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Dicta on Adrenalin(e): Myriad Problems with Learned Hand's Product-of-Nature

Pronouncements in *Parke-Davis v. Mulford*

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In April 1911, Judge Learned Hand ruled in a U.S. District Court for the Southern District of New York that “Adrin”—a therapeutic version of the hormone adrenaline marketed by H.K. Mulford Co.—infringed on patents licensed to Parke-Davis & Co., which sold a similar product under the

trademark “Adrenalin.”² Half a century later, in 1961, the lead sentence of Learned Hand’s front-page obituary in the *New York Times* would name him “the greatest jurist of his time.”³ Now—a full century after *Parke-Davis v. Mulford*—intense debate swirls on the legitimacy of what many per-

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² *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). The trademarked name held by Parke-Davis, “Adrenalin,” differs only slightly from a generic term for the hormone (or endocrine): “adrenaline.” Another generic name for the same hormone/endocrine is “epinephrine,” which is more commonly used in scientific circles. I will generally use “Adrenalin” when referring to the medical product and “adrenaline” when referring to the naturally occurring hormone. There is also some potential linguistic confusion regarding the gland in which this hormone is found, which is known as either the “suprarenal gland” or the “adrenal gland.” The term “suprarenal” was more commonly used in the early twentieth century, so I will generally use this name for the gland.

³ *Judge Learned Hand Dies; On U.S. Bench 52 Years*, N.Y. TIMES, Aug. 19, 1961, at 1.

ceive as Hand's central holding in the case: an isolated or purified natural substance can be a good subject for a patent.

The current controversy was sparked in May of 2009 when a consortium of medical societies, researchers, physicians, and patients filed a lawsuit aimed to invalidate patents on two sections of human DNA that serve as markers for breast cancer.⁴ These plaintiffs asserted that granting patents on naturally occurring genes "violate[d] long established legal principles that prohibit the patenting of laws of nature, products of nature, and abstract ideas."⁵ The suit was brought against Myriad Genetics, a Utah-based corporation, and the University of Utah Research Foundation, which jointly hold patents on these genes. In addition, the plaintiffs named the U.S. Patent and Trademark Office (USPTO) as a defendant, arguing that the agency should not have issued these patents in the first

place. But the USPTO was not breaking new ground in granting the patents at stake in *Myriad*. In fact, more than 2,500 patents have been issued with claims to "isolated DNA" during recent years.⁶ The validity of all these patents—and others that might be (or might not be) granted in the future—will likely turn on the final outcome of the *Myriad* lawsuit. And observers widely agree that the answer to the fundamental question raised in *Myriad* will eventually be provided by the U.S. Supreme Court.⁷

The attorneys for the patent holders in *Myriad* have built much of their defense around Learned Hand's positive assessment of the patentability of purified products of nature in *Parke-Davis v. Mulford*.⁸ Judge Robert W. Sweet—one of Hand's judicial successors in the Southern District of New York—who handled the first round of the case, was not, however, convinced.⁹ On March 29, 2010, he rocked

4 Complaint, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad*), 702 F. Supp. 2d 181 (S.D.N.Y. 2010), as amended (Apr. 5, 2010), *aff'd in part, rev'd in part*, 653 F.3d 1329 (Fed. Cir. 2011), (No. 09-CV-4515), 2009 WL 1343027.

5 *Id.* at 2. The Supreme Court has offered a similar summary of the general limits of patentable subject matter: "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); *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948)).

6 The appellant-defendants in *Myriad* claim that 2,645 patents have been granted "with claims to 'isolated DNA'" in recent years. Brief for the Appellants, Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad*), 653 F.3d 1329 (Fed. Cir. 2011), (No. 2010-1406), 2010 WL 4600106. See also, e.g., DAVID KOEPEL, WHO OWNS YOU? THE CORPORATE GOLD RUSH TO PATENT YOUR GENES (2009).

7 See, e.g., Posting of Catherine Saez to Intellectual Property Watch, *Myriad Outcome: Winds Shift Again for Gene Patenting in the U.S.*, <http://www.ip-watch.org/weblog/> (last visited Aug. 2, 2011, 3:45 pm); *Federal Circuit: Isolated Human DNA Molecules are Patentable*, PatentlyO, <http://www.patentlyo.com> (last visited July 29, 2011, 12:32 pm); Lori Valigra, *Appeals Court Says Genes Can Be Patented; More Legal Battles Likely*, <http://www.masshightech.com> (last visited Aug. 1, 2011).

8 The second paragraph of a key defendant's brief begins as follows: "As to the 'isolated DNA' claims, summary judgment in Myriad's favor is compelled by a long and unbroken line of authority . . . starting with this Court's seminal decision in *Parke-Davis & Co. v. H.K. Mulford Co.*" Myriad Defendants' Memorandum in Reply to Plaintiffs' Opposition to Myriad Defendants' Motion for Summary Judgment at 3, *Myriad*, 702 F. Supp. 2d 181 (No. 09-CV-4515), 2010 WL 1048411. This brief also contains several other references to *Parke-Davis* and ends with the following invocation of Judge Hand's 1911 statements on isolated products of nature: "It is difficult to overstate the sweeping nature of plaintiffs' arguments. Were they accepted, almost 100 years of jurisprudence would be swept away—from Learned Hand's *Parke-Davis* opinion to the USPTO's recent guidelines on the issuance of gene patents, which synthesized all of this law and reached the considered conclusion that patent claims such as Myriad's claim patent-eligible subject matter." *Id.* at 17. See also Brief for the Appellants, *supra* note 6, at 39–40.

9 Judge Sweet explicitly recognized the centrality of *Parke-Davis* to the defendants' arguments: "Myriad has relied heavily on the holding of the Honorable Learned Hand in *Parke-Davis & Co. v. H.K. Mulford Co.*" Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad*), 702 F. Supp. 2d 181, 224 (S.D.N.Y. 2010), as amended (Apr. 5, 2010), *aff'd in part, rev'd in part*, 653 F.3d 1329, 2011 WL 3211513 (Fed. Cir. 2011).

the biotech industry by ruling that the gene patents at stake in *Myriad* were invalid.¹⁰ In essence, Sweet's fifty-nine page opinion can be reduced to a single-sentence expression of agreement with the plaintiffs: "Because the claimed isolated DNA is not markedly different from native DNA as it exists in nature, it constitutes unpatentable subject matter."¹¹

The defendants in *Myriad* appealed Sweet's decision to the U.S. Court of Appeals for the Federal Circuit. For the most part, the appellants and appellees repeated the same basic arguments to the Federal Circuit that they had previously presented to Judge Sweet.¹² But the position taken by the government changed dramatically. Despite the fact that the USPTO was still officially listed as the lead defendant in the case, the Department of Justice submitted a brief in support of the original plaintiffs.¹³ And—in a clear signal of the significance of the case—the Solicitor General personally

appeared before the Federal Circuit on April 4, 2011, to argue against the legitimacy of granting patents on genes.¹⁴ In fact, this appearance marked the first time in history that the executive branch's top legal advocate personally presented an oral argument to the U.S. Court of Appeals for the Federal Circuit.¹⁵

On July 29, 2011, a three-judge panel reversed Judge Sweet's ruling in a two-to-one split decision.¹⁶ The three separate opinions issued by these appellate judges signal both a sharp divide on the basic question at stake in the case and a heavy emphasis on the importance of history to the outcome of the dispute. Judge Alan D. Lourie, who wrote the lead opinion, concluded that "the challenged [patent] claims [in *Myriad*] are drawn to patentable subject matter because the claims cover molecules that are markedly different—have a distinctive chemical identity and nature—from molecules that exist in nature."¹⁷ Lourie further argued that the act of isolating the

10 See, e.g., *Genetic Shock: A Surprising Court Ruling in America May Loosen the Drug Industry's Grip on Important Genes*, THE ECONOMIST, Mar. 30, 2010, <http://www.economist.com/node/15810599> (last visited November 6, 2011, 8:30 pm); John Schwartz & Andrew Pollack, *Judge Invalidates Human Gene Patent*, N.Y. TIMES, Mar. 29, 2010, <http://www.nytimes.com/2010/03/30/business/30gene.html> (last visited November 6, 2011, 8:30 pm).

11 *Myriad*, 702 F. Supp. 2d 181, 232.

12 See, e.g., Brief for the Appellants, *supra* note 6; Brief for the Appellees, *Myriad*, __ F.3d __ (No. 2010-1406), 2010 WL 5311467.

13 Brief for the United States as Amicus Curiae in Support of Neither Party, *Myriad*, __ F.3d __ (No. 2010-1406), 2010 WL 4853320. The official name for this court document is misleading; the government's brief clearly supports the plaintiff-appellees' position, as is shown by the following extract:

DNA merely isolated from a cell in the human body. . . . is a product of nature that is ineligible for patent protection, whether or not claimed in "isolated" form.

We acknowledge that this conclusion is contrary to the longstanding practice of the Patent and Trademark Office. . . . The district court's judgment in this case, however, prompted the United States to reevaluate the relationship between such patents and the settled principle under Supreme Court precedent that the patent laws do not extend to products of nature. . . . [T]he United States has concluded that isolated but otherwise unaltered genomic DNA is not patent-eligible subject matter. *Id.* at 17–18.

14 An audio recording of the oral arguments can be found at the Federal Circuit's website, <http://www.cafc.uscourts.gov/oral-argument-recordings/2011-04-04/all> (follow "2010-1406.mp3" hyperlink). During the final two minutes of Acting Solicitor General Neal Katyal's arguments before the Federal Circuit, one of the judges specifically asked him for his thoughts on Learned Hand's holding in *Parke-Davis v. Mulford*.

15 See, e.g., Alison Frankel, *U.S. Solicitor General to Make Unprecedented Federal Circuit Appearance in Myriad Case* (2011), <http://www.law.com/jsp/cc/PubArticleCC.jsp?id=1202483155902&US+Solicitor+General+to+Make+Unprecedented+Federal+Circuit+Appearance+in+Myriad+Case> (last visited November 6, 2011, 8:30 pm).

16 *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (Myriad)*, __ F.3d __, 2011 WL 3211513 (Fed. Cir. 2011).

17 *Id.* at __ (Lourie, J.).

genes at stake in *Myriad* (known as *BRCA1* and *BRCA2*) was sufficient to bring them within the scope of patentable subject matter: “*BRCA1* and *BRCA2* in their isolated state are not the same molecules as DNA as it exists in the body; human intervention in cleaving or synthesizing a portion of a native chromosomal DNA imparts on that isolated DNA a distinctive chemical identity from that possessed by native DNA.”¹⁸

In a vigorously argued dissent, Judge William C. Bryson began by offering a hypothetical “common-sense” answer that “most observers” would give if asked “whether an individual can obtain patent rights to a human gene”: “Of course not. Patents are for inventions. A human gene is not an invention.”¹⁹ Bryson perceived the “essence of *Myriad*’s argument” to be that “it has not patented a human gene, but something quite different—an *isolated* human gene.”²⁰ For Bryson, the basic question presented by the case is “whether the process of isolating genetic material from a human DNA molecule makes that isolated material a patentable invention.”²¹ Bryson’s conclusion was that such isolation does not transform a gene into patentable subject matter, which he buttressed by drawing an analogy to a leaf plucked from a tree:

[E]xtracting a gene is akin to snapping a leaf from a tree. Like a gene, a leaf has a natural starting and

stopping point. It buds during spring from the same place that it breaks off and falls during autumn. Yet prematurely plucking the leaf would not turn it into a human-made invention.²²

Judge Kimberly A. Moore joined Judge Lourie in reversing the lower court ruling, but her concurring opinion makes clear that she did not fully endorse Lourie’s argument that a gene is transformed into something patentable through the very process of isolation. Indeed, Moore acknowledged frankly that “[i]f I were deciding this case on a blank canvas, I might conclude that an isolated DNA sequence . . . is not patentable subject matter.”²³ For Moore, the deciding factor was the “substantial historical background” that came with the case.²⁴ She argued that this history has created “settled expectations” that courts should not upset.²⁵ And Moore offered the following short—but highly significant—summary of the basis for these “settled expectations”: “The settled expectations of the inventing community with respect to isolated DNA claims are built upon . . . judicial precedent, such as *Parke–Davis* and *Merck*, and the Patent Office’s longstanding policy and practice.”²⁶

But, as I will detail in the concluding section of this article, both the 1958 *Merck* decision and the USPTO’s official policy

¹⁸ *Id.* at __.

¹⁹ *Id.* at __ (Bryson, J., dissenting).

²⁰ *Id.*

²¹ *Id.*

²² *Id.* at __.

²³ *Id.* at __ (Moore, J., concurring).

²⁴ *Id.*

²⁵ *Id.* at __.

²⁶ *Id.* at __. The *Merck* case referenced by Moore was a 1958 dispute over the patentability of vitamin B12. *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156 (4th Cir. 1958).

for reviewing—and routinely granting—patents on genes were largely predicated on a few sentences from Learned Hand’s 1911 *Parke-Davis* opinion.²⁷ Thus, in a strong sense, the entire edifice of “settled expectations” that swung Judge Moore’s swing vote in *Myriad* rests upon language from this century-old case. In this article, I will attempt to peel away the layers of received wisdom that have accumulated around *Parke-Davis v. Mulford* to explore what actually happened and (perhaps more importantly) what did *not* happen in this case.²⁸ My fundamental finding is that the central question widely assumed to have been at the heart of the dispute—is a purified or isolated natural substance patentable?—was left essentially untouched by those presenting arguments to Judge Hand. Thus, Hand’s product-of-nature language in *Parke-Davis v. Mulford* did not flow from the pen of a jurisprudential giant who had weighed vigorously debated points and counter-points on a controversial legal question. Instead,

what we have are under-informed musings of a thirty-nine-year-old judge grappling with one of his first patent cases.²⁹

Without question, Learned Hand produced many important and profound opinions during his long and illustrious judicial career.³⁰ Hand’s product-of-nature pronouncements in *Parke-Davis* have, indeed, become important, but a careful historical examination of the decision reveals that they were profound in only one unfortunate sense: they were profoundly incorrect (by the relevant legal standards of 1911). Subsequent policies built upon Learned Hand’s *Parke-Davis* opinion—including those that undergird the gene patents at issue in *Myriad*—are, in short, erected upon an extremely shaky legal foundation.

