

## APPENDIX A

### Genetic Sequence Patents: Historical Justification and Current Impacts

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In 1980, the United States Supreme Court in Diamond v. Chakrabarty<sup>1</sup> authorized the patenting of a genetically-engineered living organism. The Court indicated that this was an invention, not a product of nature and said that “The laws of nature, physical phenomena, and abstract ideas have been held not patentable. Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter.”<sup>2</sup> Nevertheless, in an erroneous application of the case, the United States Patent and Trademark Office (USPTO) began allowing patents to be issued on genetic sequences when “isolated from their natural state and purified.”<sup>3</sup>

The proponents of gene patents claim that legal precedents allowing the patenting of isolated and purified products of nature justify the patenting of genetic sequences in which the non-coding regions of the genetic sequence have been removed. They claim that the remaining genetic sequence is an “invention” since it has been “isolated” (taken out of the body) and “purified” (had non-coding regions removed). In this project, we decided to test that claim by analyzing U.S. court cases at all levels that either specifically or indirectly address the products of nature doctrine (including all cases that specifically claim that isolation and purification transforms an unpatentable product of nature into a patentable invention). We additionally analyzed all other cases and policy arguments that gene patent proponents claim support the patenting of genetic sequences.

In analyzing the patent cases, we assessed the application of the products of nature doctrine from the late-1800s until today. We undertook research to find out what the product or

process was that was claimed in each patent and how close that product or process was to something that occurred in nature.

Our findings were striking. The precedents gene patent proponents cite to justify the patenting of isolated and purified genes often did not, in fact, support that viewpoint. They were distinguishable for various reasons:

1) In key cases, a Constitutional or §101 statutory products of nature doctrine was never raised as a challenge, under either the U.S. Constitution or §101 of the patents code. Instead the patent was challenged based on other provisions of the patent code, such as on the grounds of novelty, non-obviousness or usefulness. Those challenges are not dispositive of the products of nature issue because something can be an unpatentable product of nature and still be useful, novel and non-obvious.

2) In some cases, the original substance was not a product of nature at all. Instead, the cases involved a man-made invention that then was transformed through isolation or purification into a distinctive new man-made invention.

3) In other cases, the purported invention was not a product at all, but a process. No one disputes that a process for sequencing genes is patentable.<sup>4</sup>

4) In the remaining cases, the term “isolated and purified” meant something different than what gene patent proponents describe. Isolation and purification in those cases was accomplished by a specific multi-step combination of ingredients and processes that did not stop others from using the initial product of nature for other purposes or even from using an alternative combination of ingredients and processes to create a similar invention. This is a key observation because, in contrast to these cases, allowing patents on purportedly isolated and purified genetic sequences gives the patent holder rights to prevent anyone else from using the

original genetic sequence, because, by owning what might be thought of as the active ingredient of the genetic sequence, the patent holder can prevent anyone else from using the whole, naturally-occurring gene sequence in any way.

### Basic Provisions of U.S. Patent Law

Substantive provisions of the federal patent statute in the United States provide that for an invention to be patentable, it must be of eligible subject matter (under Article 1, sec. 8, clause 8 of the U.S. Constitution and under 35 U.S.C. §101).<sup>5</sup> It also must demonstrate utility (§101), novelty (§102) and non-obviousness (§103). The inventor must also adequately describe the invention and enable others to make and use the invention.<sup>6</sup> In return for the disclosure of the invention to the public, the inventor is granted patent protection for the invention for 20 years measured from the date of the filing of the application.<sup>7</sup>

The U.S. Supreme Court has said that a patent is not a “hunting license,” nor a “reward for the search, but compensation for its successful conclusion.”<sup>8</sup> The disclosure provisions of patent law require that an applicant satisfy four additional requirements in the patent specification: written description, enablement, best mode, and definiteness.<sup>9</sup> The patent application must also be adequately “enabled,” describing the invention fully, so that it would be technically feasible for another person skilled in that field to make and use the invention.<sup>10</sup> This requirement assures that the public gets information back in exchange for the exclusive rights granted to the patent holder. Definiteness relates to the way the claim is written: the claim must “particularly point out and distinctly claim the subject matter which the applicant regards as his invention.”<sup>11</sup>

For over a century the U.S. Supreme Court has held consistently that products of nature, laws of nature, and abstract ideas are not patentable subject matter. In June 2006, U.S. Supreme

Court Justice Breyer of the U.S. Supreme Court discussed the reason why it is important not to have patents on products of nature or laws of nature. He said:

The justification for the principle does not lie in any claim that “laws of nature” are obvious, or that their discovery is easy, or that they are not useful. To the contrary, research into such matters may be costly and time-consuming; monetary incentives may matter; and the fruits of those incentives and that research may prove of great benefit to the human race. Rather, the reason for the exclusion is that sometimes *too much* patent protection can impede rather than “promote the Progress of Science and useful Arts,” the constitutional objective of patent and copyright protection.<sup>12</sup>

### The Grant of Patents on Genetic Sequences

Contrary to U.S. Supreme Court precedent, the current policy of the United States Patent & Trademark Office (USPTO) is to grant patents for human genetic material, including full-length gene sequences, gene mutations, and fragments of genetic material. The theory of the USPTO is that the act of isolation and purification of this material from the human body removes it from the unpatentable “products of nature” realm.<sup>13</sup> According to the USPTO, “[w]hile descriptive sequence information alone is not patentable subject matter, a new and useful purified and isolated DNA compound described by the sequence is eligible for patenting, subject to satisfying the other criteria for patentability.”<sup>14</sup> Then Director of the Biotechnology Examination Technology Center at the United States Patent & Trademark Office, John Doll wrote in May 1998 that a patent application for a DNA sequence must be distinguished from its nonpatentable naturally-occurring counterpart, in that the “patent application must state that the invention has been purified or isolated or is part of a recombinant molecule or is now part of a vector (Doll, 1988 page 689).” In 2001, in its Utility Examination Guidelines, the USPTO stated: “Thus, an inventor’s discovery of a gene can be the basis for a patent on the genetic composition isolated from its natural state and processed through purifying steps that separate the gene from other molecules naturally associated with it.”<sup>15</sup>

Patents on human genes or gene parts differ in terms of whether the inventors could credibly argue that they have “isolated and purified” the gene. In some instances, the patent holder has merely patented a gene mutation exactly as it occurs in nature, in clear violation of the “product of nature” doctrine. In others, the patent applicant has removed the non-coding region, but the remaining genetic sequence still has the same effect as the naturally-occurring gene.<sup>16</sup> For example, not only could the patented (“isolated and purified”) sequence be used for diagnosis of a particular disease, so could the original whole sequence as it occurs in nature.

While the current policy of the USPTO is to grant patent rights for genetic material, the U.S. Supreme Court has not yet made a determination on the issue of whether human genetic material is patentable subject matter. In fact, U.S. Supreme Court precedent is to the contrary.

#### Article 1, Section 8, Clause 8 and U.S. Patent Law

Article 1, section 8, clause 8 of the United States Constitution provides that Congress shall have the power “To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries;...” This paper argues that the issuance of patents on human nucleotide sequences is contrary to Article 1, section 8, clause 8 on several related grounds. First, genetic sequences are not “discoveries.” At the time Article 1 was drafted, the term “discovery” covered a subset of inventions and required some level of inventiveness. A genetic sequence is not a “discovery” of an “inventor” as those terms were used in the late eighteenth and throughout the nineteenth century.

Second, this paper argues that human genetic sequences do not qualify for patent protection because they are not patentable subject matter under either Article 1 or 35 U.S.C. §101. Over the last few decades, a few lower courts have failed to apply the precedent of the

U.S. Supreme Court that forbids patents on products of nature.<sup>17</sup> They have also ignored the U.S. Supreme Court precedent in effect since the late 1800's holding that the act of purifying a naturally occurring substance does not put it in the realm of patentable subject matter.<sup>18</sup>

Third, this paper points out that the small number of cases that the proponents of gene patents point to as creating exceptions to the products of nature doctrine are distinguishable and do not lead to a conclusion that gene sequences are patentable "purified and isolated" products of nature. In addition, this paper argues that the policies underlying Article 1 of the U.S. Constitution do not support patents on human genetic sequences. The underlying goal of Article 1, section 8, clause 8 was to "encourage the progress of science," a goal that is not met in the case of human gene patents.

#### Meaning of the Term "Discoveries" in Article 1

Some proponents of gene patents might attempt to claim that a genetic sequence is patentable since Article 1, section 8, clause 8, allows patents on "discoveries." However, that interpretation would be at odds with the plain meaning of that word at the time of the drafting of the Constitution. The term "discoveries," as utilized when the Constitutional provision was written in the late eighteenth century, meant the unexpected or fortuitous creation of something new. (Demaine and Fellmeth, 2002 page 370) Human genetic material, even after it is isolated and purified, is not a "discovery" as that term is used in the Constitution because the material exists within the human body and thus does not meet the requirement set out by Article 1, section 8, clause 8.

The term "invention" was considered to include a "discovery" in that both created something original even until the late eighteenth century. (Demaine and Fellmeth, 2002 page 370)

citing Murray, 1901) The writings of a number of legal scholars support this view. One legal scholar, writing in a legal treatise, offered:

An “invention,” in the parlance of the Constitution and early patent laws, is a new creation consciously sought and successfully reduced to practice by the inventor. A “discovery,” as used in the same parlance, was intended to denote a fortuitous creation of the inventor and not merely something found by him or her. Thus, an “invention” and a “discovery” share the requirement that the inventor create something original; the difference between the two is that an “invention” is consciously sought, while a “discovery” is created unexpectedly. A discovery in that era, as used in the intellectual property law, denoted something originating from the human intellect and not merely learned in that intellect. (Demaine and Fellmeth, 2002 page 370 citing Bainbridge, 1984)

Writing in 1889, another patent law scholar offered that the word “discovery,” as used in the Constitution, reached the level of an “invention” only where there is some inventiveness involved in the discovery. (Walker, 1889 pages 2-3) He noted that someone “may invent a machine, and may discover an island or law of nature. For doing the first of these things, that patent laws may reward him, because he is an inventor in doing it; but those laws cannot reward him for doing either of the others, because he is not an inventor in doing either.” (Demaine and Fellmeth, 2002 page 370, citing Walker, 1889)

This view that the drafters of the Constitution used the two terms as requiring the creation of something original rather than merely finding something is fully supported in the text of the initial iteration of the patent laws. The Patent Act of 1793, authored by Thomas Jefferson, specifically stated that “simply changing the form or the proportions of any machine, or composition of matter, in any degree, shall not be deemed a discovery.”<sup>19</sup> Although the 1952 Patent Act<sup>20</sup> does not specifically contain this language, the 1952 act is considered by both Congress<sup>21</sup> and the U.S. Supreme Court<sup>22</sup> to merely codify all earlier patent acts. In addition, Jefferson’s statement sheds light on patent law because it was drafted around the time that Article 1 was written. It indicates that changes in form or proportions of a substance or object were not considered discoveries. Moreover, the current patent act arguably includes the same

requirements under the provisions requiring that the claimed matter at issue be an invention,<sup>23</sup> be novel<sup>24</sup> and be non-obvious.<sup>25</sup>

