, *Drosophilia melanogaster* contain a site for regulated alternative splicing of the 'double sex' gene. Depending upon the way an exon is spliced out of the same gene, protein expression may express male or female. Moreover, these isoforms may have "similar functions, distinct functions, or even antagonistic functions."[42] This is just one example of many ways one gene may function in entirely different ways. The concerns of about 85% of written comments to the PTO express these issues, yet the PTO reasserted one need only have *one specific, substantial, and credible utility.* Though written commentary overwhelmingly expressed concern about the loose rigidity of utility, academics and groups were acknowledged, but guidelines changed only slightly, if at all.

Of those who submitted public commentary in 2000, the two most influential bodies were the NIH and Incyte Genomics. NIH and Incyte stand at hypothetical ends of the biotechnology patent spectrum. Incyte sought commercial gain through the granting of patents while NIH's first priority was to further public health through innovation in genomic science. However, NIH also adopted a position to protect private companies in

[41] Sean A Johnston. Genentech Inc. "Public Comments on the United States Patent and Trademark Office "Revised Interim Utility Examination Guidelines" 64 FR 71440, Dec. 21, 1999, corrected 65 FR 3425, Jan. 21, 2000. http://www.uspto.gov/web/offices/com/sol/comments/utilguide/genentech.pdf
[42] Watson, et al. *Molecular Biology of the Gene*. New York: Pearson Education, 2003. 397.

realizing industrial growth was a function of investment. The NIH moved to enforce utility guidelines which would satisfy the academic and research community more than the market. NIH requested a well-established utility not only be described by the three-pronged litmus test, but also detailed as "readily apparent."[43] This request was adopted by the PTO. Furthermore, Jack Spiegel, legal and biological council for the NIH, raised the issue in the *prima facie* requirement that it required the examiner to reject a claim of utility rather than the claimant to prove a utility. The PTO struck the *prima facie* requirements in the *Revised Guidelines* and asserted it was up to the claimant to prove utility. One issue the NIH was not influential on was that of utility based upon homology. Spiegel made a convincing argument

> Granting patents based upon the highest known homology at the time of filing undermines confidence in the patent system by giving an already unpredictable art the appearance of a patent guessing game.[44]

From a scientific perspective, this statement is absolutely true. Homologous regions serve merely as predictors, but deceptive ones at that. Some homologous regions are merely evolutionary vestiges and serve no function, something which would only be discovered after further experimentation was performed. From a legal perspective, however, it seemed utility on homology was upheld by the PTO, asserting it was a viable factor in predicting utility in many cases. For example, in claiming broad scope patent on certain materials, there is sufficient predictability of utility, like in G-protein coupled receptors which all act to facilitate some level of intercellular signaling. Though the utility is broad,

---

[43] Jack Spiegel. "Comment 44, Letter to Q. Todd Dickinson." March 22, 2000.Located in the Clinton Presidential Archives: Domestic Policy Council - Chris Jennings, Senior Health Policy Adviser Files.

[44] Jack Spiegel. "Comment 44, Letter to Q. Todd Dickinson." March 22, 2000.Located in the Clinton Presidential Archives: Domestic Policy Council - Chris Jennings, Senior Health Policy Adviser Files.

it generally functions to encompass the activity of all of said proteins. Though the targets of these proteins are highly varied, the scope of utility is universal. However, some broad scope claims do not serve to properly characterize all sub-sets in the group. For example, in *In re Ziegler*, one may recall a rejection of a polypropylene based on a utility claim as 'plastic-like.' This logic somewhat upholds the viability of utilizing homology as a utility definer in biotechnological materials as it is necessary to define some utility using such methodology, but it is not sufficient. The unpredictability inherent in the sequence or material demands further experimentation beyond predicted homology and therefore such systems may indeed be viable. This is of course by legal precedent, and does not correctly follow the science. Though all G-protein coupled receptors may function in signal transduction, that stated utility (from a science perspective) is obvious and serves no function in producing knowledge, processes, or material which may or may not aid in medical or genomic research. The scope is just too broad, but interestingly, not so in the PTO's perspective.