The Patent Examiner

Paradoxically, perhaps the clearest sign in *Parke-Davis* of young Judge Hand’s intellectual ability was the self-confident admission he offered at the conclusion of

²⁷ See *infra* pp. 396–397 for my discussion of *Merck*; see *infra* pp. 397–398 for my discussion of the USPTO gene-patenting policies, which were released in 2001.

²⁸ Other legal scholars have given Hand’s decision in *Parke-Davis v. Mulford* considerable attention—with varying degrees of approval or disapproval—but no one has previously engaged in a detailed historical analysis of the case. See, e.g., Michael D. Davis, *The Patenting of Products of Nature*, 21 RUTGERS COMPUTER & TECH. L. J. 293, 325–332 (1995); Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 336–339 (2002); Graham Dutfield, *Who Invents Life: Intelligent Designers, Blind Watchmakers, or Genetic Engineers?*, 5 J. INTELL. PROP. L. & PRAC., 531, 533–534 (2010); John F. Duffy, *Innovation and Recovery*, 14 MARQ. INTELL. PROP. L. REV., 237, 266 (2010) (concluding that “Hand’s opinion in *Parke-Davis* is a perfect example of the right approach to patent law”); Robin Feldman, *Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law*, 63 STAN. L. REV. 1377, 1396–1398 (2011); Richard Seth Gipstein, *The Isolation and Purification Exception to the General Unpatentability of Products of Nature*, 4 COLUM. SCI. & TECH. L. REV. 1, 5–44, 65–67 (2003); Eric W. Gutttag, *The Patentability of Microorganisms: Statutory Subject Matter and Other Living Things*, 13 U. RICH. L. REV. 247, 253 (1979); Ashley McHugh, *Invalidating Gene Patents: Association for Molecular Pathology v. U.S. Patent & Trademark Office* 62 HASTINGS L.J. 185, 209–210 (2010); Eric J. Rogers, *Can You Patent Genes? Yes and No*, 93 J. PAT. & TRADEMARK OFF. SOC’Y 19, 33 (2011); Andrew W. Torrance, *Synthesizing Law for Synthetic Biology*, 11 MINN. J. L. SCI. & TECH. 629, 639 (2010); Allen K. Yu, *Why It Might Be Time To Eliminate Genomic Patents, Together with the Natural Extracts Doctrine Supporting Such Patents*, 47 IDEA 659, 678–679, 702 (2007).

²⁹ Hand was appointed to the bench in April 1909. A catalogue of Hand’s many decisions related to patent law during his long and illustrious judicial career reveals that *Parke-Davis v. Mulford* was only Hand’s sixth case involving patent law (he would eventually rule on a total of 140 patent cases). See PAUL H. BLAUSTEIN, *LEARNED HAND ON PATENT LAW*, 273–286 (1983) (an edited collection of snippets from Hand’s patent opinions as they pertain to various topics in patent law; numbers generated from tallying the “Table of Cases”). See GERALD GUNTHER, *LEARNED HAND: THE MAN AND THE JUDGE* (1994), for the definitive general biography on Learned Hand.

³⁰ See, e.g., *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office (Myriad)*, 702 F. Supp. 2d 181, 225, n.46 (S.D.N.Y. 2010), as amended (Apr. 5, 2010), *aff’d in part, rev’d in part*, ___ F.3d ___, 2011 WL 3211513 (Fed. Cir. 2011). (citing some of the frequent “invocation[s] of Judge Hand” in the Second Circuit).

his opinion: "I cannot stop without calling attention to the extraordinary condition of the law which makes it possible for a man without any knowledge of even the rudiments of chemistry to pass upon such questions as these."³¹ Roughly a decade before Hand issued his decision in *Parke-Davis*, a patent examiner with considerably more knowledge of chemistry—and physiology and medicine and patent law—than thirty-nine-year-old Learned Hand had deliberated repeatedly on the validity of the Adrenalin patent application.

James B. Littlewood was charged with reviewing the application for "Glandular Extractive Products and Process of Producing the Same," which was filed at the U.S. Patent Office on November 5, 1900.³² Littlewood was born in Ashton, England, on June 25, 1843.³³ At age eleven, he immigrated with his parents to Illinois³⁴ and settled near the small town of Newark, roughly 60 miles southwest of Chicago.³⁵ On June 13, 1861—twelve days before turning eighteen—Littlewood mustered into service with the Twentieth Illinois Infantry

Regiment to fight for the Union in his adopted country.³⁶ He remained with this regiment for the duration of the Civil War, participating in a number of battles including Shiloh and Vicksburg.³⁷ After serving four years as a "good soldier," Littlewood resettled in Washington, D.C., where he earned an M.D. from Georgetown University in 1868.³⁸

Two years later, in 1870, Littlewood took up employment as a clerk at the Patent Office.³⁹ He joined the ranks of patent examiners in July of 1881 with a promotion from First Class Clerk to Third Assistant Examiner.⁴⁰ During the subsequent ten years, Littlewood continued to climb the bureaucratic ladder at the Patent Office and was eventually named Chief of the Division of Chemistry in July of 1891.⁴¹ In the academic year following this promotion, Littlewood added luster to his patent credentials by enrolling as one of seventeen "Special Students in the Law of Patents" for the inaugural year of a course of study—which would later become a Master of Laws program in

31 *Parke-Davis*, 189 F. at 115.

32 Littlewood to Takamine, Dec. 7, 1900, Transcript of Record at 877–878, *Parke-Davis & Co. v H.K. Mulford & Co.*, 196 F. 496 (2d Cir. 1912) (No. 4363). The complete file wrappers associated with the patents at issue in *Parke-Davis v. Mulford* are reproduced in the nearly 1,000-page bound Transcript of Record, which was prepared for the appeal to the Second Circuit Court of Appeals (on file at the National Archives at New York City, Second Circuit Court of Appeals Case No. 4363, Box 1684) [hereinafter Transcript of Record].

33 HISTORY OF THE MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, 1817–1909 292 (1909) (brief biographical entry on Littlewood).

34 *Government Loses Trusted Employee* [sic]: *Regret Expressed at Death of Dr. Littlewood: An Expert in Chemistry: Was Chief Examiner of this Division in Patent Office for Many Years*, WASH. TIMES, Feb. 8, 1906, at 2 (obituary, including late-life photographic portrait, gives Littlewood's age at time of immigration to Illinois).

35 HISTORICAL ENCYCLOPEDIA OF ILLINOIS AND HISTORY OF KENDALL COUNTY 774–775 (Newton Bateman & Paul Selby eds., 1914) (lists Littlewood as member of 20th Illinois Infantry Regiment, which was recruited from the vicinity surrounding Newark, and gives history of unit).

36 *Id.*

37 *Id.*

38 ANDREW BROWN, COMPANY K, TWENTIETH REGIMENT, ILLINOIS INFANTRY ROSTER AND RECORD (1894) (brief entry on Littlewood describes him as "a good soldier" and provides some information on his post-war resettlement in Washington); *Deaths*, 46 JAMA 529, 530 (1906) (short obituary on Littlewood; gives Georgetown graduation date)

39 *Government Loses Trusted Employee*, *supra* note 34, at 2 (1906 obituary states that Littlewood employed at Patent office for 36 years).

40 *Promotions in the Patent Office*, 45 SCI. AM. 193 (1881).

41 *Notes from the Departments*, WASH. POST, July 22, 1891, at 5. I am grateful to Claire Duggan for her assistance in locating this article.

Patent Law—at Columbian University School of Law (now George Washington University Law School).⁴² Littlewood's professor for this series of lectures was also his boss, Commissioner of Patents William E. Simonds.⁴³ According to the Columbian University "Catalogue" for 1891/1892, Simonds "deliver[ed] a course of lectures on the Law of Patents, in which, after tracing the origin and growth of our Federal Patent system, he discuss[ed] as far as practicable the nature of Patent Property and the general nature of Patent Practice considered in its special modes of procedure."⁴⁴

Littlewood's career as a patent examiner ended in February of 1906, when he died suddenly of heart disease at age 62.⁴⁵ A *Washington Times* obituary described him as one of the "most experienced and trustworthy" employees at the Patent

Office.⁴⁶ At the time of his death, he had worked at the nation's patent agency for 36 years and had been Chief of its Division of Chemistry for fifteen years.⁴⁷ Littlewood had already occupied this lofty perch in the federal patent bureaucracy for nearly a decade when the Adrenalin patent application arrived at his desk in November of 1900.

The Patent Applicant⁴⁸

Whether by chance or design, the application had been sent to the Patent Office on the 46th birthday of the inventor, Jokichi Takamine.⁴⁹ Examiner Littlewood would go on to raise serious questions about the patent application, but no one could doubt that the applicant had led a fascinating life during his first 46 years.⁵⁰ Jokichi Takamine was born to a prominent

42 CATALOGUE OF THE OFFICERS AND STUDENTS OF THE COLUMBIAN UNIVERSITY FOR THE ACADEMIC YEAR 1891-92 20 (1892) (Littlewood listed among "Special Students in the Law of Patents"); GW Law: History, <http://www.law.gwu.edu/School/Pages/History.aspx> (timeline gives 1891 as the year a "course of lectures in patent law, given by the U.S. Commissioner of Patents, is established as a regular part of the curriculum" and 1897 as when a "Master of Laws degree program in Patent Law and Patent Law Practice begins").

43 COLUMBIAN CATALOGUE, 1891-92, *supra* note 42, at 6, 36. Simonds was Commissioner of Patents from July 1891 to April 1893. He also taught patent law at Yale Law School from 1884 through 1893. In addition, Simonds wrote a number of authoritative books on the subject in the late nineteenth century. See Joseph A. Kurz, *William Edgar Simonds*, 3 J. PAT. OFF. SOC'Y 407 (1920-1921).

44 COLUMBIAN CATALOGUE, 1891-92, *supra* note 42, at 36.

45 *Deaths*, *supra* note 38, at 530.

46 *Government Loses Trusted Employee*, *supra* note 34, at 2.

47 *Id.*

48 The biographical information presented here on Takamine is more extensive than is necessary to understand the historical and legal arguments made in this article, but Takamine's life does not lend itself to brief summation. I encourage impatient or time-pressed readers to skim (or skip) this section and proceed to the next section beginning on p. 373.

49 Patent application cover letter (Nov. 3, 1900; filed Nov. 5, 1900), Transcript of Record, *supra* note 32, at 861.

50 AGNES DE MILLE, *WHERE THE WINGS GROW* (1978) (personal memoir of famous mid-twentieth-century choreographer, who lived near Takamine estate in rural New York as a child, contains extensive biographical information on Takamine); K.K. KAWAKAMI, *JOKICHI TAKAMINE: A RECORD OF HIS AMERICAN ACHIEVEMENTS* (1928) (hagiographic biography commissioned by Takamine's widow shortly after his death); TAKAMINE: DOCUMENTS FROM THE DAWN OF INDUSTRIAL BIOTECHNOLOGY, *JAPANESE WRITINGS OF JOKICHI TAKAMINE IN FACSIMILE WITH FACING ENGLISH TRANSLATION* (1988) (preface by J.W. Bennett contains biographical information); Joan W. Bennett, *In Search of Dr. Jokichi Takamine and the Origins of Industrial Mycology*, *INOCULUM: NEWSL. MYCOLOGICAL SOC'Y AM.*, Dec. 2002, at 6-9; Joan W. Bennett, *Adrenalin and Cherry Trees*, *MDD: MOD. DRUG DISCOVERY*, Dec. 2001, at 47-48; Joan W. Bennett & Yutaka Yamamoto, *Dr. Jokichi Takamine: Japanese Father of American Biotechnology*, http://www.deerland-enzymes.com/files/Dr_Jokichi%20Takamine_Bio.pdf; W.R. Bett, *Jokichi Takamine (1854-1922): Discover of Adrenaline*, 162 *CHEMIST & DRUGGIST* 523 (1954); Tetsumori Yamashima, *Jokichi Takamine (1854-1922), the Samurai Chemist, and His Work on Adrenalin*, 11 *J. MED. BIOGRAPHY* 95 (2003); Roger Pulvers, *Jokichi Takamine: A Man with Fire in His Belly Whatever the Odds*, *JAPAN TIMES*, June 28, 2009, <http://search.japantimes.co.jp/cgi-bin/fl20090628rp.html> (last visited November 6, 2011, 8:30 pm). Takamine has sufficient stature in his homeland—and his biography is sufficiently compelling—that a feature-length movie dramatizing his life has recently been produced in Japan. SAKURA SAKURA, *see*, <http://sakurasakura.jp/index.html> (last visited November 6, 2011, 8:30 pm).

Japanese family on November 3, 1854, the same year that the Japanese Imperial government ended a 200-year-old policy of international seclusion by signing a trade treaty with the United States (under threat of naval attack from an American armada anchored in Tokyo Bay). The arc of Takamine's life would reflect the growing cultural, scientific, technological, and economic connections between Japan and the United States during the several decades that followed. But to say that Takamine's life *reflected* these changes is an understatement; Takamine himself played an important personal role in *effecting* the greatly increased level of connection between Japan and the U.S. during the late nineteenth and early twentieth centuries.⁵¹

When Jokichi Takamine was only twelve years old, the samurai lord of Kaga province, on Japan's west central coast, chose to send this bright young boy (the son of the local leader's personal physician) to study "foreign science" in Nagasaki, hundreds of miles from home.⁵² At sixteen, Takamine enrolled in medical school in Osaka, intending to follow his father into medical practice.⁵³ Two years later, Takamine redirected his studies to chemistry at the College of Science and Engineering in Tokyo.⁵⁴ In 1879, at age 24, Takamine was one of eleven students cho-

sen to continue his scientific education abroad at the expense of the Imperial government.⁵⁵ Takamine spent four years at Strathclyde University in Glasgow, Scotland, where he continued his study of chemistry and developed a particular interest in fertilizer science and technology.⁵⁶

In 1883, Takamine returned to Japan and found employment at the recently established Ministry of Agriculture and Commerce, where he was charged with helping to adapt the insights of western science and technology to Japanese farming and manufacturing.⁵⁷ But this stay in his homeland was short-lived; the following year, the Japanese government sent Takamine to the World Exposition and Cotton Centennial in New Orleans as an official observer.⁵⁸ Takamine was meant to absorb as much information as possible to bring back to Japan to aid in the national push toward westernization. During nearly a year in New Orleans, Takamine learned a great deal about western technology, and he became smitten with a western woman: the 16-year-old daughter of the upper-class family in whose French Quarter mansion he boarded. Before returning to Japan, Takamine became engaged to this young southern belle, Caroline Field Hitch.⁵⁹

Takamine left his fiancée in Louisiana

51 Late in life, Takamine became extremely active as an informal ambassador between Japan and the U.S. See, e.g., Jokichi Takamine, 7 (3) *American and Japanese Co-operation*, PROC. ACAD. POL. SCI. CITY N.Y., July 1917, at 10-13.