Apart from the original Constitutional provision and the relevant patent law that followed, the writings of the people involved in drafting Article 1 shed light on what the necessary connection was between an inventor and the subject matter for which he sought a patent. In a portion of the 1788 Federalist Papers, James Madison wrote “[t]he copyright of authors has been solemnly adjudged, in Great Britain, to be a right of common law. The right to useful *inventions* seems with equal reason to belong to the inventors.” (Madison, 1788) It follows that the drafters viewed the British law to be the touchstone for intellectual property and sought to establish the same values in U.S. law. Even today, the British Patents Act, using the term “discovery” in its modern sense, provides that “a discovery, scientific theory or mathematical method” is not an invention.<sup>26</sup> Furthermore, the “presentation of information” is not an invention under the British Act.<sup>27</sup>

Like those of Britain, the patent laws of many other leading countries distinguish “discoveries” from “inventions.”<sup>28</sup> The European Patent Convention (EPC) requires such an “inventive step,” excluding mere “discoveries” from patentable subject matter.<sup>29</sup> The EPC offers both that “discoveries, scientific theories and mathematical methods” are not regarded as patentable subject material.<sup>30</sup> Likewise, the European Directive on the Legal Protection of Biotechnological Inventions provides that “a mere discovery cannot be patented” because inventions “must involve an inventive step.”<sup>31</sup>

#### U.S. Supreme Court Precedent

The U.S. Supreme Court precedents have clearly and consistently held that products of nature are not patentable.<sup>32</sup> In 1948, Funk Brother Seed Co. v. Kalo Inoculant Co. confronted

the §101 question of patentability head on and held that naturally-occurring products of nature are excluded from patentable subject matter.<sup>33</sup> Funk focused on whether mixtures of certain bacteria were patentable.<sup>34</sup> 35 U.S.C. §101 presents the categories of inventions that are patentable, providing “[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title...”<sup>35</sup> In Funk, a patent had issued for mixed cultures of root nodule bacteria capable of inoculating the seeds of leguminous plants.<sup>36</sup> The crux of the Court’s finding was that the combination of the bacteria species did not produce new bacteria, nor did it cause a change in any of the six species of bacteria, but served more of a packaging function.<sup>37</sup> The Court stated that “[e]ach species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee.”<sup>38</sup> The Court further offered, in perhaps the most oft cited language of the case, "Patents cannot issue for the discovery of the phenomena of nature. . . . [They] are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none."<sup>39</sup>

In 1980, the U.S. Supreme Court applied the product of nature doctrine in the area of biological organisms in Diamond v. Chakrabarty, holding that where an inventor introduced new genetic material within a bacterium cell, he had produced (i.e. genetically engineered) something that was not a product of nature and was thus patentable subject matter under 35 U.S.C. §101.<sup>40</sup> The Court clearly stated again that naturally-occurring products of nature were not patentable.<sup>41</sup> The Court said that the “patentee has produced a new bacterium with markedly different

characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly it is patentable subject matter under § 101.”<sup>42</sup> Specifically, the inventor had added new genetic material into the cell of a bacterium, producing something that did not occur in nature. The court further stated:

The laws of nature, physical phenomena, and abstract ideas have been held not patentable. Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that  $E=mc^2$ ; nor could Newton have patented the law of gravity. Such discoveries are ‘manifestations of . . . nature, free to all men and reserved exclusively to none.’<sup>43</sup>

Despite the fact that Chakrabarty only allowed the patenting of a “nonnaturally occurring” living bacterium – and clearly indicated that products of nature are not patentable – it is often cited as opening the door for patents covering human genetic material. This may be the result of a misinterpretation of a line in the opinion, that “anything under the sun that is made by man” is patentable.<sup>44</sup> The line is from a 1952 Senate report that actually says “[a] person may have ‘invented’ a **machine or manufacture**, which may include anything under the sun that is made by man, but it is not necessarily patentable under section 101, unless the conditions of the title are fulfilled.”<sup>45</sup>

With an unbroken line of U.S. Supreme Court cases holding that products of nature are unpatentable, a question arises as to when a natural substance becomes subsequently transformed by the hand of man to become patentable. Is “isolation” and “purification” enough, according to Supreme Court precedents? The answer is a resounding “no.”

The U.S. Supreme Court has held that purification of an already existing natural product did not make it patentable subject matter. In the 1874 decision in American Wood-Paper Co. v. Fibre Disintegrating Co., the plaintiff had been awarded a patent that claimed refined cellulose (vegetable pulp) derived from straw, wood, and fibrous sources to use in the production of paper.<sup>46</sup> The refined cellulose was thus a purified form of a known substance that was a product

of nature. The alleged infringing company produced paper via refined cellulose using a similar method, but utilized mainly bamboo pulp rather than vegetable pulp.<sup>47</sup> The company argued that they were not infringing the patent for refined cellulose because the plaintiff patent holder's claims were invalid because they lacked invention.<sup>48</sup> The Court found for the defendant in that purification of a preexisting substance does not create a new, patentable product, determining that the primary characteristics and function of the product were not significantly different from what existed in nature.<sup>49</sup> The Court stated:

There are many things well known and valuable in medicine or in the arts which may be extracted from...substances. But the extract is the same, no matter from what it has been taken. A process to obtain it from a subject from which it has never been taken may be the creature of invention, but the thing itself when obtained cannot be called a new manufacture.<sup>50</sup>

Furthermore, the Court stated:

[I]t is quite obvious that a manufacture, or a product of a process, may be of no novelty, while, at the same time, the process or agency by which it is produced may be both new and useful...and therefore, patentable as such. And it is equally clear, in cases of chemical inventions, that when, as in the present case, the manufacture claimed as novel is not a new composition of matter, but an extract obtained by the decomposition or disintegration of material substances, it cannot be of importance from which it has been extracted [i.e. because the vegetable pulp was not a new composition of matter, it is irrelevant that the patent applicant extracted it from sources never before utilized.]<sup>51</sup>

It is important in the context of gene patents that the U.S. Supreme Court in American Wood-Paper Co. focused on the patentable subject matter requirements of §101 and found that merely removing the pulp from straw, wood, or other natural sources did not make it a “new composition of matter” worthy of patent protection. In the case of genetic material, this would parallel to a scientist isolating a gene from the human body and merely removing the non-coding regions. The fact that it is removed and purified to some level does not make it patentable subject matter under §101.

In 1884, the U.S. Supreme Court reiterated the basic concept of the American Wood Paper purification doctrine in Cochrane v. Badische Anilin & Soda Fabric.<sup>52</sup> There, the patentee

had made a synthetic version of a dye that already existed in nature (alizarine), but with a brighter hue. This case applied the purification doctrine where there was a non-living product of nature. Although the Court acknowledged that the synthesizing process may be patentable, it held that the resulting dye itself was not because the brighter hue was an insubstantial difference from the original product of nature and therefore unpatentable.<sup>53</sup> The fact that the patent applicant was able to synthetically replicate an existing product of nature, even with a brighter hue than observed in nature, did not make it patentable subject matter. The Court rejected a claim for “[a]rtificial alizarine, produced from anthracine or its derivatives by either of the methods herein described, or by any other method which will produce a like result.”<sup>54</sup> The Court found that it was an already known product of nature and that “calling it artificial alizarine did not make it a new composition of matter, and patentable as such, by reason of its having been prepared artificially for the first time from anthracine, if it was set forth as alizarine, a well known substance.”<sup>55</sup>

Initially, the USPTO and lower courts also determined that products of nature were not patentable even if they were transformed in some way. Fifteen years after American Wood Paper, the Patent Commissioner was asked to determine a similar issue regarding a product of nature, the patentability of a purified tree fiber. In Ex Parte Latimer, the patentee sought to patent purified pine needle fiber as a “new article of manufacture” for use in textiles, claiming “cellular tissues of the *Pinus australis* eliminated in full lengths from the silicious, resinous, and pulpy parts of the pine needles and subdivided into long, pliant filaments adapted to be spun and woven.”<sup>56</sup> Essentially this meant that the needle fibers had been cut and stretched for easier manipulation in spinning and weaving. The Commissioner decided that although the purified pine needles were very valuable, they were not patentable because they were extracted from a

natural source and thus naturally occurring.<sup>57</sup> The Commissioner said it “cannot be said that the applicant in this case has made any discovery, or is entitled to patent the idea, or fact, rather, that fiber can be found in the needle of the *Pinus australis*.”<sup>58</sup>

In 1928, the Third Circuit dealt with a case involving a patent for purified tungsten in General Electric Co. v. DeForest Radio Co.<sup>59</sup> In its natural state, the metal tungsten oxide has limited uses because it is extremely brittle.<sup>60</sup> But in its purified state, it is ductile and can be drawn into wire for use as a filament in light bulbs or vacuum tubes.<sup>61</sup> At issue with respect to products of nature were two product claims: (1) substantially pure tungsten having ductility and high tensile strength; and (2) a form of tungsten metal pliable at room temperature.<sup>62</sup> While the court recognized that the purified tungsten had much more useful characteristics than tungsten in its natural state, the court noted that those characteristics were given by nature rather than the inventor.<sup>63</sup> The patentee had only isolated and purified tungsten from its brittle oxide form normally found in the earth.<sup>64</sup> The court noted:

[w]hat he discovered were natural qualities of pure tungsten. Manifestly he did not create pure tungsten, nor did he create its characteristics. These were created by nature and on that fact finding the reasoning as to the validity of the product claims will be based.<sup>65</sup>

Additionally, in questioning whether the purified tungsten was human-made and thus eligible subject matter for a patent, the court said:

Naturally we inquire who created pure tungsten. [The patent applicant]? No. It existed in nature and doubtless has existed there for centuries. The fact that no one before [the patent applicant] found it there does not negative its origin or existence.<sup>66</sup>

This case is a prime example of the “products of nature” doctrine applied to an isolated and purified form of a naturally-occurring metal. The court invalidated both claims on the grounds that they were products of nature, not an invention.<sup>67</sup> Here, it is interesting that the court highlighted the fact that even though no one had previously “found” the pure form of tungsten, it does not make it patentable, for it existed there as a product of nature. Applying this to the gene

patent realm, where a scientist extracts a gene from the body and takes out the non-coding regions to leave only the coding regions, it is unpatentable subject matter even if claimed to be “isolated” and “purified,” for the gene itself and its coding regions existed prior to the scientist identifying them.

The Third Circuit in the tungsten case noted that the patent applicants had taken tungsten “as it is found in the earth, its native abode, and by his process converted it into pure tungsten or tungsten that is substantially pure, and doubtless, was first to discover that when pure it has characteristics, notably those of ductility and high tensile strength, which are wholly different from the characteristics of the impure oxid of tungsten, notable among which is extreme brittleness.”<sup>68</sup> The gene patent holder has done even less. All the gene patent holder did was to take the gene from its natural abode, the body, and discover existing traits. When the gene was “purified,” these traits did not change.