Incyte Genomics introduced an entirely different perspective. Their requests stood out in the lump of responses as overwhelmingly in favor of less stringent requirements on utility. Moreover, their propositions seem to echo in meaning, not exact words, the directives of the PTO for favoritism of patent over science. Incyte, like Celera Genomics, Pacific Biosystems, and the like, are large biotech firms whose livelihood depends on patent protection. Incyte pushed for the redefining of what was considered 'unpatentable' under the category of 'general utilities'.[45] Those groups of materials seen unfit to be broadly characterized by a patent claim were included in with those groups

[45] Incyte Genomics. Letter to the Director the USPTO. June 19, 2000.

who, by Incyte standards, held some patentability despite their broad scope. Incyte provided a 'fishing rod' analogy to express the point of contention:

> The PTO presumably would issue a patent on a novel and nonobvious fishing rod notwithstanding the lack of any disclosure of the particular fish it might be used to catch. The Training Materials would appear to warrant a rejection, however, on the grounds that the use of the fishing rod is applicable to the general class of devices used to catch fish.[46]

Be it net, pole, or shotgun, the utility was the same in this case. Is there an inherent danger in promulgating broadness? The science says yes: biotechnological materials rarely have just one utility. Again, remembering this *one utility* stipulation, Incyte made a shocking claim from court history: "It is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works."[47] This also broadened the scope of utility claim. It is beneficial to understand the conclusive function of the protein, but to what end? If there is no means for understanding mechanism or systems functioning, then there is no way to study, for example, inhibitory drugs on the protein except blind guesswork. The patent may be legally viable as such, but creates difficulties in the scientific realm.

Perhaps the most powerful component of the Incyte commentary was the assertion of low standard utility. Incyte emphasized, in arguing applicants need only a 'substantial likelihood' of utility, "Unless there is proof of 'total incapacity,' or there is a 'complete absence of data' to support the applicant's assertion of utility, the utility requirement is met."[48] Though there are certain restrictions on this ruling, such as the claim for 'throwaway utilities' [something like a knockout mouse utilized as snake food], the stage for patents was not set upon utility foremost. The main claim of Incyte was

[46] Incyte Genomics. "Letter to the Director the USPTO." June 19, 2000.
[47] *In re Cortwright,* 165 F.3d 1353, 1359. (Fed. Cir. 1999) [quoting *Newman v. Quigg,* 977 F. 2d 1575, 1581. (Fed Cir. 1989)]
[48] *Brooktree Corp. v. Advanced Micro Devices, Inc.,* 977 F. 2d 1555, 1571 (Fed. Cir. 1992).

examiners must not reject utilities based on fears of broad, yet specific and substantial claims which encompassed many groups. Incyte also cited 'substantial utility' [real world utility] may be claimed on materials unless "further research would be required to determine a practical utility."[49] This statement elaborated on the definition of utility in its application to research tools. Incyte claimed research tools were replete in the patent record in forms such as spectrophotomers to argue for allowing the patents of ESTs and cDNA libraries regardless of their utility as research tools. The PTO considered both of these matters and concluded a claimant must have a 'credible' utility, or a practical one. The Incyte details on utility however, were well read as stated:

> There is no legal requirement that utility be specific or unique to the claimed invention. Thus, the Training Materials should be revised to explain that specific utility is demonstrated by a practical use that confers a specific benefit. [50]

Here answered the PTO, a claimant must well-establish a specific, substantial, and credible utility that was readily apparent [not necessarily known].[51] To this degree, neither Incyte, nor the PTO established any illegality of patenting genes, ESTs, or other disputed claims. Moreover, because only one known utility must be established, the PTO potentially 'dead-ended' further characterizations of biological materials under patent law. Incyte benefited for they depended on the commercial benefits achieved under protection.

It was the duty of the PTO to assess this commentary and provide revisions reflecting both court precedent and public opinion. It became clear the utility requirement under 35 USC § 101 needed revision due to the lack of specificity in examination. Many comments expressed concerns with patenting genes, especially ESTs, noting its utility

[49] Incyte Genomics. "Letter to the Director the USPTO." June 19, 2000.

[50] Incyte Genomics. "Letter to the Director the USPTO." June 19, 2000.

[51] 66 FR 1092

primarily as a tool used to extract "nucleic acids whose utility was not known, and the function of the corresponding gene [was] not known".[52] Comments also related examination procedures might grant nonspecific and nonsubstantial utility despite precedent law in the opposite.[53] In response, the PTO offered new solutions in 1999.