52 Yamashima, *supra* note 50, at 95-96.

53 *Id.* at 96.

54 *Id.*

55 *Id.*

56 *Id.* When Takamine attended this Scottish university, it was known as "Anderson's College."

57 *Id.*

58 *Id.* The 1884 event was named to commemorate the 100th anniversary of the first shipment of cotton from the U.S. to England, but the exhibits covered a vast array of agricultural and industrial technology. John Kendall, *History of New Orleans 457-467* (1922), available at http://penelope.uchicago.edu/Thayer/E/Gazetteer/Places/America/United_States/Louisiana/New_Orleans/Texts/KENHNO/29*.html (digital copy of "Chapter XXIX, The World's Cotton Centennial Exposition"). (last visited November 6, 2011, 8:30 pm).

59 See DE MILLE, *supra* note 50, at 137-149, for a detailed rendering of Takamine's stay in New Orleans and extensive information on the Hitch family.

and sailed back to Japan determined to secure sufficient means to support an American wife accustomed to a life of luxury and style.⁶⁰ In 1886, Takamine was appointed Vice Commissioner of the Japan Patent Office (JPO), shortly after enactment of the country's first comprehensive patent law.⁶¹ It is unclear exactly when and where Takamine had acquired sufficient expertise to serve in this capacity, but his early leadership at the JPO sends an important historical signal: Jokichi Takamine had a serious professional interest in patent law. But the security of a government position did not suit Takamine's entrepreneurial style. Around a year later, Takamine resigned from his JPO post to establish the Tokyo Artificial Fertilizer Company, Japan's first fertilizer production facility.⁶²

With financial support from others who had invested in his fertilizer factory, Takamine left Japan for the third time in 1887 to visit fertilizer operations in Europe and the U.S., searching for technological improvements that he could use in Japan.⁶³ Near the end of his world fertilization tour, Takamine returned to New Orleans, where he married eighteen-year-old Miss Hitch on August 10, 1887. The marriage was reportedly the first-ever union between an American bride and a Japanese groom.⁶⁴ The honeymoon offered

a further demonstration of the groom's keen interest in patents: the day after the wedding ceremony, the couple departed for Washington, so that Takamine could spend time at the U.S. Patent Office studying American patent law.⁶⁵

After Takamine finished his studies at the Patent Office, the couple departed Washington for the west coast (this trip included a slightly more romantic—and conventional—detour to Niagara Falls), where they boarded a ship bound for Japan.⁶⁶ Caroline bore two sons in quick succession (1888 and 1890) in Japan, but she was not happy. In addition to the general difficulties associated with living in a foreign land where she understood little of the culture and less of the language, she was not warmly received by her husband's family, and she did not enjoy living near her husband's odiferous fertilizer plant.⁶⁷

Takamine soon hit upon an idea that would allow him to bring his wife back to America by reversing the flow of technology-transfer between the U.S. and Japan. Takamine's mother's family had owned a sake distillery, and he realized that he might be able to build a business in the U.S. by applying the Japanese techniques of sake distillation to making American whiskey and beer. Cultures around the world and across millennia have developed techniques for converting sugars into

60 *Id.* at 148–149.

61 A biographical entry for Takamine in a list of "Ten Great Japanese Inventors" at the Japanese Patent Office website states that "he was appointed by the Patent Office Commissioner Korekiyo Takahashi to the post of Vice Commissioner of the Patent Office in year 19 of the Meiji Era [i.e., 1886]." Ten Great Japanese Inventors, http://www.jpo.go.jp/cgi/linke.cgi?url=/seido_e/rekishi_e/judaie.htm (last visited November 6, 2011, 8:30 pm). Some other sources, including Takamine's obituary in the *Patent and Trade Mark Review*, state that Takamine served as "Acting Commissioner" of the JPO at this time. *Jokichi Takamine*, 20 PAT. & TRADE MARK REV. 335 (1922).

62 Bennett, *In Search of Dr. Takamine*, *supra* note 50, at 6.

63 *Id.*

64 DE MILLE, *supra* note 50, at 147.

65 *Id.* at 153.

66 *Id.*

67 *Id.* at 155–163.

alcohol through the fermenting powers of yeast. But before this process can begin, the starchy portions of plants such as wheat, corn, or rice must be converted to sugar. Enzymes known as diastases (also called “amylases”) are the biochemical work horses that carry-out this starch-to-sugar transformation. In the West, diastatic enzymes are traditionally obtained from malt, usually derived from germinating barley. Sake distillers in Japan obtained their starch-converting enzymes from a kind of filamentous fungus commonly called “koji mold” (*Aspergillus oryzae*) grown on rice. Takamine understood that the koji form of diastase had much greater enzymatic power than the malt-based diastase used to make American whiskey and beer. Further, Takamine had obtained a Japanese patent on an improved technique for producing the koji enzyme by culturing the mold on wheat bran rather than rice.⁶⁸

With financial support from his American in-laws, Takamine moved his wife and two young sons to the United States in 1890 to establish a distillery in Peoria, Illinois, the “Whiskey Capital of the World” at the time.⁶⁹ At first, the business showed significant promise, with Takamine enjoying some success selling his own “Bonzaï” whiskey to the public

and the koji diastase enzyme to other distilleries.⁷⁰ But malt producers predictably felt threatened by Takamine’s alternative starch-converting enzyme and initiated a move to ban the use of the fungal product. The great blow came in 1894 when Takamine’s distillery was burned to the ground under suspicious circumstances.⁷¹

In the same year, Takamine was granted an American patent on his improved process for producing diastase from mold.⁷² Rather than continue to fight for entrée into the American alcohol industry, Takamine decided to seek a medical application for his fungal form of diastase. He thought that the enzyme—which so effectively converted starch to sugar—might aid in treating indigestion by helping to convert starchy foods to easily digestible sugar. Takamine prepared the enzyme in tablet form and named the product “Taka-Diastase.” In 1897, Takamine struck a deal with Parke-Davis and Company, one of the world’s largest pharmaceutical concerns, which agreed to manufacture, market, and distribute the pills, with Takamine getting a slice of the profits.⁷³ The product was a great success, becoming what one biographer has called “the Alka Seltzer of the 1890s.”⁷⁴ Takamine’s deal with Parke-Davis also included a generous stipend for the

68 Bennett *In Search of Dr. Takamine*, *supra* note 50, at 7; Bennett & Yamamoto, *supra* note 50, at 2; Yamashima, *supra* note 50, at 97

69 See DE MILLE, *supra* note 50, at 164-171, for details on the extensive involvement of Takamine’s mother-in-law in his early business enterprises in the United States. See Brian Fox Ellis, *Peoria’s Whiskey Barrons*, Nov./Dec. 2009, <http://www.peoriomagazines.com/as/2009/nov-dec/peoria-s-whiskey-barons> (last visited November 6, 2011, 8:30 pm) for information on Peoria’s prominence as place of whiskey production.

70 DOCUMENTS FROM THE DAWN, *supra* note 50, at ix-x.

71 *Id.* at x; Yamashima, *supra* note 50 at 98.

72 Process of Making Diastatic Enzyme, U.S. Patent No. 525,823 (filed Feb. 23, 1894) (issued Sept. 11, 1894).

73 Bennett, *In Search of Dr. Takamine*, *supra* note 50, at 7; de Mille, *supra* note 50 at 168-169; Yamashima, *supra* note 50, at 98. See *Fifty Years of Manufacturing Pharmacy and Biology: The Story of Parke, Davis & Company*, 88 AM. J. PHARMACY 503 (1916) for general information on the early history of Parke-Davis. (The surnames identifying this corporation are variously separated by a comma and a hyphen. I have chosen to use a hyphen because this is label given to the company in the case under study: *Parke-Davis v. Mulford*.)

74 Bennett, *In Search of Dr. Takamine*, *supra* note 50, at 7.

Japanese scientist to conduct research for the pharmaceutical giant. With these funds secured, Takamine decided to move his family from Illinois to New York City, where he established a research laboratory on East 103rd Street.⁷⁵

Purifying “Adrenaline”; Inventing “Adrenalin”

The visionary general manager of Parke-Davis, William M. Warren, seems to have been responsible for putting Takamine on the scientific path that would lead to Adrenalin.⁷⁶ For roughly two years, Takamine toiled with many pounds of adrenal glands obtained from slaughtered sheep and cattle, but he did not have much success in isolating a pure, stable version of the hormone secreted by the gland.⁷⁷

Takamine eventually decided to turn toward his homeland to seek scientific talent that could help with the challenge. Sensibly—even shrewdly—Takamine focused his recruiting efforts on Keizo Wooyenaka, a promising 23-year-old chemist who had been a doctoral student of Nagayoshi Nagai at Tokyo University’s School of Pharmacy. Professor Nagai was ten years Takamine’s senior and had been in the vanguard of Japanese scientists who had trained in the west. Most signif-

icantly, Nagai had achieved both contemporaneous and lasting fame for his 1885 achievement of isolating a stimulant he named “ephedrine” from the shrub *Ephedra distachya*. Takamine seems to have believed that a standout Nagai student would be well qualified to participate in the process of isolating another natural stimulant—this time from a gland rather than a plant. He was right. Within six months of Wooyenaka’s February 1900 arrival at Takamine’s laboratory, success was at hand.⁷⁸ Takamine would later publish this summary of the multi-step process devised in his laboratory for preparing Adrenalin:

Its preparation is accomplished by disintegrating the suprarenal glands of sheep and oxen, extracting them in water which has been rendered weakly acid by the addition of a few drops of . . . acid, at 95° C. The solid residue is pressed and re-extracted. The liquid is filtered and then concentrated by evaporation. Alcohol is then added until no further precipitation occurs. The filtrate is then evaporated *in vacuo* and treated with ammonia . . . until the solution is distinctly alkaline. Adrenalin crystallises [sic] out in

⁷⁵ Bennett, *In Search of Dr. Takamine*, *supra* note 50, at 7; DE MILLE, *supra* note 50, at 169–172; Yamashima, *supra* note 50, at 98.

⁷⁶ In April 1910, in a deposition taken for Parke-Davis v. Mulford, Frank G. Ryan gave credit to Warren for putting Takamine on this research trail. When Ryan was deposed, he was president of Parke-Davis, but when Takamine began work with the suprarenal gland, Ryan was Chief Pharmacist for Parke-Davis. Deposition of Frank G. Ryan, Apr. 5, 1910, Transcript of Record, *supra* note Error! Bookmark not defined., at 309 (“The General Manager of Parke, Davis & Co., Mr. William M. Warren, requested Dr. Jokichi Takamine to endeavor to find out what active principle was contained in the suprarenal gland”). See Harry B. Mason, *William M. Warren: His Untimely Death Last Month—The Inspiring Story of His Life and Success—The Beautiful Tribute Paid to His Memory by His Business Associates*, 17 BULL. OF PHARMACY 492 (1903), for biographical information on Warren.

⁷⁷ Yamashima, *supra* note 50, at 98.

⁷⁸ *Id.* at 98–100; DE MILLE, *supra* note 50, at 172–173; Aiko Yamashita, *Research Note on Adrenaline by Keizo Uenaka in 1900*, 23 BIOMEDICAL RES. 1, 1–3 (2002) (“Uenaka” is an alternative English spelling of “Wooyenaka”).

the course of a few hours and may be purified by dissolving in acid and re-precipitating.⁷⁹

Patent Prosecution— Round One (of Seven)

As was his general pattern, Takamine moved promptly toward seeking patent protection for the scientific and technical breakthroughs associated with Adrenalin. He had legal assistance in this endeavor from Harry E. Knight and William E. Knight, who were second- (or perhaps third-) generation patent attorneys in the New York office of Knight Brothers, which was among the oldest patent-law firms in the country, having been founded by two other Knights in 1843.⁸⁰ The original application, which was officially filed on November 5, 1900, was for a combination product-and-process patent. The introductory section of the patent “Specification” attempted to cast Adrenalin as a new product and Takamine’s process as a novel form of production:

This invention relates to a *new crystalline product* consisting of the active and hemostatic principle of the Suprarenal Glands in a concen-

trated form, which possesses a remarkable power of raising blood pressure of animals when injected into veins, and also has the property of contracting blood vessels when applied to the vein either directly or by means of subcutaneous injection, *and* the invention comprises a *process for producing such product* in an economical and practical manner.⁸¹

In the balance of the patent application, however, purification rather than production was the predominant theme. Takamine and his lawyers pointed to the “well known and established fact that the Suprarenal Glands or Capsules of various animals, including man, contain peculiar constituents, which have remarkable astringent, hemostatic, and other valuable properties.”⁸² They went on to explain that “[t]he usual method of utilizing these properties [was] to dessicate [sic] the gland and grind the whole mass into powder form.”⁸³ This powder could then be used “to stop bleeding” by applying it “to the desired spot,” or “to affect the heart, it [could] be administered through the mouth.”⁸⁴ As an alternative, the “fresh

79 Jokichi Takamine, *The Isolation of the Active Principle of the Suprarenal Gland*, 27 J. PHYSIOLOGY, PROC. PHYSIOLOGICAL SOC’Y XXIX–XXX (1901). Some retrospective grumblings have been raised that Wooyenaka should have been credited as a co-inventor—or even sole inventor—for the process of obtaining Adrenalin from the adrenal gland. DE MILLE, *supra* note 50 at 177–179; Yamashita, *supra* note 98 at 2–3. The issue of Wooyenaka’s status as an inventor of Adrenalin was, however, never raised during either the patent application process—which covered the first few years of the twentieth century—or the years of patent litigation that would soon follow. It is interesting to note that Wooyenaka served as an observer during the proceedings related to Parke-Davis v. Mulford. Deposition of Charles F. Chandler [expert for Parke-Davis], Nov. 11, 1909, Transcript of Record, *supra* note 32 at 243 (“The last named gentleman [Wooyenka] is an associate of Dr. Takamine . . . and has been attending the examinations in this case on behalf of the complainant.”).