The U.S. Circuit Court of Patent Appeals (CCPA), now the Federal Circuit, also followed the reasoning laid out in American Wood Paper for naturally-occurring substances. The CCPA explicitly proffered in 1938 that even if a new product had properties superior to those of the old product, the “mere purification of known materials does not result in a patentable product.”<sup>69</sup> In In re Merz, the Court denied a patent on purified ultramarine dye produced with a new process even though dye was brighter in color than other types of aquamarine.<sup>70</sup> “No new use is claimed for [the applicant’s] purified ultramarine. It is the same old aquamarine with the same old use even though it may have brighter color and be more desirable as a pigment than formerly.”<sup>71</sup>

Likewise, the CCPA found in In re Marden (Marden I) that purified uranium treated to enhance ductility could not be patented because it was merely a purified form of a product of nature, but the process could be patented.<sup>72</sup> The Court held the substance unpatentable because

the ductility of uranium is “one of its inherent characteristics”<sup>73</sup> and is not a characteristic created “by some chemical reaction or agency which changes its inherent characteristics.”<sup>74</sup> In a companion case, In re Marden (Marden II), the same Court also denied a patent for purified vanadium because it was “not new in the inventive sense, and, it being a product of nature, no one is entitled to a monopoly of the same.”<sup>75</sup> Both sides in that case conceded that the patent was for nothing more than purified vanadium where “ductile or malleable vanadium is nothing more or less than vanadium freed from all of its impurities and that all pure vanadium is ductile.”<sup>76</sup> The court further stated that the “quality of purity of vanadium or its ductility is a quality of a natural product and as such is not patentable.”<sup>77</sup>

An analysis of precedents makes clear that the USPTO erred in granting patents on genetic sequences. Merely taking out the non-coding region of a gene does not sufficiently transform it from the original product of nature. Even more so than cellulose, purified tungsten oxide, and the other products dealt with in the case law, the valuable characteristics of the purported invention—the ability of genetic sequences to bind to a complementary strand or produce proteins—were “created by nature”<sup>78</sup> not the inventor. Even when cDNA is created, that structure serves a mere “packaging function”<sup>79</sup> for the product of nature.

### Why are Genetic Sequences Patentable?

Despite compelling precedent to the contrary, the proponents of gene patents have been able to convince the U.S. Patent and Trademark Office to grant patents on genes. They have done so based on a single argument—saying that while products of nature are not patentable, “isolated and purified” refinements of products of nature are. They have relied on a few lower court cases that depart from the U.S. Supreme Court precedent that holds that products of nature,

and even isolated and purified refinements of nature, do not meet the §101 requirement that the “invention” be patentable subject matter.

Gene patent proponents point out that patents on strawberry flavor, vitamin B<sub>12</sub>, adrenaline, and an insecticide made of a plant root have all been upheld, even though these substances are products of nature. These are all lower court cases which give them less precedential value than cases from the U.S. Supreme Court. Some of the cases do not correctly apply the law. But, equally importantly, all of them involve products and processes that are clearly distinguishable from a genetic sequence.

There are additional reasons why the “isolated and purified” argument is flawed. Not all human gene patents involve genes or parts of genes in which the non-coding region has been removed. Some patent applicants are being granted patents on naturally-occurring human nucleotide sequences (genes or parts of genes) that have been isolated (i.e. taken out of the body), but have not been purified (that is, changed from the form in which they exist in the body).<sup>80</sup> Gene patents are being granted on the actual sequence of mutations and genes as they occur in the body. See, for example, Patent No. 5,654,155 (issued Aug. 5, 1997) and Patent No. 6,762,293 (issued July 13, 2004) or any of the many patents on single nucleotide polymorphisms.

And even in cases where certain non-coding regions of the genetic sequences have been removed, the item being patented is negligibly changed from its naturally-occurring counterpart. Indeed, it functions the same way a gene would function in the body. This creates several problems. The patent on a gene without the non-coding region prohibits anyone else from using the genetic sequence with the non-coding region (the naturally-occurring counterpart of the “invention”) – for example, a version of the breast cancer gene acquired from someone else. Moreover, allowing a patent on a supposedly “isolated and purified” gene runs afoul of the idea,

expressed by the U.S. Supreme Court in American Wood-Paper Co. v. Fibre Disintegrating Co.,<sup>81</sup> that an isolated and purified product of nature is not patentable if the product functions in a way that is not significantly different than what occurs in nature. Exploring in detail the main cases cited by gene patent proponents brings to light additional distinctions.

#### Insecticide from a Plant Root

Prior to the U.S. Supreme Court's decision in Chakrabarty, which reiterated the products of nature argument, the Seventh Circuit Court of Appeals in 1939 in Dennis v. Pitner<sup>82</sup> held that mixtures of naturally-occurring chemicals were patentable subject matter where the inventor discovers a new quality of an existing product. However, this case did not involve a distinct analysis into patentable subject matter as required by §101. Instead, the court erroneously conducted only an investigation into whether the resulting product was useful.

In Dennis, the plaintiffs were granted a patent that contained claims covering an insecticide made from an extract of the root of the cube plant, a plant indigenous to Peru and other South American countries.<sup>83</sup> The claims at issue in the case read as follows: (1) An insecticide and vermifuge comprising ground cube root with the fibrous elements removed; (2) An insecticide and vermifuge comprising an extract of cube; and (3) An insecticide and vermifuge comprising concentrated extract of cube root and a carrying agent.<sup>84</sup> Although the patent was ultimately held invalid by the court due to various prior art references that indicated the insecticide qualities of the plant, the court spoke in *dicta* about the products of nature doctrine. The Seventh Circuit Court of Appeals said "(t)he discovery of a natural phenomenon, or of a quality or attribute of a well-known article, which discovery is of value to mankind, may be entitled to patent protection."<sup>85</sup>

The reasoning used by the court in this case runs afoul of the U.S. Supreme Court precedents in that it results in the insecticide being classified as patentable subject matter based on its perceived utility without even examining it for patentable subject matter under the products of nature doctrine. The Seventh Circuit Court of Appeals, in attempting to then distinguish which products of nature were patentable and which were not, suggested that the discovery of cube root as an insecticide was potentially patentable because it:

necessitated the co-acting of two or more things. The insecticide needed the breath of the insect upon which the powdered cube root could act before it became an effective insecticide. ... Seldom is there any discovery of a new phenomenon of an old chemical product that does not call for the old product's contact with a material to which it must be applied by human agencies before the phenomenon occurs. In all such cases the discoverer is well outside of the rule which excludes the issuance of patents to those who have merely discovered a law or principle of nature or fundamental truth.<sup>86</sup>

Applying this reasoning, human genetic material would not fall within the Dennis case's category of patentable products of nature because it does not involve the "co-acting of two or more things."<sup>87</sup> The court makes a distinction between something that has been known before (an "old chemical product") and a chemical product that when paired with something (i.e. the plant extract paired with the insect's breath) creates a result (i.e. the insect dying), the latter product being patentable while the former is not.<sup>88</sup> It could be argued that human gene sequences are merely "old chemical products" since the patent applicants are often claiming only the sequence information itself rather than any interaction between the sequence and something else introduced by the patent applicant that creates a "new phenomenon."

### Adrenaline

Virtually every speech or article given in defense of the patenting of genes refers to the patentability of adrenaline, based on the 1911 federal district court case, Parke-Davis & Co. v. H.K. Mulford Co.<sup>89</sup> Some law professors even have alleged that because a famous jurist, Judge

Learned Hand, authored the lower court opinion in the case, it must be right. (They seem to have forgotten about Justice Oliver Wendell Holmes and Buck v. Bell.<sup>90</sup>)

But Judge Learned Hand gets it wrong almost from the beginning of his opinion, where he states, without support, “even if it were merely an extracted product without change, there is no rule that such products are not patentable.”<sup>91</sup> He made this statement in 1911 after American Wood Paper Co. was decided – a case which held that a purified product of nature was not patentable and which was relied upon by the patent examiner in the case to hold that purified adrenaline was unpatentable.

The judge held that purified adrenaline, extracted from the suprarenal gland and purified in a form that was more stable and concentrated and made the product more valuable both therapeutically and commercially, met the statutory requirement of novelty.<sup>92</sup> The patent stated that the therapeutic benefit of the purified form of the adrenaline was that it could be introduced into the human body without the complications associated with the less pure forms.<sup>93</sup> Relying on Union Carbide Co. v. American Carbide Co.<sup>94</sup> and Kuehmsted v. Farbenfabriken of Elberfeld Co.,<sup>95</sup> Judge Learned Hand stated that the inventor was “the first to make it available for any use by removing it from other gland-tissue in which it was found, and, ... it became for every practical purpose a new thing commercially and therapeutically.”<sup>96</sup>

However, neither of those cases are on point. Both Union Carbide Co. v. American Carbide Co.<sup>97</sup> and Kuehmsted v. Farbenfabriken of Elberfeld Co.,<sup>98</sup> involved human-made substances that had already satisfied the patentable subject matter inquiry. They were not products of nature but both human-made chemicals that did not and could not exist in nature without an individual having created them. Thus, Judge Learned Hand used two cases that dealt with human-made substances as precedent and applied them to a case involving a purified form

of a substance that is contained within the human body. The case that should have been used as precedent was American Wood-Paper Co. v. Fibre Disintegrating Co., where the Court held that a more purified form of something naturally occurring does not make it patentable subject matter.<sup>99</sup> If this line of reasoning had been applied, the patent in Parke-Davis would have been invalidated because it was nothing more than a purified naturally-occurring substance. Similar to tungsten, adrenaline was much more valuable and useful in its purified state, but the valuable characteristics were not given to adrenaline by the patent applicant.<sup>100</sup>

Moreover, even if Learned Hand's opinion had reflected the law at that time, the U.S. Supreme Court's subsequent decisions in Funk Bros and Chakrabarty, both decided after the adrenaline case, make clear that Hand's position should no longer be viewed as valid law.

#### Vitamin B<sub>12</sub>

Also prior to the U.S. Supreme Court's decision in Chakrabarty, the Fourth Circuit Court of Appeals in Merck & Co. v. Olin Mathieson Chemical Corp.<sup>101</sup> in 1958 upheld a patent on a specific form of B<sub>12</sub>, a product of nature, where the inventor claimed "a vitamin B<sub>12</sub>-active composition comprising recovered elaboration products of the fermentation of a vitamin B<sub>12</sub>-activity producing strain of Fungi selected from the class consisting of Schizomycetes, Torula, and Eremothecium, the L.L.D. activity of said composition being at least 440 L.L.D units per milligram and less than 1 million L.L.D. units per milligram."<sup>102</sup>

The defendant in an infringement suit asserted that the patent covered a product of nature, a Vitamin B<sub>12</sub> compound. The court held the patent claim valid, relying on the logic of the Parke-Davis adrenaline case. Despite the intervening case law of Funk Brothers and the cases holding uranium, ductile vanadium, and tungsten unpatentable, the court held a specific preparation of B<sub>12</sub> patentable because "it had never existed before."<sup>103</sup> The preparation required a

complicated series of previously-unknown steps, involving the specific addition and extraction of various materials. The court made clear that “[t]he claims do not cover vitamin B<sub>12</sub> from liver or any source other than the specified fermentations.”<sup>104</sup>

This is not an adequate precedent for genetic sequence patents because it only covers a substance that has been isolated and purified through a specific, previously-unknown process. In contrast to the specific B<sub>12</sub> recovery process, the process used for sequencing genes is not itself novel. It is routine. And, unlike in the instance of B<sub>12</sub>, the reach of the genetic sequence patents is too broad, allowing the holder to block the use of the genetic sequence even by those who have used a different method of sequencing the gene.