The 'useful invention' or utility requirement added a new litmus test, credibility. Section 2 of the Examination Guidelines for the Utility Requirement noted:

> Review the claims and the supporting written description to determine if the applicant has asserted for the claimed invention any specific and substantial utility *that is credible*.[54]

In the frame of context, credible would most aptly mean realistic, or proposal of an invention that not only had a practical utility, but a realistic means of imposing its benefits. Thus, ESTs, in being a useful tool in DNA isolation, do not qualify as a credible utility in that they do not serve realistic and immediate benefits by themselves, but rather in conjunction with more laboratory work and other chemicals and genes that are discovered in consequence. Moreover, the PTO asserted

> Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record (e.g. test data, affidavits or declarations from experts in the art, patents or printed publications) that is probative of the applicant's assertions.[55]

That is, a professional in the field may assert from the proposed assertion of utility that the invention was indeed specific and substantial. Utility should, in conjunction with the three prongs, describe how to use the invention. Moreover, a patent application should be nonobvious to a person skilled in the art. The credibility clause still seemed frustratingly

[52] 64 Fed. Reg. 71440 (Dec. 21, 1999).
[53] Brenner v. Manson, 383 US 519, 534-535, 148 USPQ 689, 695 (1966).
[54] 64 Fed. Reg. 71440 (Dec. 21, 1999).
[55] 64 Fed. Reg. 71440 (Dec. 21, 1999).

vague from a scientific perspective because one may see a scientific tool as a credible utility while another does not.

The PTO also called for comments on the aforementioned guidelines of 1999 along with concerns about the written description and extension of comment period. The opening for public commentary lasted from Dec. 21, 1999 until March 22, 2000. Overall, the new guidelines provided a means for patent officers to reject claims to vague chemical processes or genes coding for unknown proteins or proteins of unknown and specific function. These guidelines still seemed vague due to the fast pace of biotechnology. Some difficulty the PTO did not address was practical utility might seem non-obvious and credible to one in the field at the time, but with exponentially increasing research capabilities, the utility might become obvious in a short time. Also, the specificity in conjunction with credibility might still be lacking and patentable. For example, a claim to a tumor suppressor gene might relay a credible utility to prevent cancer, but what if there was no description beyond the structure and some known properties? From a science perspective, how a gene works within a biological system is as important, if not more so, than the isolated gene itself. Drug therapies and methods to cure disease seem more credible than isolated genes in a petree dish, however all seem legally viable. Again, no definite boundaries were set.

The PTO specifically addressed commentary providing their opinions. The newest guidelines out of the PTO attempted to verify the patentability of genes under current laws and practices. This verification was the result of 35 individual and 17 organizational responses to the PTO's request for comments. The inherent difficulty in the patentability

of genes was the characteristics of genes as a result of manufacture and of nature, as previously described.

Essentially, a gene is indeed a product of nature, not a product of matter, but only within the organism. In the case a gene has been isolated by the hands of man, then the product is indeed a product of matter and therefore patentable as long as it meets the other criteria of a patent (utility, novelty, non-obviousness). Interestingly, comment 3 of the publication suggested "the USPTO should seek guidance from Congress as to whether naturally occurring genetic sequences are patentable subject matter."[56] The response from the PTO was two fold: citing *Diamond v. Chakrabarty*, and any biological sequence or chemical isolated from its natural components does not qualify as natural. As it stands, a protein isolated by process may be patentable. Does this logic parallel to other natural products? Is pine wood patentable when cut from the tree and isolated from its natural state? The follow-up to the proposed difficulties is somewhat feebly explained in comment 4 which establishes:

> The patent system promotes progress by securing a complete disclosure of an invention to the public, in exchange for the inventor's legal right to exclude other people from making…the composition for a limited time. That is, a patent owner can stop infringing activity by others for a limited time.[57]

The inherent danger in this statement is the unintentional stifling of *progress* by making patented genes and chemical unattractive to private-sector communities who have the ability and capital to make medical breakthroughs, but not the rights to the genes involved.

[56] Fr 66 1092. January 5, 2001.
[57] Fr 66 1092. January 5, 2001.