80 Takamine’s Adrenalin patent application contained a document granting power of attorney for prosecution of the application to Harry E. Knight and William E. Knight of the Knight Brothers firm located at 20 Broad Street in New York. Jokichi Takamine to Commissioner of Patents, Nov. 3, 1900 (filed Nov. 5, 1900), Transcript of Record, *supra* note 32, at 862. I have not been able to locate significant biographical information on either of these two attorneys. See THE NEW YORK STOCK EXCHANGE: BANKS, BANKERS, BUSINESS HOUSES, AND MONEYED INSTITUTIONS OF THE GREAT METROPOLIS OF THE UNITED STATES 142 (1886), for general information on the Knight Brothers firm.

81 Patent Application, filed Nov. 5, 1900, *supra* note 80, at 863 (emphasis added).

82 *Id.*

83 *Id.* at 863–864.

84 *Id.* at 864.

glands" had been "treated with water, so as to extract the soluble constituents," which were then "sterilized or treated with some antiseptic agents, with the view of making more or less permanent solution."⁸⁵ The basic problem with the existing suprarenal gland preparations was contamination:

It will be readily seen that the dessicated [sic] powder contains a very large amount of foreign substance other than [the] active principle, and also that the [aqueous] extract, while somewhat purer in comparison than the dessicated [sic] powder, still contains a large percentage of foreign substance consisting of both organic and inorganic bodies, which have considerable deteriorating effect upon the active principle contained therein.⁸⁶

Takamine acknowledged that other scientists had made "[v]arious attempts . . . to isolate the active principle from inert foreign substances contained in the glands."⁸⁷ And the patent application described at some length two different techniques recently proposed in publications by "Professor John J. Abel of Johns Hopkins University" and "Otto V. Furth of Strassburg."⁸⁸ But this prior art was dismissed because "neither authors have succeeded in isolating the active principle

[of the suprarenal gland] in pure crystalline forms."⁸⁹

The original patent application included nine claims. The first seven concerned process; the last two were directed to the product. The product claims are transcribed below:

8. The product, Adrenalin, consisting of the active principle of the Suprarenal Glands, in a white, solid, crystalline form, difficultly soluble in water, soluble in acid and alkaline solutions, possessing hemostatic, astringent and reducing properties, producing a characteristic green reaction with ferric salt, and red coloration with iodine all substantially as set forth [in the process claims].

9. The product consisting of a salt of the alkaloid Adrenalin, the active principle of the Suprarenal Glands, which has all the chemical and physiological reactions characteristic of the active principle of the Suprarenal Glands and is obtained by dissolving Adrenalin in acid, evaporating the liquid and crystallizing the solution which is separated from the mother liquor and drying, all substantially as described [in the process claims].⁹⁰

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.*

⁸⁸ *Id.* at 864-866.

⁸⁹ *Id.* at 866.

⁹⁰ *Id.* at 872-873.

Examiner James B. Littlewood sent a response to Takamine's patent application only a little over a month after it was first filed at the Patent Office.⁹¹ Littlewood had a few quibbles with the process claims, which the applicants would be able to solve without much difficulty.⁹² And the examiner had two objections to the product claims—one was easily rectified; the other would not be settled for two and a half years. First, Littlewood objected to the use of the "coined" word "Adrenalin" in the patent, clarifying that "[a]n applicant can not [sic] be permitted to use coined terms in an application for a patent, other protection being provided by law."⁹³ Of course, this "other protection" was trademark registration, an option that Parke-Davis would later pursue for the term "Adrenalin."⁹⁴ Littlewood's second objection to the product claims clearly shows that the examiner did not accept Takamine's assertion in the introductory section of the patent application that a "new product" was being "produced." Instead, Littlewood focused on the balance of the application, where Takamine described his process as a break-through technique for "isolating"

the pre-existing "active principle" of the suprarenal gland. The examiner bluntly rejected both product claims:

Claim 8 is drawn to a product of nature, merely isolated by applicant, and hence is not drawn to such patentable invention as required by statute (ex parte Latimer, 46 O.G., 1638; Badische Anilin v. Cochran, 27 O.G., 813). The claim is rejected.

Claim 9 discloses nothing regarding the properties of the substances to be covered (Badische, cited), except that it has the same properties as the natural principle. The natural principle not being patentable, neither is this. The claim is rejected.⁹⁵

Patent Prosecution— Round Two (of Seven)

Takamine and his attorneys took nearly a year to file an amended application in response to Littlewood's critique.⁹⁶ They tweaked the process claims in accordance

⁹¹ Littlewood to Takamine, Dec. 7, 1900, Transcript of Record, *supra* note 32, at 877–878.

⁹² *Id.*

⁹³ *Id.* at 877.

⁹⁴ "Adrenalin," Trade-Mark for Hemostatic, Astringent, Blood-Pressure Raising, and Stimulating Preparations, U.S. Trade-Mark No. 53,934 (filed Aug. 22, 1905) (registered June 12, 1906).

⁹⁵ Littlewood to Takamine, Dec. 7, 1900, Transcript of Record, *supra* note 32, at 878. See *infra* pp. 378–379, for a discussion of *Ex parte Latimer*. Littlewood had the parties reversed in the other case he cited, which is an 1884 Supreme Court decision generally known as *Cochran v. Badische Anilin & Soda Fabrik*. Littlewood's "27 O.G. 813" citation is to page 813 in volume 27 of the *Official Gazette of the United States Patent Office*. The standard *Supreme Court Reporter* citation is 111 U.S. 293 (1884). In this case, the Supreme Court invalidated a product patent that had been granted on a type of red dye (alizarine), which had long been derived from the roots of madder plants (alizarine had been used to color the "red coats" of British soldiers during the Revolutionary War). A product patent had been granted on a synthetically generated form of alizarine, but the Supreme Court struck it down because the chemical was not "a new composition of matter": "While a new process for producing it was patentable, the product itself could not be patented, even though it was a product made artificially for the first time, in contradistinction to being eliminated from the madder root. Calling it artificial alizarine did not make it a new composition of matter, and patentable as such, . . . if it was . . . alizarine, a well-known substance." 111 U.S. at 311.

⁹⁶ Knight Bros. (for Takamine) to Commissioner of Patents, Amendment, Oct. 22, 1901 (filed Oct. 24, 1901), Transcript of Record, *supra* note 32, at 879–883.

with the examiner's suggestions and trimmed the word "Adrenalin," but otherwise they left the product claims completely unaltered.⁹⁷ They also submitted a brief "Argument," which was not much more than an attempt to brush-off Littlewood's product-of-nature objections. They did not discuss the cases he cited, and they somewhat blithely asserted that "the compounds here named do not exist in a state of nature," adding—almost acerbically—that "[t]he product as it exists in nature is certainly not a white, solid, crystalline body."⁹⁸

Two weeks later, on November 7, 1901, Littlewood fired back a response that seemed to suggest he did not appreciate the rather casual attempt that had been made to rebut his concerns that Adrenalin was an unpatentable natural product.⁹⁹ Littlewood once again asserted that he "regarded [Adrenalin] as unpatentable under *ex parte* Latimer."¹⁰⁰ And he pointed toward two additional cases to buttress his arguments. First, he quoted from *Ex parte Patzer*, a decision of the Patent Examining Board, to support the basic notion that natural substances cannot be patented: "Natural articles and their obvious physical constituents are not inventions or discoveries by man. They are

objects on which human invention or discovery may be utilized."¹⁰¹

Littlewood also referred to an 1874 U.S. Supreme Court case, *American Wood-Paper Co. v. Fiber Disintegrating Co.*, in which the justices had disallowed a product patent on the pulp used to make paper.¹⁰² Pulp is essentially a slurry of cellulose that is left after wood is broken-down and processed during the early stages of paper-making. The inventors in this case had devised a strictly chemical means for removing non-cellulosic elements from raw pulp; all previous paper-making techniques had required both chemical and mechanical action to remove the extraneous woody matter from pulp. In addition to seeking a patent for the chemical purification process (which was granted), the applicants sought a patent on the resulting pulp itself. The Court disallowed the product patent because the pulp (as opposed to the process for obtaining it) was *not a new type of material*: "Paper-pulp obtained from various vegetable substances was in common use before [this] patent was granted . . . and whatever maybe be said of [the inventors'] process for obtaining it, the product was in no sense new. The . . . patent . . . is, therefore, void for want of novelty."¹⁰³

Should be: *See infra* pp. 378-379

97 *Id.* at 879-882.

98 *Id.* at 873.

99 Littlewood to Takamine, Nov. 7, 1901, Transcript of Record, *supra* note 32, at 884.

100 *Id.* *See infra* p. 49, for a discussion of *Ex parte* Latimer

101 *Id.* Littlewood's citation for *Ex parte* Patzer is exactly as follows: "~~Board dec., *ex parte* Patzer, Vol. 51, pp. 378-379.~~" I think it is likely that Littlewood intended this as a citation to the *Official Gazette of the United States Patent Office*. The decision is not, however, printed at page 81 of volume 51 of the *Official Gazette*. With expert assistance from Walt A. Johnson, Patent & Trademark Depository Librarian at the Minneapolis Central Library, I have not been able to locate this decision in any other location. I am grateful to Mr. Johnson for his assistance in this matter. He was also kind enough to raise the "where's *Patzer*?" question with several of his colleagues at other patent depository libraries across the country, who were similarly unsuccessful in locating this case. I am also grateful to these anonymous bibliographic sleuths.

102 *Id.*; *Am. Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874).

103 90 U.S. at 596. The Court's ruling in this case did not turn on whether wood pulp was a product of nature; it was enough that the material was not novel.

Printer's errors

Should be: "Board dec., *ex parte* Patzer, Vol. 51, p. 81."

Patent Prosecution— Round Three (of Seven)

On September 26, 1902, Takamine and his attorneys filed a second amended application.¹⁰⁴ Once again, they did not significantly alter their product claims,¹⁰⁵ but they seem to have received the message from Littlewood that a more thoroughgoing consideration of product-of-nature problem was expected. They produced an “Argument” on the issue that filled almost four typed pages.¹⁰⁶ They did not mention the *Patzer* case quoted by Littlewood (perhaps because the examiner had provided an incorrect—or obscure—citation for this case in his November 1901 response).¹⁰⁷ They did, however, assure Littlewood that they had “carefully examined” the other cases he had cited: “ex parte Latimer, the Wood Pulp Case, and the Badisch Anilin case.”¹⁰⁸

They explained to Littlewood that they would focus their discussion on *Ex parte Latimer* because it had been “decided subsequently and with full knowledge and reference to the other two cases.”¹⁰⁹ Thus, the Adrenalin legal team believed that *Latimer* should “be taken as the official interpretation of the doctrine involved.”¹¹⁰

The *Latimer* decision was also most directly on-point because the case concerned an attempt to patent an isolated natural substance; the other two concerned attempts to patent non-novel products that had been obtained by novel—and patentable—processes.¹¹¹

In 1888, William Latimer submitted a patent application for a new process of extracting the fibrous core from the center of the pine needles that grow to an exceptional length of ten to twenty inches on Longleaf Pines (*Pinus australis*). Once extracted from the center of the needle, the fiber could be used to make a wide variety of textile products. Latimer was quickly granted a patent on his new process for extracting the fiber,¹¹² but the examiner rejected Latimer’s parallel attempt to obtain a product patent on the fiber itself because the fibrous pine-needle core was a product of nature rather than an invention.¹¹³

Latimer appealed the examiner’s decision to the Commissioner of Patents, Benton J. Hall, in 1889.¹¹⁴ Hall shared the examiner’s judgment that the fiber was not a patentable product because, in the Commissioner’s words, “the fiber, when it

104 Knight Bros. (for Takamine) to Commissioner of Patents, Amendment, Sept. 25, 1902 (filed Sept. 26, 1902), Transcript of Record, *supra* note 32, at 885–889.

105 *Id.* at 885–886.

106 *Id.* at 886–889.

107 *See supra* note 101. Even though *Ex parte Patzer* was not discussed in this amended application, Takamine’s attorneys did not express disagreement with the basic principle stated in the passage Littlewood had quoted from the case (*see supra* p. 377).

108 Amendment, Sept. 25, 1902, *supra* note 104, at 886.

109 *Id.*

110 *Id.*

111 *Ex parte Latimer*, 1889 DEC. COMM’R PAT. 123 (1889). This decision also appeared in the *Official Gazette of the United States Patent Office* (at 46 O.G. 1638), but my citations will be to the first periodical cited, which is now more widely available.

112 Process of Making Fiber from Pine-Needles, U.S. Patent No. 397,240 (filed Dec. 10, 1888) (issued Feb. 5, 1889).

113 The examiner’s rejection of Latimer’s product-patent application is quoted at some length in *Ex parte Latimer*. *Latimer*, 1889 DEC. COMM’R PAT. at 124.