### Strawberry Flavor

Some proponents of gene patents use the case of Application of deC. Kratz<sup>105</sup> to support the position that patents should be granted on anything that can be “isolated and purified.” The case deals with a patent covering strawberry flavoring. Claim 17 of the application for a reissue of U.S. Patent No. 3,499,769, entitled “Process for Producing Strawberry Flavor Compositions and Products,” claimed a process of adding a synthetically produced substantially pure chemical, 2-methyl-2-pentenoic acid to food in order to produce a strawberry-like flavor or aroma. Claim 18 was directed to a composition made up of a synthetically-produced substantially pure chemical and some other flavor enhancing chemicals.<sup>106</sup> It claimed

A flavor modifying composition useful in imparting a strawberry flavor to a foodstuff consisting essentially of (i) from 1 to about 20% By weight of said flavoring composition of synthetically produced substantially pure 2-methyl-2-pentenoic acid and (ii) the remainder of said composition being at least one adjuvant for said 2-methyl-2-pentenoic acid, selected from the group consisting of geraniol, ethyl methyl phenyl glycidate, vanillin, ethyl pelargonate, isoamyl acetate, ethyl butyrate, naphthyl ethyl ether, ethyl acetate, isoamy butyrate, diacetyl, cinnamic acid, oil of cinnanmon and decalactone.<sup>107</sup>

The claims were rejected by the patent examiner under §103 as being obvious because “[t]he analysis of the natural constituents of foods is now conventional...” and the synthetic or substantially pure compound would be obvious over the natural constituent.<sup>108</sup> The Patent and Trademark Office Board of Appeals agreed with the patent examiner, and noted that substantially pure 2-methyl-2-pentenoic acid does not differ from that which occurs in the strawberry itself, its sole distinction being the claimed use in a composition to impart fruit flavor.<sup>109</sup>

Moreover, the examiner and the board cited a journal article (Bedoukin, 1973 page 3) which described the logic behind the ban on patents of products of nature.

“[C]onsider the case of a compound which plays a role in the flavor of peaches. The appearance of patents describing its importance in peach aroma, thereby preventing its usage by others, seems hardly fair or legal. It would be possible for a few major companies, with ample research facilities, to corner the market in the use of newly discovered natural components in plants or fruits. Each would prevent all the others, including the remaining minor firms, from developing a better product by using these natural components. The end result would certainly not be to the best advantage of the public.”<sup>110</sup>

The United States Court of Customs and Patent Appeals ruled in favor of granting the patent stating that at the time the invention was made, the prior art consisted only of the natural strawberry and its attendant taste.<sup>111</sup> Although the rejection had been made under the §103 obviousness standard, the appellate court sua sponte changed it to a §102 novelty analysis.<sup>112</sup> The court did not handle this as a §101 case. According to the appellate court, there was no basis found in the prior art for selecting 2-methyl-2-pentenoic acid and using it in compositions such as those claimed.<sup>113</sup> Moreover, because the claims were to compositions containing “substantially pure” 2-methyl-2-pentenoic acid and preparative methods thereof, and not 2-methyl-2-pentenoic acid in its “natural state,” the court held that the claims were novel since they did not cover any natural composition.<sup>114</sup>

Even though the case did not involve a §101 products of nature challenge, the court articulated a two-part test to determine whether a claimed invention so lacked novelty that it was nothing more than a natural composition.<sup>115</sup> First, the claimed composition must inherently contain the naturally-occurring compound.<sup>116</sup> Second, the claim must be of sufficient breadth to encompass both the known composition and the naturally occurring compound.<sup>117</sup> In considering the case, the Court of Customs and Patent Appeals in 1979 allowed the strawberry flavor patent claims because those claims “do not encompass natural compositions.”<sup>118</sup> In contrast, genetic sequence patents do encompass natural compositions, some directly and others due to the fact that the patent on the so-called isolated and purified sequence prevents others from using the whole natural sequence.

As in Parke-Davis & Co. v. H.K. Mulford Co., which dealt with the patentability of adrenaline, the case that should have been used as precedent was American Wood-Paper Co. v. Fibre Disintegrating Co., where the Court held that a more purified form of something naturally occurring does not make it patentable subject matter.<sup>119</sup> Neither the Court of Customs and Patent Appeals nor the inventors disputed that 2-methyl-2-pentenoic acid is a naturally-occurring constituent of strawberries, and according to Supreme Court precedent, a purified product of nature is unpatentable subject matter.<sup>120</sup>

Moreover, a recent decision by the Federal Circuit indicates that the current law is exactly as expressed by the patent examiner and patent board of appeals in this case – This purported invention does not meet the statutory requirement of non-obviousness. The Federal Circuit held that one expects a concentrated or purified ingredient to retain the same properties it exhibited in a mixture, and for those properties to be amplified when the ingredient is concentrated or purified.<sup>121</sup> Isolation of interesting compounds is a mainstay of the chemist’s

art, and if it is known how to perform such an isolation, doing so is likely the product not of innovation but of ordinary skill and common sense.<sup>122</sup>

Another ground for distinguishing the strawberry flavor patents is that a complicated process was used to create the synthesized flavor, which involved much more than just removing impurities.<sup>123</sup> Moreover, the flavor patent is narrowly applied to the particular compound claimed, in only its “substantially pure”<sup>124</sup> form and in some claims only when specific amounts are used,<sup>125</sup> while the reach of the gene sequence patents is much broader, allowing the holder to block the use of the genetic sequence even by those who have used a different method of sequencing the gene.

#### The Patenting of Genetic Material

Relying on the precedent of the out-dated and erroneous adrenaline case, proponents of human gene patents have successfully argued that the “isolation and purification” of a gene or other genetic material transforms it from a naturally-occurring product of nature to something new and useful for a specific purpose or function that does not naturally exist in nature. Amgen, Inc. v. Chugai Pharmaceutical Co. involved patent rights over the DNA sequences that encode human erythropoietin (EPO), a protein that stimulates red blood cell production.<sup>126</sup> The patent applicant claimed an isolated and purified form of a gene that codes for EPO, where “isolated and purified” meant that the applicant had identified and reproduced the coding region of the DNA outside of its natural environment. (Conley and Makowski, 2003 page 382)

The case focused on the issue of conception with regard to the specific requirement of written description, where an applicant must have a mental picture of the chemical structure or be able to define it by the method of preparation.<sup>127</sup> The Federal Circuit said that where an inventor is not able to envision the “detailed constitution of a gene so as to distinguish it from

other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e. until after the gene has been isolated.”<sup>128</sup> While acknowledging that the patent holder had not invented either EPO or the EPO gene, the court held that because they had “isolated and purified” the gene, they had fulfilled the patentability requirements of 35 U.S.C. § 102 and 112.<sup>129</sup> However, the court failed to conduct the appropriate patentable subject matter inquiry under §101. If U.S. Supreme Court precedent had been followed, the case would have resulted in a threshold finding that the sequence was in fact a product of nature and therefore not patentable subject matter. The only distinguishing factor between the claimed sequence and the sequence in human cells that code for EPO was the presence of the words “isolated” and “purified” within the patent claims, defined as removing the coding region of the relevant DNA. (Conley and Makowski, 2003 page 382) Subsequent federal cases, following Amgen, have continued to assume that specific patents covering human gene sequences are patentable where the applicant “isolated” and “purified” the gene.<sup>130</sup> Similar to the decision in Parke- Davis, the Amgen case and its progeny fail to even consider the product of nature doctrine explicitly and disregard the line of U.S. Supreme Court precedent that dictates that products of nature, even where purified, are not patentable subject matter under §101.<sup>131</sup>

Recent U.S. Supreme Court case law suggests an additional reason that genetic sequence patents might be vulnerable to a legal challenge. In 2007, the U.S. Supreme Court in KSR International Co. v. Teleflex, Inc.,<sup>132</sup> clarified the standards by patent applicants must meet to show their invention is non-obvious. Now it is more difficult to prove that the invention is non-obvious.

A subsequent decision in September 2007 by the U.S. Court of Appeals for the Federal Circuit stands for the proposition that an isolated and purified active ingredient may be obvious

unless the purification creates unexpected results.<sup>133</sup> The case arose as a patent infringement action over the pharmaceutical compound ramipril.<sup>134</sup> Addressing the question of what is the proper analysis for a claimed composition that is a purified form of a mixture that existed in the prior art, the Federal Circuit stated that “[i]f it is known that some desirable property of a mixture derives in whole or in part from a particular one of its components, or if the prior art would provide a person of ordinary skill in the art with reason to believe that this is so, the purified compound is prima facie obvious over the mixture even without an explicit teaching that the ingredient should be concentrated or purified.”<sup>135</sup> The court also said “[o]rdinarily, one expects a concentrated or purified ingredient to retain the same properties it exhibited in a mixture, and for those properties to be amplified when the ingredient is concentrated or purified.”<sup>136</sup> Further, the court said “[i]solation of interesting compounds is a mainstay of the chemist’s art,”<sup>137</sup> and that “[i]f it is known how to perform such an isolation doing so ‘is likely the product not of innovation but of ordinary skill and common sense.’”<sup>138</sup>

The Federal Circuit ultimately found Aventis’s ‘722 patent obvious, finding that a chemical compound in the prior art (SCH 31925) contained the claimed 5(S) ramipril and that it was either understood that 5(S) ramipril was the active ingredient, or that there was sufficient reason to look to 5(S) ramipril.<sup>139</sup> Aventis was unable to show unexpected results to rebut the prima facie case of obviousness.<sup>140</sup>

Proponents of gene patents argue that genetic sequences are patentable because they are isolated and purified and thus not in their naturally occurring state. However, after Aventis, it appears likely that gene patents will be found to be obvious and hence unpatentable because 1) the desirable property of a gene is derived from its coding region, therefore creating a prima facie case of obviousness; and 2) a prima facie case of obviousness could not be rebutted by

arguing unexpected results because an “isolated” and a “purified” gene retains the properties it exhibited in its natural form.

Since the method of isolation and purification has been used before, the method would be disclosed in the prior art. A person of ordinary skill in the art could then infer to isolate and purify a particular gene. For this reason, after KSR and Aventis, “isolated” and “purified” genetic sequences might be found to be unpatentable because they could not meet the requirement of non-obviousness.

### Why Haven't Gene Patents Been Challenged?

It is likely that if the U.S. Supreme Court were to hear a case involving genetic sequence patents, the Court would find them to be unpatentable products of nature. However, it is difficult for such a challenge to arise under U.S. law. The actors in the gene patent drama do not have an incentive to challenge the patentability of genes. The litigation about gene sequence patents generally has involved two parties who each claim to be the inventor of the genetic sequence. Both sides want genetic sequences to be patentable.

There are numerous scientific organizations and consumer groups in the United States that believe that genetic sequences are unpatentable products of nature.<sup>141</sup> But under U.S. law, generally only someone who is infringing the patent can challenge the patent (by arguing the invalidity of the patent as a defense to the infringement). Plus, the average patent lawsuit costs almost five million dollars. (American Intellectual Property Law Association, 2007 page 22) In Europe, members of the public (rather than just competing companies who infringe a patent) do have a voice in the patent application process or the right to challenge existing patents. In Europe, as a result of the opposition procedure which can be initiated by third parties, the patent

was revoked in approximately 41% of the cases, and in 30% of the cases the patent rights were restricted. (Graham, Hall, Harhoff, and Mowery, 2002)

### Underlying Policies of Article 1

The patent and copyright laws in the United States were developed in order to support the creation and sharing of ideas with an aim to distributing that knowledge to all citizens. The drafters of the Constitution, Article 1, section 8, clause 8 sought to give Congress the power to promote this widespread distribution of knowledge in the most effective way possible. The idea was to promote a large number of inventions in order to encourage other inventors to build on that knowledge and benefit society as a whole through dissemination of the information. However, patents for human genetic material directly threaten that idea, impeding further innovation.