Perhaps one of the most pertinent and ignored comments in the new guidelines was in comment 5. Concerns raised by the public communicated fear "a gene will be allowed a broad patent covering any number of possible applications even though those uses may be unattainable and unproven," a stark contrast to Incyte's claim.[58] The public claim referenced phenomenon in biology such as redundancy, homology, conservancy, alternative splicing, and more to imply one gene patent may stifle the correct and most detailed characterization of protein function, not only in isolated form, but in systemic form (which is the most specific, substantial, and credible). If researchers characterized a protein, by patent law, he/she is only required to assert one utility. However, once the gene is patented, all other utilities, discovered before or after the patent, do not have to be expressed. Epidermal growth factor (EGF) and related EGF-R though related, bind different ligands and function differently. The supposition of one utility based on ligand binding would perhaps not challenge further characterization of how each one functions. The public sector may only learn one of these characteristics through the beauty of full disclosure in patent application. The PTO expressed its reasoning:

> progress is promoted because the original inventor has the possibility to recoup research costs, others are motivated to invent around the original patent, and cause a new chemical is made available as a basis for future research.[59]

Politically, it seems the PTO was influenced by private sector interests and commercial benefits. If genes could not be patented, then the public sector would be able to collaborate on specific proteins rather than invent around them, a frustrating result of patent law. Research costs do provide an incredible hurdle which is easily solved by enabling the patentability of genes, but genes are small money makers in comparison to pharmaceuticals and therapies. Most patented genes are used as research tools to

[58] Fr 66 1092. January 5, 2001.
[59] Fr 66 1092. January 5, 2001.

understand systems and develop drug treatments which function on the system. The PTO had no choice but to allow such patents, for disallowing them would open up the field of international competition, making researchers pay international licensing agreements for genes they could have patented in the US.

Also, Comments 8-10 suggest DNA should not be adopted as patentable material. The PTO rebuts DNA may be patentable if it is: isolated or purified, maintains some specific, substantial, and credible utility, and adheres to the other statutory requirements. The patentability of DNA is a slippery slope. Through methods of isolation, DNA may prove to be useful in hybridization or genomics studies. Oppositely, a segment of DNA may appear multiple times within a genome, encoding different proteins. However, is the DNA marker itself a credible utility? It seems a DNA marker is another tool used to identify a potential candidate gene for which gene therapies may be developed. It is not inherently commercially beneficial. Though the PTO agrees patents need not have a commercial benefit, there seems to be a disjunction between the reasoning in comment 5 {patents have the "possibility to recoup research costs"). [60] Moreover, DNA is most invaluable in natural form because further experimentation and observation must be used to properly characterize its function. Furthermore, if DNA is isolated from this environment, it may not always perform as nature intended it to. Thus, while helpful in *in vitro* experimentation, the patenting of DNA sequences may isolate segments of DNA which will be poorly or shallowly characterized in lab treatments. This hypothetical problem could create slow progress in the scientific community, and also perhaps, in the private realm.

[60] See *In re Langer*, 503 F 2d. 1380,1393, 183 USPQ 288, 298 (CCPA 1974).

Also, the 'one practical utility' rule also applies for DNA. Comments suggested these patents might provide a similarly broad scope like gene patents. Interestingly, the PTO answered:

> Where a new use is discovered for a patented DNA composition, which new use may qualify for its own process patent, notwithstanding that the DNA composition itself is patented.[61]

Recalling the PTO was in favor of patenting both biological processes and materials to ward off international patent infringement, it seems logical the PTO would also agree to patent the DNA composition itself, especially in some isolated form. Thus, it seems plausible the ability to patent a new utility on an existing patent would be nonexistent. Researchers would have little room to discover new utilities without licensing agreements. The PTO reasserted in comment 12 "there is no basis to deny patent applications claiming DNA compositions, or to limit a patent's scope in order to allow free access".[62] The PTO was at the mercy of statues and the court system, not what would most benefit the science.

The issue of utilities based on homologies raised some interesting issues as well. In patent processes, many have complained this method of establishing utility may not be specific enough. Moreover, they suggested if such a method was used, then the utility should be established as file-specific by the computer which matched the homology.[63] The PTO did not really answer this problem. Rejections to utility claims were only viable if the patent officer could prove some "inherently unbelievable or…implausible scientific principles".[64] They follow "a patent examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the

[61] Fr 66 1092. January 5, 2001.
[62] Fr 66 1092. January 5, 2001.
[63] Fr 66 1092, January 5, 2001.
[64] *In re Brana*, 51 F. 3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995).

assertion."[65] It was the task of the examiner to deny patent, not the task of the applicant to prove utility. The inherent difficulty is proving a negative, rather than establishing a positive. More scientific data than simply computer analyzed homology tests should grant patentability given the nature of homologous regions. Many DNA compounds contain non-homologous regions which may or may not have been characterized.