114 Benton J. Hall (1835–1894) served as Commissioner of Patents from April 11, 1887, until March 31, 1889. Hall was appointed by President Grover Cleveland and was succeeded by an appointee of President Benjamin Harrison. *See* L.J. Farley & Leroy A. Palmer, *Benton J. Hall*, 3 J. PAT. OFF. SOC’Y 309 (1920–1921).

was made free" through a process of "dis-integrate[ing] and remov[ing] the material constituting the [needle's] sheath . . . [was] in nowise changed or different in its natural construction."¹¹⁵ Hall also added that it would not matter if the fiber had been a newly discovered natural product: "I am not aware of any instance in which it has been held that a natural product is the subject of a patent, although it may have existed from creation without being discovered."¹¹⁶ The Patent Commissioner sketched-out the problematic policy implications of allowing patents on natural objects by imagining a scenario in which patents were granted on the natural constituents of various trees:

The result would be that an alleged inventor in Germany would acquire a patent which would give him the exclusive use of the *Pinus sylvestris* [Scots Pine], the applicant in this case would secure a patent for the fiber of the *Pinus australis*, and thus, successively, patents might be obtained upon the trees of the forest and the plants of the earth, which of course would be unreasonable and impossible.¹¹⁷

Hall did, however, point to a way in which Latimer would likely be able to obtain a patent on his product, which necessitated bringing about some—even very minor—change in the condition of the fiber:

If the applicant's process had another final step by which the fiber thus withdrawn or separated from the leaf or needle in its natural state were changed, either by curling it or giving it some new quality or function which it does not possess in its natural condition as fiber, passing through the exigencies of such a process would be treated and *become something new or different from what it is in its natural state*. Natural fibers, hair, and many other substances have been allowed as patentable products which have been changed by some such treatment.¹¹⁸

Takamine's attorneys quoted this same paragraph in their attempt to convince Littlewood that Adrenalin was a patentable product (and they underlined the passage that I have emphasized).¹¹⁹ They concluded by arguing that "[t]here is a much greater distinction between a mere curling of a natural fibre . . . and the complete transformation which applicant has accomplished and defined in his claims."¹²⁰ But, in specifying how Adrenalin had undergone a "complete transformation," Takamine's legal team circled back to almost exactly the same language that had worked so poorly with Littlewood roughly a year earlier: "The active principle of the glands does not exist in nature as a white, solid, crystalline substance."¹²¹

¹¹⁵ *Latimer*, 1889 DEC. COMM'R PAT. at 126.

¹¹⁶ *Id.* at 127.

¹¹⁷ *Id.* at 126.

¹¹⁸ *Id.* at 127 (emphasis added).

¹¹⁹ Amendment, Sept. 25, 1902, *supra* note 104, at 888.

¹²⁰ *Id.* at 889.

¹²¹ *Id.*

Three weeks later, on October 17, 1902, Littlewood replied with news that all the process claims were now in allowable shape, but he was not convinced by the applicant's discourse on the product claims.¹²² He assured Takamine that "[t]he argument of the applicant ha[d] been carefully read," but Littlewood was essentially unmoved.¹²³ He encapsulated his rejection in one sentence: "The examiner does not assert that the active principle exists, freed from impurities in nature; neither did Latimer's fibre; but it did exist and therefore is not patentable."¹²⁴ Even more bluntly, Littlewood-Latimer wrote that the application was "fatally defective" because "the product . . . to all appearances is simply separated from impurities."¹²⁵

Patent Prosecution— Round Four (of Seven)

Just before Christmas 1902, Takamine and his attorneys notified Littlewood that they would restrict the patent application under consideration to the process claims, and they informed the examiner that it was the "applicant's intention to file a divisional application for the product claims."¹²⁶ Not surprisingly, the process-patent application moved toward approval without significant difficulty.¹²⁷

On January 14, 1903, three weeks after announcing their intention to divide their application, Takamine and his attorneys submitted a separate application for the Adrenalin product patent.¹²⁸ They had run into something like a brick wall with Littlewood's October response to their product patent claims for Adrenalin, but rather than trying to run around the wall—or jump over it or knock it down—they tried to pretend it did not exist. The new application contained claims that were almost identical to those that Littlewood had deemed "fatally defective" only a few months earlier, and the application contained no new arguments to rebut Littlewood's product-of-nature objections.¹²⁹

Four weeks later, Littlewood dryly—but firmly—reminded Takamine of the brick wall's existence: "It is noted that [the] claims . . . are drawn to the active principle [of the suprarenal gland] itself. . . . [T]he applicant is aware of the views of the [Patent] Office as previously set forth in the original application of which this [application] is a division."¹³⁰

Patent Prosecution— Round Five (of Seven)

This time Takamine's legal team did not wait a year to reply to Littlewood's

¹²² Littlewood to Takamine, Oct. 17, 1902, Transcript of Record, *supra* note 32, at 890.

¹²³ *Id.*

¹²⁴ *Id.*

¹²⁵ *Id.*

¹²⁶ Knight Bros. (for Takamine) to Commissioner of Patents, Amendment, Dec. 22, 1902 (filed Dec. 23, 1902), Transcript of Record, Transcript of Record, *supra* note 32, at 891–892.

¹²⁷ Commissioner of Patents to Takamine, Notice of Allowance on Patent Application for "Process of Obtaining a Product from Supra-renal Glands," April 15, 1903, Transcript of Record, *supra* note 32, at 899; Process of Obtaining Products from Suprarenal Glands, U.S. Patent No. 730,175 (filed Nov. 5, 1900) (issued June 2, 1903).

¹²⁸ Takamine to Commissioner of Patents, Patent Application, Jan. 10, 1903 (filed Jan. 14, 1903), Transcript of Record, *supra* note 32, at 826–833.

¹²⁹ *Id.* at 832.

¹³⁰ Littlewood to Takamine, Feb. 14, 2003, Transcript of Record, *supra* note 32, at 834.

“views.” They filed an amended application for a product patent on March 14, 1903, only two months after Littlewood had made his continued product-of-nature concerns known.¹³¹ In the “Remarks” that accompanied this amended application, they once again quoted the entire paragraph from *Latimer* in which Commissioner Hall had directed that a slight change in the fiber would likely bring the product into the sphere of patentable subject matter. But this time they underlined the passage stating that patentability could be achieved “by curling [the fiber] or giving it some new quality or function which it does not possess in its natural condition.”¹³² In a sense, Takamine’s legal team was trying to convince Littlewood that Adrenalin was a *curled* version of the hormone existing in the suprarenal gland. Toward this end, they altered the claims to eliminate the phrase “active principle,” and they inserted the phrase “stable and concentrated form.” A comparison of the first claim from the January 14, 1903, application and the March 14th amendment shows the changed approach:

January 14th:

1. The herein-described product, consisting of the active principle of the suprarenal capsules of glands, having a white color, solid and crystalline in form.¹³³

March 14th:

1. A substance possessing the herein-described physiological characteristics and reactions of the suprarenal glands in a stable and concentrated form, and practically free from inert constituents.¹³⁴

In the explanatory material accompanying the March application, Takamine’s lawyers came up with several ways to distinguish Adrenalin from the natural substance existing in the suprarenal gland. They tossed out their old standbys—“its crystalline form; its color”—but they also pointed to the “alkaline reaction” of Adrenalin, stating that the “natural product [was] neutral or acid,” which “indicat[ed] that [the natural substance] is in combination with other elements in some form” in Adrenalin.¹³⁵ And they tried to place particular emphasis on the “permanence and stability” of Adrenalin, contrasting it with “the natural product,” which they said was “subject to decomposition and deterioration.”¹³⁶

Two weeks later, Littlewood wrote with a “rejection” of the amended application. He had either missed the subtlety of the arguments, or he simply did not believe that Takamine had produced a *curled* hormone. Littlewood directed his dissatisfaction in particular to the first claim of the March 14th amended application, asserting that “Claim 1 as it stands would be met by any suprarenal gland.”¹³⁷

131 Knight Bros. (for Takamine) to Commissioner of Patents, Amendment, Mar. 13, 1903 (filed March 14, 1903), Transcript of Record, *supra* note 32, at 835–848.

132 *Id.* at 847.

133 Application, filed Jan. 14, 1903, *supra* note 128, at 832.

134 Amendment, filed Mar. 14, 1903, *supra* note 131, at 842.

135 *Id.* at 847.

136 *Id.* at 846.

137 Littlewood to Takamine, Rejection, Mar. 30, 1903, Transcript of Record, *supra* note 32, at 849.

Patent Prosecution— Round Six (of Seven)

On April 29, 1903, a month after receiving what must have been a frustrating response from Littlewood, Takamine and his lawyers filed another amended application that contained only two very insignificant changes in the claims.¹³⁸ The “Remarks,” however, covered three typed pages.¹³⁹ The crucial passage was a direct response to Littlewood’s concerns about Claim 1 of their amended March application:

With regard to the objection to Claim 1, as being met by the suprarenal gland, we would respectfully point out that the substance as claimed is distinguished from the glands by the language that it is in stable and concentrated form and free from inert constituents.

Applicant believes himself to be the first to produce the described product in a permanent, stable and free from inert constituents.¹⁴⁰

Patent Prosecution— Round Seven (of Seven)

In 1903, April 29th fell on a Wednesday. The following Monday, May 4th, Takamine

and his attorneys held an “oral interview” with Littlewood at the Patent Office in Washington.¹⁴¹ No records exist that capture the exact nature of the exchanges at this meeting. But only two days later the Adrenalin legal team filed an amended application that they believed was “in compliance with the Examiner’s requirements” as formulated during the conference.¹⁴² In the “Remarks” section of this filing, they said that Claim 1 had been “amended to clearly express the property of the applicant’s substance as being stable, permanent, and freed from all deteriorating, decomposable and organic material with which it is associated in the glands.”¹⁴³ In actuality, the only change to Claim 1 is shown below:

1. A substance possessing the herein-described physiological characteristics and reactions of the suprarenal glands in a stable and concentrated form, and practically free from inert ~~constituents~~ and associated gland tissue.¹⁴⁴

Changes to the other claims were of a similar, fairly trivial nature.¹⁴⁵ Eight days later, on May 14, 1903, Littlewood sent a notice to Takamine that the patent for “Glandular Extractive Products” had been “examined and ALLOWED.”¹⁴⁶

¹³⁸ Knight Bros. (for Takamine) to Commissioner of Patents, Amendment, Apr. 28, 1903 (filed Apr. 29, 1903), Transcript of Record, *supra* note 32, at 851–853.

¹³⁹ *Id.*

¹⁴⁰ *Id.* at 852.

¹⁴¹ In an amended application written the day after the meeting with Littlewood, Takamine’s attorneys stated the following: “Pursuant to an oral interview had with the Examiner in charge of the above application [on] May 4th, 1903, . . .” Knight Bros. (for Takamine) to Commissioner of Patents, Amendment, May 5, 1903 (filed May 6, 1903), Transcript of Record, *supra* note 32, at 854.

¹⁴² *Id.*

¹⁴³ *Id.* at 855.

¹⁴⁴ *Id.* at 854.

¹⁴⁵ *Id.* at 854–855.

¹⁴⁶ Commissioner of Patents to Takamine, Notice of Allowance on Patent Application for “Glandular Extractive Products,” May 14, 1903, Transcript of Record, *supra* note 32, at 859.

After the requisite paying of fees and filing of forms, patent number 730,176 was officially granted on June 2, 1903.¹⁴⁷ But the precise extent of this victory should be understood: Takamine's lawyers did not succeed in convincing Littlewood that an isolated or purified product of nature was worthy of a patent (in fact, they never really attempted to argue this position). Instead, Takamine's legal team finally convinced—or wore down—Littlewood to accept the idea that “Adrenalin,” the medical product, was something different than a purified or isolated version of “adrenaline,” the hormone.

Adrenalin in the Medical Marketplace

Parke-Davis began advertising and selling to physicians and pharmacists a 1:1,000 solution of Adrenalin at least as early as June of 1901.¹⁴⁸ An October 1901 newspaper article touting the introduction of a new medical product discovered by “Dr. Jokichi Takamine, a well known and highly educated Japanese,” hailed Adrenalin as “the most powerful medicine known,” but quickly added that it might also be “the most expensive.”¹⁴⁹ The price was \$1.00 for a one ounce bottle, but the dilution rate for the product meant that there was approximately one grain of pure Adrenalin in each \$1.00 bottle of solution.¹⁵⁰ There are 7,000

grains per pound, so—doing a little math—the newspaper explained that “[p]hysicians buy it at . . . \$7000 a pound” (in 2011 dollars, the cost would be nearly \$200,000 per pound).¹⁵¹

The same article also somewhat breathlessly asserted that “unlimited possibilities” for medical applications existed, listing several uses that had already been discovered or were hoped-for: pre-surgery applications of Adrenalin solution allowed “operations [to be] performed on the nose, ear and eye without the spilling of a drop of blood”; “adrenalin is a most powerful cardiac stimulant, and it has been hinted by physicians that it may be possible to resuscitate persons who have died of heart failure”; and “it may be possible to perform amputations without loss of blood, which is so disastrous to the patient.”¹⁵² Time would largely bear out the clinical promise of Adrenalin. For example, in 1913 Parke-Davis published a book-length review of the various clinical applications for the product that ran to almost 150 pages.¹⁵³

In 1910, the president of Parke-Davis, Frank G. Ryan, offered the following matter-of-fact, yet superlative, assessment of the Adrenalin as a pharmaceutical product:

Adrenalin and its solution have been unqualifiedly the most pronounced success, both from a com-

¹⁴⁷ Glandular Extractive Product, U.S. Patent No. 730,176 (orig. filed Nov. 5, 1900) (divided & filed Jan. 14, 1903) (issued June 2, 1903).

¹⁴⁸ Parke-Davis began placing advertisements for “Adrenalin the Active Principle of the Suprarenal Gland” at least as early as June 1901. See, e.g., Half-Page Adrenalin Advertisement, *MED. NEWS: WEEKLY MED. J.*, June 29, 1901, at 20.

¹⁴⁹ *A New Chemical*, *L.A. TIMES*, Oct. 1, 1901, at 15 (reprinted from the *N.Y. HERALD*).