The U.S. Supreme Court spoke on the motivation for the creation of a patent system in Graham et al. v. John Deere Co. of Kansas City et al.<sup>142</sup> After an extensive examination of constitutional history, the Court wrote:

...Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available. Innovation, advancement, and things which add to the sum of useful knowledge are inherent requisites in a patent system which by constitutional command must ‘promote the Progress of...useful Arts.’ This is the *standard* expressed in the Constitution and it may not be ignored.<sup>143</sup>  
[emphasis in opinion]

That same case addressed, in dicta, the need for a “discovery” to have a new and useful aspect to be afforded patent protection of an “invention”:

The patent monopoly was not designed to secure to the inventor his natural right in his discoveries. Rather, it was a reward, an inducement, to bring forth new knowledge. The grant of an exclusive right to an invention was the creation of society—at odds with the inherent free nature of disclosed ideas—and was not to be freely given. Only inventions and discoveries which furthered human knowledge, and were new and useful, justified the special inducement of a limited private monopoly.<sup>144</sup>

Many of the founders of the U.S. were wary of the patent system; they often wrote and spoke on the topic as a means to clarify the role of patents with respect to scientific

developments. Thomas Jefferson, the first administrator of the patent system, and author of the 1793 Patent Act, was concerned about the power of monopolies over science (Shulman, 1999 page 29). He believed that “ingenuity should receive a liberal encouragement.” (Jefferson, 1971 pages 75-76) He eventually became an ardent supporter and helped create the patent system, yet never sought a patent over any of his inventions. On the purpose and nature of the patent system, Jefferson once wrote:

He who receives an idea from me, receives instruction himself without lessening mine; as he who lights his taper at mine, receives light without darkening me. That ideas should freely spread from one to another over the globe, for the moral and mutual instruction of man, and improvement of his condition, seems to have been peculiarly and benevolently designed by nature, when she made them, like fire, expansible over space, without lessening their destiny in any point, and like the air in which we breathe, move, and have our physical being, incapable of confinement or exclusive appropriation.<sup>145</sup>

James Madison, writing in the Federalist (No. 43), argues that Article 1 and the development of patent laws would add to “the public good.” (Madison, 1961 pages 271-272)

It would be very difficult to argue that the granting of patents on genetic sequences has added to the public good. Patent law is supposed to be a bargain in which the patent holder gets the exclusive right to make, use, or sell the invention in exchange for publishing in the patent the description of the invention. Under U.S. patent law, the inventor can exclude anyone else from making, using, or selling the invention for 20 years. The inventor also has a right to charge a royalty to anyone who uses, makes, or sells the invention. This works well with a nuts and bolts invention. If you make a wooden mousetrap, I can use your description to invent a better one with metal, etc. However, the system breaks down if what you patent is information – such as the sequence of a gene. Then you have a right to prevent others from using that information entirely. Innovation is stifled and the basic patent bargain (exclusivity in exchange for information) is thwarted.

If a researcher wants to study a gene, he or she must obtain a license or infringe and risk treble damages. In fact, the researcher may have to obtain multiple licenses if patents have been granted on mutations in the gene. Some gene patent holders have stopped research on “their” genes by researchers at top universities, such as Yale, U.C.L.A. and the University of Pennsylvania. This is contrary to the purpose of the patent law – which is to stimulate innovation, not retard it. Gene patents are also the reason Americans are offered genetic tests that are inferior to those available in other countries. In countries where the breast cancer genes and hemochromatosis genes were not patented, and thus were freely available for all researchers to analyze, more mutations were discovered, allowing for better diagnostic testing.

In addition to hampering the development of diagnostics, gene patents hamper the development of cures. When a non-profit foundation and the American Neurological Association wanted to finance research to find a cure for a particular genetic disease, researchers were unwilling to undertake the work because of the potential for legal action against them by the holder of the patent.

In addition, gene patents interfere with medical care. Gene patents increase the cost of the diagnosis and treatment of genetic diseases. The patent holder can charge whatever it wants for any test analyzing the patented gene—even if that test uses a technology that was not invented by the patent holder. Myriad, which holds the patent on the BRCA1 and BRCA2 genes, charges \$2,900 for its genetic test for breast cancer. Already, one in four laboratories has stopped performing certain genetic tests because of patent restrictions or excessive royalty costs. (Cho, Illangasekare, Weaver, Leonard, and Merz 2003 pages 3-8) Half had not developed a test for fear of running afoul of patent law.

Furthermore, when a single entity controls all testing of a gene sequence, it might not provide the highest quality test or it may decide, for commercial reasons, not to offer testing for all the known mutations in the gene sequence. According to a study published in 2006, the test Myriad employs to detect breast cancer risk can miss mutations that help cause the disease. (Pollack, 2006 page 20) Myriad's protocol was to "sequence the exons and flanking regulatory regions of each gene and...to test for 5 specific larger mutations in BRCA1." (Walsh et. al, 2006 page 1379-1388) Because many mutations are inherently undetectable by short-range polymerase chain reaction (PCR)—the process Myriad used—Myriad's test was unable to detect them. (Walsh et. al, 2006 page 1379-1388)

In the study, researchers sampled DNA from 300 members of high-risk families in which four or more members had been diagnosed with either breast or ovarian cancer. (Walsh et. al, 2006 page 1379-1388) All 300 patients had received negative test results from Myriad. (Walsh et. al, 2006 1379-1388) The research team used six methods to search DNA for breast cancer gene mutations. (Walsh et. al, 2006 1379-1388) The researchers found that 12% of the patients studied carried rearrangements of BRCA1 or BRCA2 that were not included in Myriad's array. (Walsh et. al, 2006 1379-1388)

Some believe the number of missed mutations to be even higher. (Benowitz, 2002 page 80) According to Institute Curie geneticist Dr. Dominique Stoppa-Lyonett, the Myriad test may miss up to 20% of the expected BRCA1 mutations. (Benowitz, 2002 page 80) Myriad's patents extend to all methods of diagnosing the risk for hereditary breast and ovarian cancers based on comparing an individual's sequence with the company's BRCA sequences. (Benowitz, 2002 page 80) Stoppa-Lyonett claims that the company's patent is too broad because it prohibits

alternative techniques, such as DNA combing, from being used to detect mutations. (Benowitz, 2002 page 80)

Although alternative, less expensive methods exist to identify breast cancer gene mutations in a patient's DNA that could identify more mutations, they are not used clinically for genetic testing for breast cancer in the U.S. because of the Myriad patents. (Stockstad, 2006 page 20) Since Myriad does not make use of the other methods the researchers used, they are effectively cutting off the public from their use entirely. Dr. Mary-Claire King, a senior author of the 2006 study, maintained in an interview that "a fuller testing process would include more than one technology, and competition would enable that to develop." (Pollack, 2006 page 20)

The ability of a patent holder to prevent health care providers from using a patented genetic sequence denies people crucial medical information. Most drugs only work on a percentage of patients who use them. An asthma inhaler might only work on three of ten people to whom it is prescribed, causing the other seven to suffer symptoms of asthma and pay for an inappropriate drug until the right medication can be found. Genetic testing can help to distinguish those people for whom a drug will work from those people for whom it will not work, but, if the same entity holds the patents on the drugs and the gene sequences, it may prevent use of the gene sequence because the identification of people for whom the drug will not work will limit the market for the drug.

One company has filed for patent protection on a genetic sequence that could be analyzed in the blood of a prospective patient to determine whether their asthma drug will work for that patient. (Anand, 2001 page B.1) The company, however, has said that it will not develop the test – or let anyone else develop the test. (Anand, 2001 page B.1) While such a test would be crucial to doctors in determining which patients would benefit from the use of the asthma inhaler and

which patients would benefit from a different drug or treatment, it would also diminish the market for the company's drug because a trial use of its asthma inhaler would no longer be needed to determine if it would be an effective treatment.

In addition to the negative impact that gene patents have on access to and the quality of genetic testing, the possibility of patenting genes has caused some physicians and university researchers to view patients as treasure troves. Doctors, health care institutions, researchers and hospitals have gone to court to gain ownership of patients' cell lines, tissue, and genes in order to commercialize them, even over the patients' objections. Genetic research is being undertaken on people without their consent as researchers prospect for genes.

Without their knowledge or consent, the mutations in Dan Greenberg's and David Green's Canavan gene mutations were patented.<sup>146</sup> This prevents either man from donating their Canavan gene for use by other researchers and allows the patent holder to have a monopoly on (and charge whatever it wants for) assessing whether either man's children have inherited their father's mutation.

Moreover, the rationales given for the patenting of other health care products (such as drugs) do not support the patenting genes. Genes are inherently different than drugs. The approximately 30,000 genes in our bodies control several hundred-thousand biological proteins. (Greenpeace, 2004) Their main function is as encoded information. (Greenpeace, 2004)

There are fewer downsides to granting a patent on a drug or a medical device than granting a patent on a gene. The nature of genes makes them impossible to invent around. (Matthijs and Halley, 2002 page 784) In the case of drugs and pharmaceuticals, the disclosure of a new drug in a patent may motivate other researchers to find chemical analogs that may work better or in slightly different ways. (Boseley, 2007) Patented genetic sequences invite no such

innovation. A patent for a particular gene sequence patents the information contained in the sequence – for example the As, Ts, Cs, and Gs of the genetic code – and is therefore impossible to invent around. (Matthijs and Halley, 2002 page 784)

The discovery of genes does not require the same incentives as drug development. Molecular biologists were attempting to identify genes long before the U.S. Patent and Trademark Office adopted the position that genes could be patented. As opposed to the development of drugs, which is undertaken primarily with private funds (for which investors expect a commercial return), the discovery of genes has been undertaken with vast quantities of public funds.

Moreover, there are no expensive clinical trials when a gene is discovered and knowledge about the sequence of the gene is used to identify whether a particular patient has a mutation in that gene. In some cases, testing has begun almost immediately after a disease gene has been identified. Because the U.S. Food and Drug Administration (FDA) does not regulate the clinical services of genetic tests (as opposed to the sale of genetic diagnostic kits or gene therapies), there is no costly FDA approval process. Thus, even if one of the purposes of the patent law were to provide financial incentives for invention, the need to financially compensate a gene-discoverer is not as great as the need to compensate the developer of a drug that must take it through costly clinical trials, with only a small number of drugs actually becoming commercially-viable products.

Gene patents do not seem necessary to encourage technology transfer in the move from gene discovery to the availability of a genetic diagnostic test. As soon as information about the discovery of the hemochromatosis gene was published, laboratories began testing for mutations in the gene. After a patent on the gene was granted seventeen months later, 30% of the 119 U.S.

laboratories surveyed reported discontinuing or not developing a genetic test for the disease. The patent holder was asking for an up-front fee of \$25,000 from academic laboratories and as much as \$250,000 from commercial laboratories, plus a fee of \$20 per test. (Merz, Kriss, Leonard, and Cho, 2002 page 578) The patent interfered with clinical adoption of the test and potentially compromised the quality of testing by limiting the development of higher quality or lower cost alternative testing methods.