After responding to concerns, the PTO issued their final Utility Revision during the Clinton Administration. Section 2a of the 1999 version was moved to section 1c of the 2001 version. This section described a 'well-established utility' if someone skilled in the art may immediately appreciate the invention claimed (unchanged) and the utility must be specific, substantial, and credible (changed in 2001).[66] In the written description, a utility must be somewhat apparent and credible, a new change aimed at quenching some of the merely descriptive patent claims. Section 2.2.c of the 2001 guidelines asserted an applicant must prepare a 'readily apparent well-established utility,' that is, a known utility, not a hypothetical one or one that awaited proper characterization. [67] Section 2.2.d.2 clarified the use of the word 'nexus' from the 1999 guidelines by adding, "the applicant has the burden to establish a probative relation between the submitted evidence and the originally disclosed properties of the claimed invention."[68] It was now up to the applicant to prove the utility was well-established given the previously disclosed claims. Also, section 3 of the same section elaborated proof of no utility should provide documentary evidence "regardless of publication date".[69] This addendum is somewhat out of place. Given the long history of PTO references to laws passed decades

[65] Fr 66 1092. January 5, 2001.
[66] Fr 66 1092. January 5, 2001.
[67] Fr 66 1092. January 5, 2001.
[68] Fr 66 1092. January 5, 2001.
[69] Fr 66 1092. January 5, 2001.

ago, it seemed this statement was well understood. Perhaps the influx of new technology might have cast doubt onto the applicability of past cases, despite logical parallels.

Moreover, the PTO added a few word changes to some sections. To Section 3.1.b., 'known' was changed to 'well-established'.[70] This was an interesting application of addendum mainly because the striking of known implied loosely that a utility may not need be fully known, rather just one utility be *well-established.* The examination has become somewhat less stringent here, rather than more so. Also, the *prima facie* establishment was also struck from the 1999 guidelines entirely. Section 3.3.b.1-3 asserted a need for an explanation why the utility was well established, facts which determined this conclusion, and an evaluation of the evidence record. This deletion falls in line with the new burden of the claimant to establish utility.

After all of the directives to significantly change examination guidelines, very few revisions were actually made. Most revisions reflected the comments of Incyte Pharmaceuticals and the NIH itself. The hope for scientific justice lay in case-by-case analysis in courts more than the PTO. The exorbitant overhead of research, it would seem, would only be paralleled by the costs of endless litigation. The PTO took a tiny step in better representing the fundamentals of science, but left gaping holes of unanswered biological questions covered by a thin legal blanket.

Just one presidential statement about the status of patents and biotechnology caused great fear, losses, and uncertainty in the markets. The PTO attempted to solve the conundrum of allowing unfettered access to science while still providing protection to inventors. The utility guideline were necessarily lacking in specificity because needed to keep pace with rapidly developing technology. Vicariously, the universality opened the

[70] Fr 66 1092. January 5, 2001.

patent guidelines to overly broad scope, which in turn impeded specificity of patent protection, leaving some genes locked in the twenty year closet, open only to exorbitant licensing. The patent protect also grossly underappreciated the mechanisms by which genomic information functions. Legally, the revisions accurately involved both legal precedent and public commentary. However, scientifically, both the definition of utility and what may be allowed for patent application remained frustratingly broad. The biotechnology sector is exponentially growing and contributes billions of dollars to the GNP. The PTO patent revisions of the 1990's did little to provide guidelines for proper examination of biotechnological patents primarily in the inability to determine boundaries for what constitutes a specific, substantial, and credible utility. Moreover, the stipulation of just one necessary utility undercuts the worth of biological materials as organic materials with constantly evolving characteristics. The sterility of isolating DNA in a petree dish and claiming rights parallels the sterility of the PTO in addressing biotechnological research not as a systemic understanding, but an isolated one. Biotechnology cannot be adequately reflected in patent law because the fluidity of the prior is stifled by the rigidity of the later.