¹⁵⁰ *Id.*

¹⁵¹ *Id.*

¹⁵² *Id.*

¹⁵³ PARKE, DAVIS & CO., *ADRENALIN: ITS PROPERTIES, PHYSIOLOGIC ACTION, MODE OF USE, AND THERAPEUTIC HISTORY: CONDENSED CLINICAL REPORTS SHOWING ITS WIDE RANGE OF APPLICABILITY* (1913).

mercial and therapeutic stand-point[,] of any product introduced by our house. The rapidity with which its value was recognized by the medical profession has no equal in our experience.¹⁵⁴

In short, Adrenalin was a *blockbuster* drug—decades before the term was invented.¹⁵⁵

Takamine's patent licensing agreement with Parke-Davis guaranteed him five percent of the wholesale price of all Adrenalin sold by the company.¹⁵⁶ He leveraged this revenue stream—along with his continuing royalties on the sale of Taka-Diastase—to invest in a number of companies in both Japan and the U.S.¹⁵⁷ He was spectacularly successful. Within the first decades of the twentieth century, Takamine amassed a fortune estimated at \$30 million—or roughly half a billion dollars by present-day standards.¹⁵⁸ He built two homes that were emblematic of his tremendous wealth. The Japanese government had recreated a lavish Japanese estate, including a grand house and gardens, as part of their national exhibit at the 1904 World's Fair in St. Louis. At the

conclusion of the fair, Takamine received permission from Japanese officials to finance the transfer of the entire estate piece-by-piece (including a number of trees) to a twenty-acre country haven, one-hundred miles north of New York City.¹⁵⁹ A few years later, Takamine had a five-story mansion erected on Riverside Drive in Manhattan, with each floor constructed to represent a different period in Japanese design history (one could time-travel from eighth to the eighteenth century while riding the elevator from the first to the fifth floors).¹⁶⁰

Patent Litigation

As with most litigation—patent and otherwise—the infringement suit filed by Parke-Davis against H.K. Mulford was driven by financial concerns. Not long after the product patent was granted for Adrenalin, sales began to drop, which Parke-Davis attributed to competition from other pharmaceutical companies that had entered the market with their own suprarenal gland preparations.¹⁶¹ Indeed, this growing competition might

¹⁵⁴ Ryan Deposition, *supra* note 76, at 311–312.

¹⁵⁵ See NICOLAS RASMUSSEN, ON SPEED: THE MANY LIVES OF AMPHETAMINE 8 (2008), for a historical argument that Parke-Davis's Adrenalin was "the first important new drug to emerge from [late nineteenth-century] advances in physiology" and that this "milestone" drug was a "special landmark for American medicine because it was invented in the United States, and commercialized by an American company, at a time when that nation lagged woefully behind Europe in both medical science and pharmaceuticals."

¹⁵⁶ Ryan Deposition, *supra* note 76, at 312.

¹⁵⁷ DE MILLE, *supra* note 50, at 182.

¹⁵⁸ Pulvers, *supra* note 50.

¹⁵⁹ DE MILLE, *supra* note 50, at 117–120.; KAWAKAMI, *supra* note 50, at 68–71. This estate, which Takamine called "Sho-Foo-Den," (Japanese for "Pine Maple Hall," which has been transliterated into English under various spellings), received contemporaneous attention as an architectural and aesthetic achievement. See, e.g., Grace Tabor, *Shoo Foo Den: The Japanese House and Garden of Dr. Jokichi Takamine at Merriwold Park, N.Y.*, COUNTRY LIFE, Dec. 1914, at 59–63 (accompanied by several photographs, including one color print).

¹⁶⁰ KAWAKAMI *supra* note 50, at 63–67.

¹⁶¹ In April 1910, Parke-Davis President Frank Ryan was asked during a deposition if he could explain why the sales of Adrenalin were "greater in 1903 and 1904 than in years subsequent." Ryan answered that he had "always attributed it to the fact that competition had come into the market with similar products." Ryan Deposition, *supra* note 76, at 311. Sales figures introduced as evidence showed that Parke-Davis sold \$192,589 worth of Adrenalin in 1904 and \$129,995 in 1905. *Id.* at 310 (a roughly 30% drop in sales, which in 2011 dollars represents about \$1.6 million).

have motivated Takamine's legal team to pick up the pace of patent prosecution in the spring of 1903. Close observers of the pharmaceutical industry began to sense an impending legal battle, as is shown by the text of a short notice titled "The Suprarenal War," which appeared in the "News and Comment" section of the August 1904 issue of the *Practical Druggist and Pharmaceutical Review of Reviews*:

Parke, Davis & Co. have taken steps to protect their patent-rights in adrenalin, the active principle of the suprarenal capsules. Notice has already or will be shortly served on all the alleged infringers (American and foreign). Among those said to be infringing on their rights are Armour & Co., manufacturers of suprarenalin; Eli Lilly & Co., manufacturers of sanguetine; H.K. Mulford & Co., manufacturers of adrin; Frederick Stearns & Co., manufacturers adnephtrin; Henry K. Wampole & Co., manufacturers of hemostatin; [and] John Wyeth & Brother, manufacturer of caprenalin. The outcome of these cases will be looked for with keen interest by the trade.¹⁶²

The first shot in the "Suprarenal War" had, in fact, been fired two months before this piece appeared in print. And Parke-Davis had decided to focus its legal firepower

on a single opponent, rather than take-on "all the alleged infringers": its largest competitor Philadelphia-based H.K. Mulford Co., maker of Adrin.¹⁶³ Parke-Davis hired a veteran patent litigator, Livingston Gifford of the New York firm Gifford & Bull, to lead the legal charge against Mulford.¹⁶⁴ On June 8, 1904, Gifford sent a letter to Mulford notifying the company "that in manufacturing and selling the substance 'Adrin' you are infringing upon . . . the . . . letters patent issued to Dr. Takamine and now owned by . . . Parke Davis & Co."¹⁶⁵ On behalf of Parke-Davis, Gifford "respectfully request[ed]" that Mulford "immediately discontinue such infringement."¹⁶⁶

Mulford employed the services of an experienced, Philadelphia-based, patent litigator, Charles Howson of the firm Howson & Howson, to deal with the legal challenge from Parke-Davis. Howson, who had started his career in 1859 as a fourteen-year-old clerk in his father's patent practice,¹⁶⁷ replied to Gifford's letter with news that, "after careful consideration of the subject," Mulford had decided that "they [were] not infringing on any rights of your clients under said letters patent . . . and therefore, of course, cannot comply with your request that they discontinue making their product 'Adrin.'"¹⁶⁸

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¹⁶² *The Suprarenal War*, 16 PRACTICAL DRUGGIST & REV. REVIEWS 328 (1904) (emphasis added).

¹⁶³ See LOUIS GALAMBOS & JANE ELIOT, NETWORKS OF INNOVATION: VACCINE DEVELOPMENT AT MERCK, SHARP & DOHME, AND MULFORD, 1895-1995 9-32 (1995) for general historical background on H.K. Mulford Company.

¹⁶⁴ See WHO'S WHO IN AMERICAN HISTORY, Vol. 1, 452 (1943), for biographical information on Gifford.

¹⁶⁵ Gifford & Bull to H.K. Mulford Co., June 8, 1904, Transcript of Record, *supra* note 32, at 16 ("Gifford & Bull" was the name of Gifford's law firm).

¹⁶⁶ *Id.*

¹⁶⁷ *Howson, Charles* [obituary], 29 ANN. REP. PA. BAR ASS'N 66 (1923).

¹⁶⁸ Howson & Howson to Gifford & Bull, Transcript of Record, *supra* note 32, at 17.

The legal battle was joined. But it is crucial to understand that Mulford did not wage its battle behind a patentable-subject-matter banner. Instead, Mulford charged forward behind thematic flags that are much more familiar in patent litigation. H.K. Mulford—the man for whom his company was named—believed his firm would win by showing that Takamine did not deserve priority for the invention (or discovery) of the purified version of the hormone found within the suprarenal gland. Mulford used a technique for purifying adrenaline that had been developed by John J. Abel, a prominent professor of pharmacology at Johns Hopkins University (Takamine had detailed—and dismissed as imperfect—Abel’s work in the prior-art section of his patent application).¹⁶⁹ In the fall of 1905, as the move toward taking depositions for the Adrenalin litigation was starting to take shape, President Mulford sent Francis E. Stewart, Mulford’s scientific

director, to visit Abel in his laboratory at Hopkins. Stewart had instructions to inquire about Abel’s willingness to testify for Mulford in the patent dispute. Stewart reported back that the patent-averse academic did not want to entangle himself in this corporate squabble. Mr. Mulford’s reaction to the news is telling:

I am exceedingly sorry that Prof. Abel expresses himself as being unwilling to be a witness, however, his published work will be sufficient as it certainly shows *priority* and would prove to any fair court that P. D. & Co. were not entitled to [a] product patent.¹⁷⁰

H.K. Mulford—the man and the company—believed that Takamine and Parke-Davis were not entitled to a product patent for Adrenalin, but this belief seems to have had virtually nothing to do with a concern that

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¹⁶⁹ The question of whether Takamine or Abel deserved credit for discovering the technique of isolating the active principle of the adrenal gland received considerable attention from both litigants in *Parke-Davis v. Mulford*. The question has also subsequently drawn the attention of various biographers of the two men and others who have given the matter historical attention. See, e.g., JOHN PARASCANDOLA, *THE DEVELOPMENT OF AMERICAN PHARMACOLOGY: JOHN J. ABEL AND THE SHAPING OF A DISCIPLINE* 57–58 (1992); Horace W. Davenport, *Epinephrin(e)*, 25 *PHYSIOLOGIST* 76, 78–81; Sanford S. Singer, *Abel and Takamine Independently Isolate Adrenaline*, in *GREAT EVENTS FROM HISTORY II: SCIENCE AND TECHNOLOGY SERIES*, VOL. 1, 1888–1910 16–20 (Frank N. Magill ed., 1991); Carl Voegtlin, *John Jacob Abel, 1857–1938*, 67 *J. PHARMACOLOGY & EXPERIMENTAL THERAPEUTICS* 373, 378–382.

¹⁷⁰ H.K. Mulford to F.E. Stewart, October 16, 1905, Box 8, Folder 7, Francis Edward Stewart Papers, Wisconsin Historical Society Archives, Madison, Wis. (emphasis added). I am grateful to Vicki Fama for her skilled work on my behalf in this archival collection. General biographical information on Stewart is available in the front matter of the finding aid for this collection. <http://digital.library.wisc.edu/1711.dl/wiarchives.uw-whs-mss00606>. (last visited November 6, 2011, 8:30 pm) Stewart, who was both a pharmacist and physician, had been the scientific director for Parke-Davis before taking-up employment with Mulford. He was extremely outspoken on matters of patent and trademark law affecting the medical and pharmaceutical profession, and he was a particularly vocal proponent of the position that U.S. law should not allow patents to be granted on *any* medical products. It seems unlikely that either Parke-Davis or Mulford fully shared this position. Stewart’s views have been detailed in a recent historical article. Joseph M. Gabriel, *A Thing Patented is a Thing Divulged: Francis E. Stewart, George Davis, and the Legitimization of Intellectual Property Rights in Pharmaceutical Manufacturing, 1879–1911*, 64 *J. HIST. MED. & ALLIED SCI.* 135 (2009). Stewart specifically mentioned the Adrenalin patents, and the related litigation, in a number of his publications proposing various reforms in patent law affecting the pharmaceutical industry, but he never raised the question of whether the Adrenalin patent should be invalidated because it related to an isolated product of nature. Instead, Stewart focused on the issue of the trademarked name “Adrenalin” being confused with—or used as—the generic term for the medical product (or hormone). He also used the Adrenalin patent as an illustration of the general evil (as he saw it) of granting patents on medical products. See, e.g., F.E. Stewart, *Patents and Trade Marks in Their Relation to Pharmaceutical Science and Practice*, 58 *PROC. AM. PHARMACEUTICAL ASS’N* 648, 662 (1910); F.E. Stewart, *Materia Medica Monopoly a Hindrance to Materia Medica Science*, 1 *J. AM. PHARMACEUTICAL ASS’N* 614, 616–617 (1912); F.E. Stewart, *Report of the P.P.A. [Pennsylvania Pharmaceutical Association] Committee on Patents and Trademarks*, 2 *J. AM. PHARMACEUTICAL ASS’N* 1149, 1151 (1913).

Adrenalin was merely a purified product of nature. The official "Answer" that Charles Howson would eventually submit to Judge Learned Hand multiplied the number of arguments against the validity of Takamine's product patent, but nowhere in this six-page document did Howson directly assert that Takamine should not have been granted a patent because the substance was nothing more than an isolated product of nature. The only place where Howson came close was in the eleventh of twelve numbered points of argumentation:

11. . . . Defendant says that the alleged new Glandular Extractive Product set forth and purporting to be patented in and by said Letters Patent No. 730,176 is not an art, manufacture or composition of matter patentable under the laws of the United States, wherefore said Letters Patent were improvidently granted and are null and void.¹⁷¹

Howson did not amplify the point any further, he did not even name the problem as arising from the "product-of-nature" doctrine, and he did not cite the crucial precedent of *Ex parte Latimer*. The general nature of the arguments that Howson emphasized can be better gleaned from the second numbered point of his "Answer" (written in legalese characteristic of the age):

2. . . . Defendant denies that Jokichi Takamine . . . was, or is, the original or first inventor or discoverer of the alleged new Glandular Extractive Product in said Bill of Complaint mentioned; denies that said alleged product was not known or used by others in this country before the alleged invention or discovery thereof by the said Takamine, or had not before said alleged invention or discovery thereof by the said Takamine, or more than two years prior to this application for Letters Patent thereon, been patented or described in any printed publication in this or any foreign country for more than two years prior to such application, or that it had not been abandoned.¹⁷²

These are the type of arguments that a patent litigator with decades of experience would be very accustomed to make. Questions about whether an invention was not eligible for a patent because it was nothing more than a pre-existing natural substance were rare. Indeed, the examiner who had originally refused Latimer's product patent acknowledged the exotic nature of the issue: "This exact question, so far as [I am] aware, has never been considered by the courts or by [Patent] Commissioners."¹⁷³ And entire books on the U.S. patent system could be written during this period without any mention of this aspect of patentability. In fact, Charles Howson had coauthored

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¹⁷¹ Answer of the H.K. Mulford Company, Defendant to the Bill of Complaint of Parke, Davis & Company, Complainant, Transcript of Record, *supra* note 32, at 396.