Originally, U.S. patent law forbade patents on health care inventions. (Portman, 1996 page 99) That changed in 1954. But when there is enough of an outcry from the public or the medical community, Congress and the courts<sup>147</sup> still protect health over patents in many instances. For example, in the mid-1990's, a doctor patented a method for performing cataract surgery and sued another doctor for using the technique without paying a royalty.<sup>148</sup> The American Medical Association amended its Code of Ethics to forbid doctors from patenting medical procedures (Merz, Cho, Roberston and Leonard, 1997 page 303) because it found that these patents compromised patient care. (Lee, 1997 page 703) Responding to the concerns raised by patients and by the medical profession, the U.S. Congress then created an exception in the patent law so that health care providers are not subject to patent infringement suits when they use a patented medical or surgical technique.<sup>149</sup> It would be well within the scope of Congress's authority to ban patents on nucleotide sequences to undo the mistake made by the patent office in granting them and to protect the public. This is the approach taken under a bill to ban gene patents, H.R. 977, which is currently pending in the U.S. Congress.

### Conclusion

A close analysis of the history of the U.S. patent laws and their interpretation by the U.S. Supreme Court over the past 150 years indicates that genetic sequences are unpatentable

products of nature. It is likely that, if the U.S. Supreme Court were to hear a case involving a products of nature challenge to gene patents, the Court would invalidate the patents. Allowing unhindered access to genetic sequences not only contributes to the public good, but could spur innovation.

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## Footnotes

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<sup>1</sup> 447 U.S. 303 (1980).

<sup>2</sup> Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980), citing Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

<sup>3</sup> United States Patent & Trademark Office, Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (2001).

<sup>4</sup> It would, of course, have to meet the other patent criteria of non-obviousness, usefulness, and novelty.

<sup>5</sup> Under 35 U.S.C. §101, any “new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement” is eligible subject matter for a patent. 35 U.S.C. §101 requires first that there be an invention and lists three additional requirements: novelty, utility, and statutory subject matter (i.e. “process, machine, manufacture, or composition of matter”). 35 U.S.C. §101. These three requirements have been determined to be “separate and distinct.” In re Bergy, 596 F.2d 952, 960 (CCPA 1979). The subject matter inquiry focuses on whether the invention claimed by the applicant is (or is not) a statutory process, machine, manufacture, or composition of matter, where the presence or absence of novelty and utility should not factor into the determination. John M. Conley and Robert Makowski, “Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part II),” 85 J. Pat. & Trademark Off. Soc’y 371, 374 (2003).

<sup>6</sup> 35 U.S.C. §112. Proper disclosure includes written description, enablement, best mode, and definiteness requirements.

<sup>7</sup> 35 U.S.C. §154.

<sup>8</sup> Brenner v. Manson, 383 U.S. 519, 536, 86 S. Ct. 1033, 1042 (1966). In the case of genetic material, the Federal Circuit has said “when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.” Amgen v. Chugai Pharmaceutical, 927 F.2d 1200, 1206 (Fed. Cir. 1991). USPTO 2001 guidelines regarding written description further clarify this requirement. United States Patent & Trademark Office, Guidelines for Examination of Patent Applications Under the 35 U.S.C. §112, ¶1, “Written Description” Requirement, 66 Fed. Reg. 1066 (2001). “Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. Patents and printed publications in the art should be relied upon to determine whether an art is mature and what the level of knowledge and skill is in the art. In most technologies which are mature, and wherein the knowledge and level of skill in the art is high, a written description question should not be raised for original claims even if the specification discloses only a method of making the invention and the function of the invention. In contrast, for inventions in emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession. For example, disclosure of only a method of making the invention and the function may not be sufficient to support a product claim other than a product-by-process claim. Furthermore, disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention.” Id. at 1106 (citations omitted).

<sup>9</sup> 35 U.S.C. §112.

<sup>10</sup> 35 U.S.C. §112.

<sup>11</sup> 35 U.S.C. §112.

<sup>12</sup> Laboratory Corp. of America Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 126-27 (2006) (J. Breyer, dissenting)

<sup>13</sup> See United States Patent & Trademark Office, Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (2001). “An isolated and purified DNA molecule that has the same sequence as a naturally-occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally-occurring compound.” Id.

<sup>14</sup> United States Patent & Trademark Office, Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (2001). The guidelines provide “[a]n isolated and purified DNA molecule that has the same sequence as a naturally occurring

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gene is eligible for a patents because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound.” *Id.*

<sup>15</sup> Utility Examination Guidelines, 66 Fed. Reg. 1092 (2001).

<sup>16</sup> Aside from the issue of patentable subject matter, current patent law requires that genetic material must also have a beneficial utility to society that is “substantial, specific, and credible” in order to be afforded patent protection. United States Patent & Trademark Office, Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (2001). Clarifications to the USPTO Utility examination guidelines in 2001 state:

If a patent application discloses only nucleic acid molecular structure for a newly discovered gene, and no utility for the claimed isolated gene, the claimed invention is not patentable. But when the inventor also discloses how to use the purified gene isolated from its natural state, the application satisfies the “utility” requirement. That is, where the application discloses a specific, substantial, and credible utility for the claimed isolated and purified gene, the isolated and purified gene composition may be patentable.

United States Patent & Trademark Office, Utility Examination Guidelines, 66 Fed. Reg. 1092, 1093 (2001).

<sup>17</sup> *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948).

<sup>18</sup> *American Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. (23 Wall.) 566 (1874).

<sup>19</sup> Patent Act of 1793, Ch. 11, 1 Stat. 318-323 (February 21, 1793), Sec. 2.

<sup>20</sup> 35 U.S.C. § 101 et seq.

<sup>21</sup> S. Rep. No. 82-1979, reprinted in U.S.C.C.A.N. 2394.

<sup>22</sup> *Diamond v. Chakrabarty*, 447 U.S. 303, 308-309 (1980). The court found that “the Patent Act of 1793, authored by Thomas Jefferson, defined statutory subject matter as ‘any new and useful art, machine, manufacture, or composition of matter, or any new or useful improvement [thereof].’ Act of Feb. 21, 1793, § 1, 1 Stat. 319. The Act embodied Jefferson’s philosophy that ‘ingenuity should receive a liberal encouragement.’ 5 Writings of Thomas Jefferson 75-76 (Washington ed. 1871). See *Graham v. John Deere Co.*, 383 U.S. 1, 7-10 (1966). Subsequent patent statutes in 1836, 1870, and 1874 employed this same broad language. In 1952, when the patent laws were recodified, Congress replaced the word ‘art’ with ‘process,’ but otherwise left Jefferson’s language intact. The Committee Reports accompanying the 1952 Act inform us that Congress intended statutory subject matter to ‘include anything under the sun that is made by man.’ S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952); H. R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952).”

<sup>23</sup> 35 U.S.C. §101.

<sup>24</sup> 35 U.S.C. §102.

<sup>25</sup> 35 U.S.C. §103.

<sup>26</sup> Patents Act of 1977, 1977 Chapter 37, §1(2)(a); United Kingdom Patent Office, at <http://www.patent.gov.uk/patent/howtoapply/index.htm>.

<sup>27</sup> Patents Act of 1977, 1977 Chapter 37, §1(2)(d); United Kingdom Patent Office, at <http://www.patent.gov.uk/patent/howtoapply/index.htm>.

<sup>28</sup> See, e.g., See European Patent Convention, Article 99 (1998), available at <http://www.european-patent-office.org/legal/epc/>, at Article 52(2); Hungarian Law on the Protection of Inventions by Patents, Art. 1, §2(a), available at <http://www.hpo.hu/Magyar/ipjvtv/shlaw.cgi?e9533:1pC> (last visited Feb. 19, 2004)(nothing that “discoveries, scientific theories, and mathematical methods” are not patentable); See also, Carlos M. Correa, “Internationalization of the Patent System and New Technologies,” 20 *Wisc. Int’l L.J.* 523, 528 (2002); Ikechi Mgbeoji, “Patents and Traditional Knowledge of the Uses of Plants: Is A Communal Patent Regime Part of the Solution To the Scourge of Bio Piracy?,” 9 *Ind. J. Global Legal Stud.* 163, 181 n. 74 (2001).

<sup>29</sup> See European Patent Convention, Article 99 (1998), available at <http://www.european-patent-office.org/legal/epc/>, at Article 52(2).

<sup>30</sup> See European Patent Convention, Article 99 (1998), available at <http://www.european-patent-office.org/legal/epc/>, at Article 52(2).

<sup>31</sup> Directive 98/44/EC of the European Parliament and of the Council of the European Union on the Legal Protection of Biotechnological Inventions, July 6, 1998, Article 16.

<sup>32</sup> See for example, *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948); *American Wood-Paper Co v. Fibre Disintegrating Co.*, 90 U.S. (23 Wall.) 566 (1874); *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). Recently, in *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred International*, a 2001 case involving a plant patent, the U.S. Supreme Court cited *Chakrabarty* for the long-standing notion that under the product of nature doctrine the “relevant

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distinction” for §101 purposes is not “between living and inanimate things, but between products of nature, whether living or not, and human-made inventions.” J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred International, 534 U.S. 124, 134 (2001), quoting Diamond v. Chakrabarty, 447 U.S. 303, 313 (1980). This case dealt with the Plant Variety Protection Act, where the product of nature doctrine was revisited in an effort to analyze the original Plant Patent Act of 1930.

<sup>33</sup> Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948). Funk asserted that patents cannot be awarded for “manifestations of ... nature, free to all men and reserved exclusively to none.” Id. The Court relied on existing precedent in this decision. O’Reilly v. Morse, 15 How. 62, 112-121 (1854); Le Roy v. Tatham, 14 How. 156, 175 (1853).

<sup>34</sup> Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).

<sup>35</sup> 35 U.S.C. §101. The term “invention” is defined in 35 U.S.C. §100 as an “invention or discovery.”

<sup>36</sup> Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 128 (1948). The claim read: “An inoculant for leguminous plants comprising a plurality of selected mutually non-inhibitive strains of different species of bacteria of the genus *Rhizobium*, said strains being unaffected by each other in respect to their ability to fix nitrogen in the leguminous plant for which they are specific.” Id.

<sup>37</sup> Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).

<sup>38</sup> Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).

<sup>39</sup> Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

<sup>40</sup> Diamond v. Chakrabarty, 447 U.S. 303 (1980). Chakrabarty court fully distinguished Funk by stating that in Funk there was merely the discovery of a natural possibility, which was the combination of root bacteria. On the other hand, in the present case, the inventor had “produced a new bacterium with markedly different characteristics from any found in nature.” Id. at 310. The Court said that “His discovery is not nature’s handiwork, but his own: accordingly, it is patentable subject matter under §101.” Id. at 310. Thus, the inventor had “intervened at the genetic level to make something that nature had not and, apparently, could not.” John M. Conley and Robert Makowski, “Back to the Future: Rethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part II),” 85 *J. Pat. & Trademark Off. Soc’y* 371, 375 (2003). See discussion of Chakrabarty *infra*.

<sup>41</sup> Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980). “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.” Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980), *citing* Parker v. Flook, 437 U.S. 584 (1978); Gottschalk v. Benson, 409 U.S. 63, 67 (1972); Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948); O’Reilly v. Morse, 15 How. 62, 112-121 (1854); Le Roy v. Tatham, 14 How. 156, 175 (1853).