¹⁷² *Id.* at 393.

¹⁷³ *Ex parte Latimer*, 1889 DEC. COMM'R PAT. 123, 124 (1889).

just such a book, which included a discourse of several pages under the heading “Conditions to Patentability” with nary a word on the product-of-nature problem.¹⁷⁴

But by far the best indicator of the extent to which product-of-nature issues did *not* play a meaningful contemporary role in *Parke-Davis* is the complete inattention to the topic during the days (and days!) when depositions were taken from the two experts involved. *Parke-Davis v. Mulford* was essentially a “battle of the experts,” and heavyweights were in each corner for this fight. Charles F. Chandler (1836–1925) was the expert for Parke-Davis. Chandler had obtained a Ph.D. in chemistry from the University of Göttingen in 1856 (the epicenter of academic chemistry in the mid-nineteenth century) and held concurrent professorships in chemistry at three New York institutions for most of his career: Columbia School of Mines (1864–1910), New York College of Pharmacy (1866–1897), and New York College of Physicians and Surgeons (now Columbia Medical School) (1872–1897). Among many highlights during his illustrious career, Chandler invented the flush toilet (for which he did not seek a patent), and he was twice consulted on how to preserve the ink in the original copy of the Declaration of Independence.¹⁷⁵

Samuel P. Sadtler (1847–1923) sat in Mulford’s corner as an expert witness. Sadtler also had a Göttingen Ph.D. in chemistry, which he obtained in 1871. And he held concurrent professorships in chemistry at two prominent institutions in Philadelphia for most of his career: the University of Pennsylvania (1874–1891) and the Philadelphia College of Pharmacy (1878–1916). In 1908, Sadtler’s peers recognized his place of professional prominence by choosing him to serve as the founding president of the American Institute of Chemical Engineers.¹⁷⁶

Parke-Davis’s expert, Chandler, sat as an expert for depositions that occurred on thirty-two separate days between May of 1906 and May of 1910 (producing transcripts covering a total of 286 pages).¹⁷⁷ Sadtler, the expert for Mulford, offered testimony on twenty-one different days between January 1907 and June 1908 (Sadtler beat Chandler in the transcript page-count by five: his transcripts filled 291 pages).¹⁷⁸ The extensive exchanges with these two giants of pharmaceutical science and chemical engineering addressed—in rather mind-numbing detail—the biochemical techniques used by Takamine and other scientists (such as Abel) to isolate a medically useful version of the hormone in the suprarenal gland.¹⁷⁹ But never during the equivalent of almost two months worth of deposition days was a single question directed to

174 H. HOWSON AND C. HOWSON, A BRIEF INQUIRY INTO THE PRINCIPLES, EFFECT, AND PRESENT STATE OF THE AMERICAN PATENT SYSTEM, TOGETHER WITH THE LAWS OF THE UNITED STATES RELATING TO PATENTS, TRADE-MARKS AND COPYRIGHTS 58–64 (1872).

175 Marston Taylor Bogert, *Biographical Memoir of Charles Frederick Chandler, 1836–1925*, 14 NAT’L ACAD. SCI. BIOGRAPHICAL MEMOIRS 125 (1931); Margaret W. Rossiter, *Charles F. Chandler Collection*, 18 TECHNOLOGY & CULTURE 222 (1977); Elizabeth Noble Shor, *Chandler, Charles Frederick*, AMERICAN NATIONAL BIOGRAPHY ONLINE (2000).

176 Jerome Alexander, *Samuel Philip Sadtler—Ulysses in Chemistry*, 16 INDUSTRIAL & ENGINEERING CHEMISTRY 195 (195); Wyndham D. Miles, *Samuel Philip Sadtler, 1847–1923*, in AMERICAN CHEMISTS & CHEMICAL ENGINEERS, vol. 2, 245 (Wyndham Miles & Robert F. Gould, eds., 1994).

177 Transcript of Record, *supra* note 32, at 17–44, 50–307.

178 *Id.* at 404–694.

179 *Id.* at 17–44, 50–307, 404–694.

the issue of whether Takamine's Adrenalin was an unpatentable product of nature.¹⁸⁰ Of course, it would have been much more likely for Mulford's attorneys to raise this topic because it could have helped them invalidate the patent, but they did not do so—in a total of 97 questions to Sadtler and 325 questions to Chandler.¹⁸¹

Learned Hand's Opinion

A 1,000-page pile of briefs, deposition transcripts, and documentary exhibits related to *Parke-Davis & Co. v. H.K. Mulford Co.* finally arrived at Judge Learned Hand's desk on February 3, 1911.¹⁸² When Livingston Gifford had sent the initial infringement letter to Mulford in June of 1904, 32-year-old Learned Hand had just been named a partner at the Wall Street law firm of Gould and Wilkie (he had left law practice in his hometown of Albany two years earlier with aspirations for big-city success).¹⁸³ Hand would soon grow weary of what he considered the intellectually empty grind of Wall Street legal practice and, in 1907, began to work political connections in a quest for a federal judgeship.¹⁸⁴ In 1909, he achieved success in this pursuit when President William Howard Taft—on the recommendation of Attorney General George Wickersham, who had previously prac-

ticed on Wall Street—nominated Hand to fill a newly created fourth trial bench in the Southern District of New York.¹⁸⁵

Hand issued his opinion in *Parke-Davis v. Mulford* on April 28, 1911—two days short of his second anniversary as a judge.¹⁸⁶ Despite Hand's forthright admission in his ruling that he had been somewhat befuddled by the technical complexity of the case, he performed yeoman's service in working through hundreds of pages of expert testimony and exhibits.¹⁸⁷ He emerged from this biochemical thicket with a pronouncement that Parke-Davis's Adrenalin patents were valid and that Mulford was infringing with the production and sale of Adrin.¹⁸⁸ This holding was essentially based on a finding that Takamine had priority in devising a technique for extracting a medicinally useful hormone from the suprarenal gland—and that both Takamine's process and product were sufficiently novel to warrant patent protection.¹⁸⁹ It also seems possible—or perhaps probable—that Hand was also somehow swayed in his decision by the practical reality that a fellow New Yorker, Jokichi Takamine, had accumulated such tremendous fame and fortune from the development and sale of Adrenalin.

Hand's opinion is, of course, now well known for his assertion that purified products of nature can be a good subject

¹⁸⁰ *Id.*

¹⁸¹ *Id.*

¹⁸² Adrenalin Patents Valid, the United States Circuit Court so Decides, 83 AM. J. PHARMACY, 347 (1911).

¹⁸³ Hand was hired by Gould and Wilkie in January 1904, but—to his significant frustration—he was placed on a six-month “probation” before being made a partner. GUNTHER, *supra* note 29, at 104.

¹⁸⁴ *Id.* at 106–133.

¹⁸⁵ *Id.* at 129–133.

¹⁸⁶ *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). Hand took his judicial oath on Apr. 30, 1909. GUNTHER, *supra* note 29, at 133.

¹⁸⁷ *Id.* at 115.

¹⁸⁸ *Id.* at 114.

¹⁸⁹ *Id.* at 114–115.

for a patent, which he stated most forcefully in the following terms:

[E]ven if [Adrenalin] were merely an extracted product without change, there is no rule that such products are not patentable. Takamine was the first to make it available for any use by removing it from the other gland-tissue in which it was found, and, while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically. That was a good ground for a patent.¹⁹⁰

However, a close examination of Hand's opinion—especially in the light of what transpired during the lengthy patent-examination process for Adrenalin—drives home the fact that the lawyers involved in this case did not argue the product-of-nature issue in a meaningful or educational fashion for this novice federal judge.

Hand offered a nodding acknowledgment in his opinion of the difficulty that Takamine had experienced in applying for a product patent a decade earlier,¹⁹¹

but Hand made significant errors of both law and fact in recounting this patent-application process. Hand claimed that “the examiner . . . [had] bas[ed] his rejection of the [Adrenalin product patent] upon his interpretation of *American Wood Paper Co. v. Fibre Disintegrating Co.*”¹⁹² But this explanation of Littlewood's rejection is wrong on two counts. First, Hand asserted that the examiner understood *American Wood-Paper* to stand for a rule “that no product is patentable, however it be of the process, which is merely separated by the patentee from its surrounding materials and remains unchanged.”¹⁹³ But this is not an accurate recitation of the *American Wood-Paper* rule, which only dictates that a *previously known* substance cannot be the subject of a product patent, even if the substance is obtained by a novel purification process.¹⁹⁴ It seems quite clear that Littlewood neither harbored nor acted upon this misunderstanding of the Supreme Court's ruling (it is unclear whether Hand himself misunderstood *American Wood-Paper* in this way).

Hand's second mistake in characterizing Littlewood's rejection of Takamine's product patent is even more significant: the extended tussle between the patent

190 *Id.* at 103. Hand cited two cases to support this section of his opinion: *Kuehmsted v. Farbenfabriken of Elberfeld Co.*, 179 F. 701 (7th Cir. 1910); and *Union Carbide Co. v. American Carbide Co.*, 181 F. 104 (2d Cir. 1910). The two cases were, however, largely irrelevant to the issue of whether a purified product of nature could be patented. *Kuehmsted* concerned the question of whether greater purification of a man-made chemical—the active ingredient in aspirin (acetyl salicylic acid)—could give rise to patentability, which the Seventh Circuit answered in the affirmative. But the *Kuehmsted* court did not offer any significant insight on whether patentability via purification could or should be extended to naturally occurring products. (Livingston Gifford, the attorney for Parke-Davis in *Parke-Davis v. Mulford*, also represented *Farbenfabriken* in *Kuehmsted*.) The *Union Carbide* case concerned a patent on a new form of crystalline calcium carbide, and did not concern purification in any sense. (The *Union Carbide* case was decided by same federal appeals court that two years later would consider the appeal of *Parke-Davis* (see *infra*, at p. 37. Two of the three judges on each panel would be the same for both cases (Lacombe and Noyes).) See Gipstein, *supra* note 28, at 18–25, for a useful technical and theoretical discussion of the relationship—or lack thereof—between these two cases and Hand's assertions regarding the patentability of purified products of nature in *Parke-Davis*.

191 *Parke-Davis*, 189 F. at 101.

192 *Id.*

193 *Id.*

194 See *supra* at p. 377.

applicant's legal team and Examiner Littlewood certainly had much more to do with *Ex parte Latimer* than *American Wood-Paper*. But Hand seems to have been utterly ignorant of this case; he did not cite it here or anywhere else in his opinion. If the Mulford attorneys had expended any significant legal energy to strike down Adrenalin as an unpatentable product of nature, Learned Hand certainly would not have been able to ignore *Latimer*.

Hand's recounting of the patent-examination process also contains another species of error, which suggests that this novice federal judge—who had left Wall Street only two years earlier—fundamentally misunderstood the deep and persistent concerns about the patentability of Adrenalin as expressed by a top patent examiner—who, by contrast, had been dealing with patents every working day for two decades. Hand implied that Littlewood had rejected Takamine's product-patent claims only once before the combined process-and-product patent was divided.¹⁹⁵ In fact, Littlewood had rejected the product-patent claims three times because of product-of-nature concerns before Takamine decided to divide-out the product-patent claims.¹⁹⁶ Then, Hand went on to maintain that when Takamine had submitted unrevised claims in the newly divided product-patent application, the examiner had "raised no objection to

the form in which these claims were given."¹⁹⁷ Here, Hand was simply wrong: Littlewood had actually rejected Takamine's claims on product-of-nature grounds twice more after the divisional application had been filed.¹⁹⁸

But the greatest shortcoming with Learned Hand's assertion that "even if [Adrenalin] were merely an extracted [natural] product without change, there is no rule that such products are not patentable"¹⁹⁹ was his failure to take *Ex parte Latimer* into account. This 1889 ruling of Patent Commissioner provided *exactly* the rule Hand proclaimed to be nonexistent.²⁰⁰ And, one should recall, even the attorneys who had handled patent-prosecution for Takamine had acknowledged in September of 1902 that *Latimer* ought to be "be taken as the official interpretation of the doctrine involved."²⁰¹ In fact, the only way that these attorneys had eventually succeeded in obtaining a product patent for Takamine was in finally convincing—or wearing down—Littlewood to accept the proposition that Adrenalin was *not* "merely an extracted product without change."

Hand concluded his problematic product-of-nature discussion by asserting that "[e]veryone, not already saturated with scholastic distinctions, would recognize that Takamine's dried glands were not merely the dried glands in a purer state,

195 *Parke-Davis*, 189 F. at 101.

196 Littlewood to Takamine, Dec. 7, 1900, *supra* note 91; Littlewood to Takamine, Nov. 7, 1901, *supra* note 99; Littlewood to Takamine, Oct. 17, 1902, *supra* note 122.

197 *Parke-Davis*, 189 F. at 101.

198 Littlewood to Takamine, Feb. 14, 1903, *supra* note 130; Littlewood to Takamine, Mar. 30, 1903, *supra* note 137.

199 *Parke-Davis*, 189 F. at 103.

200 See *supra* at p. 19. One recent commentator on *Parke-Davis v. Mulford*—who was not aware that *Latimer* played such a central role in the Adrenalin patent-examination process—has stated that "the patent in *Parke-Davis* would have been invalidated if Learned Hand had followed the rule in . . . in *Ex Parte Latimer*." Gipstein, *supra* note 28, at 33.