<sup>42</sup> Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980)

<sup>43</sup> Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980), *citing* Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948).

<sup>44</sup> Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980), *quoting* S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952) and H. R. Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952).

<sup>45</sup> Senate Report No. 1979, 82d Cong., 2d Sess. (1952) (emphasis added)

<sup>46</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 594 (1874).

<sup>47</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 607(1874).

<sup>48</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 594 (1874).

<sup>49</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 594 (1874).

<sup>50</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 593-94 (1874).

<sup>51</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 593 (1874).

<sup>52</sup> Cochrane v. Badische Anilin & Soda Fabric, 111 U.S. 293, 4 S. Ct. 455 (1884).

<sup>53</sup> Cochrane v. Badische Anilin & Soda Fabric, 111 U.S. 293, 311-312, 4 S. Ct. 455, 464-465 (1884).

<sup>54</sup> Cochrane v. Badische Anilin & Soda Fabrik, 111 U.S. 293, 296, 4 S. Ct. 455, 456 (1884).

<sup>55</sup> Cochrane v. Badische Anilin & Soda Fabrik, 111 U.S. 293, 312, 4 S. Ct. 455, 465 (1884).

<sup>56</sup> Ex Parte Latimer, 1889 Dec. Comm’r Pat. 123, 123 (1889).

<sup>57</sup> Ex Parte Latimer, 1889 Dec. Comm’r Pat. 123, 125-26 (1889).

<sup>58</sup> Ex Parte Latimer, 1889 Dec. Comm’r Pat. 123, 125, 127 (1889).

<sup>59</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>60</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 642 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>61</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 642 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>62</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 643 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>63</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 643 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>64</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 642 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>65</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 642 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>66</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 643 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

The Court further noted in response to the issue of who gave the ductility and high tensile strength to tungsten as claimed in the second portion of one of the claims, “Did [the inventor] give those qualities to ‘substantially pure tungsten’? We think not for it is now conceded that tungsten pure is ductile cold. If it possess that quality now it is certain that it possessed it always. Therefore...[it is] merely a correct description of the first part [of the claim] and the first part broadly claims as an invention a product of nature in the form of a chemical element for which a product claim is distinguished from a process claim cannot be validly awarded.” *Id.*

<sup>67</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 643 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>68</sup> General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 643 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929).

<sup>69</sup> In re Merz, 25 C.C.P.A. 1314, 1316 (CCPA 1938), where the Court denied a patent on purified ultramarine dye produced with a new process even though dye was brighter in color than other types of aquamarine. “No new use is claimed for [the applicant’s] purified ultramarine. It is the same old aquamarine with the same old use even though it may have brighter color and be more desirable as a pigment than formerly.” *Id.*, at 1317. *See also In re Marden*, 47 F.2d 957, 957-58 (CCPA 1931)(Marden I), where purified uranium treated to enhance ductility could not be patented, but the process could; In re Marden, 47 F.2d 958, 959 (CCPA 1931)(Marden II), where purified vanadium “not new in the inventive sense, and, it being a product of nature, no one is entitled to a monopoly of the same.” *Id.*, at 1059; In re Ridgeway, 76 F.2d 602 (CCPA 1935), where the PTO patent rejection was affirmed on purified chemical product (crystalline alpha alumina). The court said that a product is not saved from being unpatentable subject matter because it contains some impurities; “...a natural product with slight impurities would not be patentable as such over the same natural product slightly less pure.” *Id.*, at 603.

<sup>70</sup> In re Merz, 25 C.C.P.A. 1314, 1317 (CCPA 1938).

<sup>71</sup> In re Merz, 25 C.C.P.A. 1314, 1317 (CCPA 1938).

<sup>72</sup> In re Marden, 18 C.C.P.A. 1046; 47 F.2d 957 (CCPA 1931)(Marden I).

<sup>73</sup> In re Marden, 18 C.C.P.A. 1046, 1047, 47 F.2d 957 (CCPA 1931)(Marden I).

<sup>74</sup> In re Marden, 18 C.C.P.A. 1046, 1048, 47 F.2d 957 (CCPA 1931)(Marden I).

<sup>75</sup> In re Marden, 18 C.C.P.A. 1057, 1059, 47 F.2d 958 (CCPA 1931)(Marden II).

<sup>76</sup> In re Marden, 18 C.C.P.A. 1057, 1058 47 F.2d 958 (CCPA 1931)(Marden II).

<sup>77</sup> In re Marden, 18 C.C.P.A. 1057, 1059, 47 F.2d 958 (CCPA 1931)(Marden II).

<sup>78</sup> Thus, it would be unpatentable under the logic of General Electric Co. v. DeForest Radio Co., 28 F.2d 641, 642 (3<sup>rd</sup> Cir. 1928), *cert. denied* 278 U.S. 656 (1929) and American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566 (1874).

<sup>79</sup> Thus, it would be unpatentable under the logic of Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948).

<sup>80</sup> *See, e.g.*, Patent No. 6,762,293, “Diagnostics and therapeutics for autosomal dominant hemochromatosis.” Claim 1 of that patent reads as follows: “An isolated DNA sequence comprising SEQ ID NO: 1 or the complement.”

<sup>81</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566, 594 (1874).

<sup>82</sup> Dennis v. Pitner, 106 F. 2d 142 (7<sup>th</sup> Cir. 1939), *cert. denied* 308 U.S. 606 (1939).

<sup>83</sup> Dennis v. Pitner, 106 F. 2d 142, 143 (7<sup>th</sup> Cir. 1939).

<sup>84</sup> Dennis v. Pitner, 106 F. 2d 142, 143 (7<sup>th</sup> Cir. 1939), *citing* U.S. Pat. No. 18,667 for a “Vermifuge and Insecticide.”

<sup>85</sup> 106 F. 2d 142, 144 (7<sup>th</sup> Cir. 1939), *cert. denied* 308 U.S. 606 (1939).

<sup>86</sup> Dennis v. Pitner, 106 F. 2d 142, 145 (7<sup>th</sup> Cir. 1939).

<sup>87</sup> Dennis v. Pitner, 106 F. 2d 142, 145 (7<sup>th</sup> Cir. 1939).

<sup>88</sup> Interestingly, in its application of this language the court also contradicts itself. The relevant claims covered only the chemical make-up of the cube root, not its interaction with the insect that created a “new phenomenon.” The court allowed the patent applicant to claim not only use of the cube root as an insecticide via the interaction of the ground cube root with the breath of an insect (resulting in the death of the insect), but also the existing cube root itself even when not paired with the breath of the insect (and therefore not an insecticide).

<sup>89</sup> Parke-Davis & Co. v. H.K. Mulford & Co., 189 F.95 (C.C.S.D.N.Y 1911), *aff’d in part, rev’d in part*, 196 F. 496 (2d Cir. 1912).

<sup>90</sup> Buck v. Bell, 274 U.S. 200 (1927).

<sup>91</sup> Parke-Davis & Co. v. H.K. Mulford & Co., 189 F.95, 103 (C.C.S.D.N.Y 1911), *aff’d in part, rev’d in part*, 196 F. 496 (2d Cir. 1912). Subsequent appeal to the Second Circuit resulted in the decision being affirmed in part, reversed in part. Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156 (4<sup>th</sup> Cir. 1958).

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The reversal in part dealt merely with three claims that the Second Circuit felt were not necessary for a determination of the case at bar. Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156, 157 (4<sup>th</sup> Cir. 1958).

<sup>92</sup> Parke-Davis & Co. v. H.K. Mulford & Co., 189 F.95, 103 (C.C.S.D.N.Y 1911), *aff'd in part, rev'd in part*, 196 F. 496 (2d Cir. 1912). Within a product patent, the inventor claimed a “substance possessing the physiological characteristics and reactions for the suprarenal glands in stable and concentrated form, and practically free from inert and associated gland tissue.” U.S. Pat. No. 730,176 (issued June 2, 1903). (The patent uses “practically free from inert and associated gland-tissue” to describe the level of purity of the adrenaline. In the opinion, Judge Hand uses the terms “relatively pure” and “substantially pure” interchangeably to describe the level of purification. To determine whether Adrenaline was itself “practically free,” Judge Hand looked at the results of several chemical experiments examining the level of purity of Adrenaline. He then concluded, based on the intravenous use of Adrenaline, that it was shown to be “practically free” as described in the patent. Judge Hand also makes no mention of “concentrated form” in his decision in Parke-Davis).

<sup>93</sup> U.S. Pat. No. 730,176.

<sup>94</sup> Union Carbide Co. v. American Carbide Co., 181 F. 104 (2d Cir. 1910).

<sup>95</sup> Kuehmsted v. Farbenfabriken of Elberfeld Co., 179 F. 701 (7<sup>th</sup> Cir. 1910), *cert. denied* 220 U.S. 622 (1911).

<sup>96</sup> Parke-Davis & Co. v. H.K. Mulford & Co., 189 F.95 103, (C.C.S.D.N.Y 1911), *aff'd in part, rev'd in part*, 196 F. 496 (2d Cir. 1912).

<sup>97</sup> Union Carbide Co. v. American Carbide Co., 181 F. 104 (2d Cir. 1910).

<sup>98</sup> Kuehmsted v. Farbenfabriken of Elberfeld Co., 179 F. 701 (7<sup>th</sup> Cir. 1910), *cert. denied* 220 U.S. 622 (1911).

<sup>99</sup> 90 U.S. (23 Wall.) 566 (1874).

<sup>100</sup> In Union Carbide Co. v. American Carbide Co., the inventor had claimed a man-made substance, calcium carbide, in the crystalline form. Union Carbide Co. v. American Carbide Co., 181 F. 104, 104 (2d Cir. 1910). The Second Circuit was asked to determine the validity of the patent for this new form of calcium carbide. Previously, calcium carbide had been available only as an amorphous solution. Union Carbide Co. v. American Carbide Co., 181 F. 104, 104-105 (2d Cir. 1910). The court found that a “[m]ere change of form in and of itself does not disclose novelty,” but where there was a commercial value in the new form, there was novelty. Union Carbide Co. v. American Carbide Co., 181 F. 104, 107 (2d Cir. 1910). The court said “[c]rystalline carbide...has been a great commercial success, and has furnished the foundation for important industries.” *Id.* at 107. This case involved a human-made, not a natural, product where the court relied on a §102 novelty inquiry to find a “patentable difference in the purified form of an originally man-made chemical, the difference giving rise to a new use.” Richard Seth Gipstein, “The Isolation and Purification Exception to the General Unpatentability of Products of Nature,” 4 Columbia Science and Technology Law Review 2 (2002-2003). This is relevant in showing that the calcium carbide had already passed the §101 patentable subject matter inquiry since it was a human-made substance rather than a product of nature.

Likewise, in Kuehmsted, the Seventh Circuit set out to determine the validity of a patent for Aspirin, an already known human-made substance, but in a more purified form brought about by the addition of another substance. Kuehmsted v. Farbenfabriken of Elberfeld Co., 179 F. 701, 705 (7<sup>th</sup> Cir. 1910), *cert. denied* 220 U.S. 622 (1911).

The plaintiff had claimed infringement of a patent covering purified acetyl salicylic acid (aspirin) where the defendant marketed acetyl salicylic acid in its impure form, which was chemically the same as the plaintiff’s patented product but acted differently within the body when ingested. Kuehmsted v. Farbenfabriken of Elberfeld Co., 179 F. 701, 703 (7<sup>th</sup> Cir. 1910), *cert. denied* 220 U.S. 622 (1911). The patent at issue claims only the product, purified acetyl salicylic acid. “...I claim...a new article of manufacture the acetyl salicylic acid having the formula: O-COCH<sub>3</sub>/COOII being when crystallized from drychloroform in the shape of white glittering needles, easily soluble in benzene, alcohol and glacial acetic acid, difficulty soluble in cold water, being split by hot water into acetic acid and salicylic acid, melting at about 13500 centigrade, substantially as hereinbefore described.” U.S. Pat. No. 644077. Within the patent, the purification process is essentially described as heating salicylic acid with acetic anhydride to produce a crystalline form. “A mixture prepared from fifty parts of salicylic acid and seventy five parts of acetic anhydride is heated for about two hours at about 1500 centigrade in a vessel provided with a reflux condenser. Thus a clear liquid is obtained, from which on cooling a crystalline mass is separated, which is the acetyl salicylic acid. It is freed from the acetic anhydride by pressing and then recrystallized from dry chloroform. The acid is thus obtained in the shape of glittering white needles melting at about 1357 centigrade, which are easily soluble in benzene, alcohol, glacial acetic acid, and chloroform, but difficulty soluble in cold water.”

The court found that “a chemical formula is simply the symbolical expression of the composition or constitution of a substance...That is to say, two substances, having the same chemical formula, may differ widely, as to impurities, upon qualitative analysis.” 179 F. 701, 703-704 (7<sup>th</sup> Cir. 1910). The patented product, aspirin, was distinct from

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previous acetyl salicylic acid products in that the salicylic acid was held tightly in bond as it passed through the stomach and was set free in the intestines where it was effective as a therapeutic agent. Thus, the aspirin did not break apart in the stomach as a result of the acidic fluids as the impure form did and instead is split apart by the alkaline fluids of the intestines. 179 F. 701, 704 (7<sup>th</sup> Cir. 1910).

It is relevant to note that in both Union Carbide and Kuehmsted, the Second and Seventh Circuits, respectively, found that novelty existed where there was a new form of an already known man-made substance because of an increased commercial or therapeutic value. This is distinct from the Parke-Davis case which involved a patent for a purified form of a substance that is naturally-occurring within the human body.

<sup>101</sup> Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156 (4<sup>th</sup> Cir. 1958).

<sup>102</sup> Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156, 157 (4<sup>th</sup> Cir. 1958).

<sup>103</sup> Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156 (4<sup>th</sup> Cir. 1958).

<sup>104</sup> Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156, 160 (4<sup>th</sup> Cir. 1958)

<sup>105</sup> Application of deC. Kratz, 592 F.2d 1169 (CCPA 1979).

<sup>106</sup> Claims 17 and 18 appear as claims 13 and 14, respectively, in Processes for Producing Strawberry Flavor Compositions and Products, Reissue of Patent No. 3,499,769 (filed Sep. 14, 1966)(issued Aug. 5, 1980). No appeal was taken from the decision of the Patent and Trademark Office Board of Appeal affirming the rejection of claims 9, 10, 14 and 15 of the application for a reissue of U.S. Patent No. 3,499,769. Four less claims appear in the patent than the application, so claims 17 and 18 in the application became claims 13 and 14, respectively, in the patent. (*see* Application of deC. Kratz, 592 F.2d 1169 (CCPA 1979).)

<sup>107</sup> Quoted in Application of deC. Kratz, 592 F.2d 1169, 1172 (CCPA 1979).

<sup>108</sup> Application of deC. Kratz, 592 F.2d 1169, 1172 (CCPA 1979).

<sup>109</sup> Application of deC. Kratz, 592 F.2d 1169, 1172 (CCPA 1979).

<sup>110</sup> Quoted in the appellate decision of Application of deC. Kratz, 592 F.2d 1169, 1171 (CCPA 1979).

<sup>111</sup> Application of deC. Kratz, 592 F.2d 1169, 1172 (CCPA 1979).

<sup>112</sup> Application of deC. Kratz, 592 F.2d 1169, 1172 (CCPA 1979).

<sup>113</sup> Application of deC. Kratz, 592 F.2d 1169, 1172 (CCPA 1979).

<sup>114</sup> Application of deC. Kratz, 592 F.2d 1169, 1174 (CCPA 1979).

<sup>115</sup> Application of deC. Kratz, 592 F.2d 1169, 1174 (CCPA 1979).

<sup>116</sup> Application of deC. Kratz, 592 F.2d 1169, 1174 (CCPA 1979).

<sup>117</sup> Application of deC. Kratz, 592 F.2d 1169, 1174 (CCPA 1979).

<sup>118</sup> Application of deC. Kratz, 592 F.2d 1169, 1174 (CCPA 1979).

<sup>119</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566 (1874).

<sup>120</sup> American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566 (1874).

<sup>121</sup> Aventis Pharm Deutschland v. Lupin, LTD., 499 F.3d 1293, 1302 (Fed.Cir. 2007).

<sup>122</sup> Aventis Pharm Deutschland v. Lupin, LTD., 499 F.3d 1293, 1302 (Fed.Cir. 2007).

<sup>123</sup> Isolation Method: Taken from Mussinan and Walradt, "Organic Acids from Fresh California Strawberries," 23 J. Agric. Food Chem. 482 to 484 (1975), written by the patent holders, published after the initial application and discussed during the reissue prosecution.

#### Physical Preparation

- Fresh (not-frozen) strawberries, ground in a blender for 15 seconds.
- Slurry transferred to a glass funnel fitted with a coarse fritted disk and allowed to sit until the seeds and other particulate matter separated.
- Slurry then filtered under nitrogen pressure, then the funnel was back-flushed by forcing nitrogen back up the disk.
- Extraction
  - Filtrates were extracted in a separatory funnel in several portions.
    - Initial extraction was done with distilled diethyl ether containing 10% methanol to reduce emulsification. The resulting emulsion was broken by filtration through absorbent cotton.
    - The two succeeding extractions were carried out with virtually no emulsion.
- Acid Isolation
  - The ether phase of the acids were extracted with three volumes of 5% sodium carbonate.
  - The carbonate extract was acidified with 2N hydrochloric acid and back extracted with diethyl ether.

- The extract was dried over anhydrous sodium sulfate and concentrated by distillation.
- The solvent was evaporated with nitrogen.
- Derivation and Analysis
  - The acid salts were “esterfied” with BF<sub>3</sub>-Methanol.
  - The Reaction mixture was placed into a seperatory funnel with distilled water and extracted with three aliquots of distilled Freon 11.
  - The extract was washed with distilled water and the solvent removed under a stream of nitrogen.
  - The extract was finally analyzed using a standard Gas-Chromatography/Mass Spectrometer

<sup>124</sup> Application of deC. Kratz, 592 F.2d 1169 (CCPA 1979).

<sup>125</sup> Processes for Producing Strawberry Flavor Compositions and Products, Reissue of Patent No. 3,499,769 (filed Sep. 14, 1966)(issued Aug. 5, 1980).

<sup>126</sup> Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1203 (Fed. Cir. 1991).

<sup>127</sup> See 35 U.S.C. §112.

<sup>128</sup> Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991).

<sup>129</sup> Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991).

<sup>130</sup> See In re Wallach, 378 F.3d 1330 (Fed. Cir. 2004); Noelle v. Lederman, 355 F.3d 1343 (Fed. Cir. 2004); Carnegie Mellon Univ. v. Hoffman La Roche Inc., 148 F. Supp.2d 1004 (N.D. Cal. 2001); Chiron Corp. v. Abbott Lab., 902 F. Supp. 1103 (N.D. Cal. 1995); Univ. of Cal. V. Eli Lilly & Co., 39 USPQ (BNA) 1225 (S.D. Ind. 1995).

<sup>131</sup> Diamond v. Chakrabarty, 447 U.S. 303 (1980); Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 130 (1948); American Wood-Paper Co. v. Fibre Disintegrating Co., 90 U.S. (23 Wall.) 566 (1874).

<sup>132</sup> KSR International Co. v. Teleflex, Inc., 127 S. Ct 1727 (2007).

<sup>133</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293 (Fed. Cir. 2007).

<sup>134</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293, 1294 (Fed. Cir. 2007).

<sup>135</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293, 1301 (Fed. Cir. 2007).

<sup>136</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293, 1302 (Fed. Cir. 2007).

<sup>137</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293, 1302 (Fed. Cir. 2007).

<sup>138</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293, 1302 (Fed. Cir. 2007) (citing KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727, 1742 (2007)).

<sup>139</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293, 1302 (Fed. Cir. 2007).

<sup>140</sup> Aventis Pharma Deutschland GMBH v. Lupin, Ltd., 499 F.3d 1293, 1302 (Fed. Cir. 2007).

<sup>141</sup> See, e.g., American College of Medical Genetics, “Position Statement on Gene Patents and Accessibility of Gene Testing” (“Genes and their mutations are naturally occurring substances that should not be patented.”), available at <http://www.acmg.net/resournces/policies/pol-015.asp>.

<sup>142</sup> 383 U.S. 1, 86 S. Ct. 684 (1966).

<sup>143</sup> Graham et al. v. John Deere Co. of Kansas City et al., 383 U.S. 1, 6, 86 S. Ct. 684, 688 (1966).

<sup>144</sup> Graham et al. v. John Deere Co. of Kansas City et al., 383 U.S. 1, 8, 86 S. Ct. 684, 689 (1966).

<sup>145</sup> Graham et al. v. John Deere Co. of Kansas City et al., 383 U.S. 1, 9, 86 S. Ct. 684, 689 (1966), citing VI Writings of Thomas Jefferson, at 180-181 (Washington ed.).

<sup>146</sup> U.S. Pat. No. 5,679,635, “Aspartoacylase gene, protein, and methods of screening for mutations associated with Canavan disease.”

<sup>147</sup> Sometimes courts, too, eschew patent rights to protect public health. In City of Milwaukee v. Activated Sludge, Inc., the patentee had patented a process for treating sewage and sought an injunction to close down a municipal sewage treatment facility on the grounds of patent infringement. The Seventh Circuit refused to issue the injunction. The court specifically noted that “where, as here, the health and the lives of more than a half million people are involved, we think no risk should be taken . . . .” (City of Milwaukee v. Activated Sludge, Inc., 69 F.2d 577, 593 (7th Cir. 1934)). The court was concerned that, while both parties had strong equities, “there are many others who are indirectly concerned whose equities are even stronger than those of the parties.” Id. The U.N. Human Rights Commission in April 2001 urged all states to ensure that “the application of international agreements is supportive of public health policies which promote broad access to safe, effective and affordable preventive, curative or palliative pharmaceutical and mechanical technologies.” (*Access to Medication in the Context of Pandemics Such as HIV/AIDS*, United Nations Commission on Human Rights Resolution 2001/33, 71st meeting, April 23, 2001).

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<sup>148</sup> Pallin v. Singer, 36 U.S.P.Q.2d 1050 (D. Vt. 1995). The case was settled with a career judgment barring Dr. Pallin from enforcing the patent.

<sup>149</sup> 35 U.S. Code § 287(c).