201 Knight Bros. to Commissioner of Patents, Sept. 25, 1902, *supra* note 104.

nor would [anyone's] opinion change if [they] learned that the crystals were obtained from the glands by a process of eliminating the inactive organic substances."²⁰² Examiner James B. Littlewood, who had died in 1906, might have experienced some post-mortem bodily rotation when Hand wrote these words. In October of 1902, Littlewood had judged the Adrenalin product patent application as "*fatally defective*" precisely because of his belief that "the product . . . is simply separated from impurities."²⁰³ Perhaps most significantly, even Takamine's legal team never once attempted to argue that Littlewood's understanding of the product-of-nature rule was flawed; instead, they spent years arguing—with mixed success—that Adrenalin was something other than a purified version of the naturally occurring hormone. Littlewood does not seem to have been "saturated with scholastic distinctions" when he repeatedly rejected Takamine's product-patent application; rather, he seems to have been "saturated" with a thorough understanding of patent law and in possession of a fairly sophisticated understanding of the emerging field of endocrinology.

The final sentence of Hand's treatment of the product-of-nature issue includes another one of his characteristic rhetorical flourishes: Hand declared that whether a product falls within the bounds of patentable subject matter should be "drawn rather from the common usages

of men than from nice considerations of dialectic."²⁰⁴ But, again, this proclamation runs counter to *Ex parte Latimer*. In 1889, Patent Commissioner Hall explained that he had given Latimer's application "no little consideration" and that he had "experienced an anxiety, if possible, to secure the applicant a [product] patent."²⁰⁵ Hall had *wanted* to grant Latimer a patent because the Commissioner recognized that "[t]he alleged invention [was] unquestionably very valuable . . . and of immense benefit to the people of the country in which the *Pinus australis* grows."²⁰⁶ Hall further acknowledged the many practical advantages of the fibrous pine-needle core: "The fiber . . . is stronger, more durable, and can be produced at much less expense than jute, and will undoubtedly supersede that article in the manufacture of many fabrics."²⁰⁷ But—to borrow Learned Hand's phrase—these "common usages of men" did not convert the core of a pine needle into a patentable product. And the nation's top patent official did not resist the temptation to grant a product patent to Latimer because of "nice considerations of dialectic." Rather, Hall was restrained by a real-world concern that a patent granted on one product of nature could open the door to patents being granted on all "the trees of the forest and the plants of the earth, which of course would be unreasonable and impossible."²⁰⁸

²⁰² *Park-Davis*, 189 F. at 103.

²⁰³ Littlewood to Takamine, Oct. 17, 1902, *supra* note 122 (emphasis added).

²⁰⁴ *Park-Davis*, 189 F. at 103.

²⁰⁵ *Ex parte Latimer*, 1889 DEC. COMM'R PAT. 123, 127 (1889).

²⁰⁶ *Id.*

²⁰⁷ *Id.*

²⁰⁸ *Id.* at 126.

Appeal

Five weeks after Learned Hand issued his ruling, Mulford filed a petition to appeal the decision to the Second Circuit Court of Appeals.²⁰⁹ The petition was granted, and several months later, Charles Howson, for Mulford, and Livingston Gifford, for Parke-Davis, submitted appellate briefs of 142 pages and 198 pages, respectively.²¹⁰ In attempting to convince the Second Circuit Court to reverse Judge Hand, Howson largely repeated the arguments he had made at the trial-court level. Howson's first and foremost assertion again centered on priority:

The patentee was not the first to make the suprarenal gland or its active principle practically useful for medical surgical purposes, nor was he the first to produce a substance possessing the useful physiological properties of the suprarenal gland and practically free from "inert constituents" or "inert and associated gland tissue."²¹¹

This time around, however, Howson did muster an attempt to make an argument against the validity of the Adrenalin

patent based on the product-of-nature problem. But Howson's argument suffered from some serious weaknesses. Perhaps most significantly, the point was not given prominent placement within the brief, appearing on pages 46–49 of a 142-page document.²¹² It also is clear that Howson did not even fully engage with the objections raised by Examiner Littlewood during patent prosecution. Howson briefly mentioned that the "Patent Office record . . . shows . . . that the patentee's application was repeatedly rejected on the ground that the 'product' claims were to a 'natural' and therefore 'unpatentable' substance."²¹³ But Howson's citations of Littlewood's objections were incomplete, out of chronological order, and—in one instance—slightly incorrect.²¹⁴ But the most significant symptom of Howson's failure to fully engage with Littlewood's product-of-nature concerns is a complete absence of any reference to *Ex parte Latimer*.²¹⁵ If Howson—or one of his associates—had read the file wrapper with a notion that they might aggressively pursue a product-of-nature argument against the Adrenalin patent, they surely would have latched onto *Latimer* and trumpeted Commissioner Hall's holding. But, as with

209 Howson & Howson (for H.K. Mulford), Petition for Appeal, June 3, 1911, Transcript of Record, *supra* note 32, at 950–951.

210 Charles Howson, Brief for Defendant-Appellant, Parke-Davis v. H.K. Mulford, undated, (on file at the National Archives at New York City, Second Circuit Court of Appeals Case No. 4363, Box 1685, Folder 9364); Livingston Gifford, Brief for Complainant-Appellee, Parke-Davis v. H.K. Mulford, March 1912 [no day given], (on file at the National Archives at New York City, Second Circuit Court of Appeals Case No. 4363, Box 1685, Folder 9364).

211 This was the first bold-faced point of argumentation in Howson's brief for Mulford. Brief for Defendant-Appellant, *supra* note 210, at 5.

212 *Id.* at 46–49.

213 *Id.* at 48.

214 The citations to Littlewood's rejections appeared as follows: "(pp. 890; 878; 834; R[ecord].)" *Id.* Page 890 (Howson's first citation) is to Littlewood's *third* rejection on Oct. 17, 1902, *supra* note 122. Page 878 (Howson's second citation) is to Littlewood's *first* rejection on Dec. 7, 1900, but the relevant section of this communication actually appears at page 879, *supra* note 91. Page 834 (Howson's third citation) refers to Littlewood's *fourth* rejection (the first rejection after the product-patent application had been divided from the process-patent application) on Feb. 14, 1903, *supra* note 130. Howson did not cite two of Littlewood's five rejections: the second rejection, on Nov. 7, 1901, *supra* note 99, at 884; and the fifth rejection, on Mar. 30, 1903, *supra* note 137, at 839.

215 Brief for Defendant-Appellant, *supra* note 210, at 46–49.

Learned Hand's opinion, there is absolutely no reference to *Latimer* anywhere in Mulford's appellate brief.

The three-judge panel of the Second Circuit issued its ruling on April 22, 1912.²¹⁶ The opinion began with words of praise for the young trial judge who had produced a "most exhaustive opinion," which "set forth fully and with the greatest clearness" the "specifications, the claims, the prior art, the difficult chemical questions presented, and the nature of the complainant's and defendant's products."²¹⁷ The opening paragraph of the opinion ended with an affirmation of the essential nature of the lower court ruling: "Upon all the main fundamental questions we fully concur in all Judge Hand's reasoning and conclusions."²¹⁸ The Second Circuit panel had a few minor quibbles with Hand's opinion, but these did not affect their view of the basic holding that Adrenalin was a legitimately patented product and that Mulford's product infringed on the patents owned by Parke-Davis.²¹⁹ In historical terms, the most important point is, again, a negative one: a discussion of the potential product-of-nature problems with the Adrenalin patent is completely nonexistent in the Second Circuit's ruling.

Coincidentally, three days after the appellate decision, an in-house attorney for Parke-Davis named Charles M. Woodruff was testifying before a

Congressional committee on another matter.²²⁰ In the midst of his testimony, Woodruff announced that he had "received a telegraph" stating, "Adrenalin suit decided in our favor."²²¹ The way in which Woodruff framed the dispute—and Parke-Davis's victory—confirms the reality that the litigants perceived this as a battle over priority. It is particularly noteworthy that Woodruff twice referred to the scientific challenge of *isolating* the "active principle of the suprarenal gland"—without so much as a whiff that this had been a meaningful point of contention in the litigation:

The suprarenal glands have long been known to possess valuable hemostatic properties. . . . [I]t naturally came into the minds of chemists that these valuable properties must be due to some active principle which could be *isolated*. So, several chemists in America and Europe, some connected with colleges, but more with manufacturing establishments, under the incentive of the royalties success would mean, went to work to *isolate*, if possible, the active principle of the suprarenal gland Dr. Jokichi Takamine, a Japanese chemist . . . was employed by Parke, Davis & Co. to investigate, and he succeeded quite where others did almost. . . .

²¹⁶ *Parke-Davis & Co. v H.K. Mulford & Co.*, 196 F. 496 (2d Cir. 1912).

²¹⁷ *Id.* at 497.

²¹⁸ *Id.*

²¹⁹ *Id.* at 497–500.

²²⁰ The Pure Food and Drugs Act: Hearings Before the H. Comm. on Interstate and Foreign Commerce, 62d Cong. 231 (1912) (opening of Woodruff's testimony).

²²¹ *Id.* at 287.

Well, now, there has been a great dispute as to who was entitled to that discovery. Dr. Takamine got the substance patented and [Parke-Davis] made arrangements with him for his rights. As soon as Dr. Takamine's processes were disclosed[,] Parke, Davis & Co.'s competitors began putting the substance [onto the market] under other names than that of Adrenalin. Suit was brought against one of them to determine the *priority of invention*. . . . [T]hey denied that Dr. Takamine was entitled to the discovery. The question was submitted to the District Court of the Southern District of New York; and after all the chemical evidence was in, all the articles and everybody that could give any testimony upon the subject, the decision was in favor of Adrenalin. The decision was appealed . . . and I have just received word that the decision of the lower court has been affirmed.²²²

This rather remarkable contemporaneous encapsulation of the entire patent dispute—as expressed by someone who would have had detailed insider knowledge—places a final stamp upon a fundamental historical fact: *Parke-Davis v. Mulford* was not a legal quarrel over the patentability of isolated products of nature.

Conclusion

A few weeks before this appellate court victory, Jokichi Takamine experienced another triumph: on March 27, 1912, he attended a ceremony that was held to plant the first two cherry trees on the north bank of the Tidal Basin in Washington, D.C. Takamine had played a central role in arranging for the gift of these two trees—and 3,018 more—from the people of Japan to the United States. But, in a strong sense, these trees were actually a personal present from Jokichi Takamine to his adopted country. Takamine himself funded the entire cost of having the trees transplanted from Tokyo to Washington.²²³

Ten years later, Takamine died at the age of 67. A *New York Times* editorial commenting on Takamine's passing, labeled him as "the best known and most highly respected of all the Japanese in America."²²⁴ The editorial lauded Takamine for his "contributions to pure science, and especially to the health of both Eastern and Western nations" and praised him for having "done perhaps more than anyone else of his race in this country to bring the two peoples [of Japan and the U.S.] into better understanding."²²⁵

For a number of years, Learned Hand's opinion in *Parke-Davis* was mildly famous in legal circles for his blunt acknowledgment of his scientific shortcomings and

²²² *Id.* at 287–288 (emphasis added).

²²³ In fact, Takamine arranged for and financed the Washington cherry trees *twice*: the first shipment of trees, which arrived in early 1910, was found to be diseased and had to be burned. National Park Service, Cherry Blossom Festival: History of the Cherry Trees, <http://www.nps.gov/cherry/cherry-blossom-history.htm> (last visited November 6, 2011, 8:30 pm).

²²⁴ *Dr. Takamine*, N.Y. TIMES, July 24, 1922, at 10.

²²⁵ *Id.*

his proposed cure for the situation: a court composed of “technical judges to whom technical questions are submitted and who can intelligently pass upon the issues without blindly groping among testimony upon matters wholly out of their ken.”²²⁶ This early articulation of the need for a more technically skilled bench would at least partially come to fruition several decades later with the establishment of the United States Court of Appeals for the Federal Circuit.

Hand’s assertions about the patentability of purified products of nature in *Parke-Davis* would essentially lay dormant and unnoticed until 1958, when they were retrieved by a Fourth Circuit Court appellate panel grappling with the patentability of vitamin B₁₂.²²⁷ These judges were faced squarely with the question of whether this newly identified and isolated dietary factor was an unpatentable product of nature.²²⁸ Presumably with guidance from an appellate brief in support of the patentability of vitamin B₁₂, this court reached back to Hand’s product-of-nature pronouncements in *Parke-Davis*.²²⁹ Significantly, the panel explicitly identified Adrenalin as a product of nature:

Adrenalin is a concentrate of the blood pressure raising principle in the suprarenal glands of living ani-

mals. It certainly is a *product of nature* in the sense the B₁₂ active compositions here may be said to be products of nature.²³⁰

But, once again, Examiner James B. Littlewood—who had been dead more than fifty years at this point—would not have been pleased with this assertion. Littlewood had allowed the Adrenalin product patent only after Takamine’s lawyers had spent over two years convincing him that Adrenalin was something other than a product of nature.

The judges in the 1958 vitamin B₁₂ case missed this subtlety and, instead, quoted Learned Hand’s entire product-of-nature declaration from *Parke-Davis*, including the crucial—and highly problematic—sentence: “But, even if it were merely an extracted product without change, there is no rule that such products are not patentable.”²³¹ Largely on the strength of this language, it seems, the Fourth Circuit held that the B₁₂ product patent was valid.²³² Of course, by 1958, Learned Hand had achieved near god-like status in legal circles, and his figure had come to loom especially large in patent law.²³³ Somewhat understandably, the Fourth Circuit judges failed to take account of the fact that when Learned Hand wrote his decision in *Parke-Davis* he was less than

²²⁶ *Parke-Davis*, 189 F. at 115. For contemporaneous attention to Hand’s *Parke-Davis v. Mulford* opinion, see Felix Frankfurter, *Hours of Labor and Realism in Constitutional Law*, 29 HARV. L. REV. 353, 373, n.66 (1915–1916) (quoting Hand’s call for technically skilled judges in support of Frankfurter’s claim that “substantially disputed questions of fact [require] the invention of some machinery by which knowledge of the facts . . . may be at the service of the courts as a regular form of the judicial process”); William Hard, *Better Business*, 30 EVERYBODY’S MAG. 339, 344–345 (1914) (quoting Hand’s admissions in *Parke-Davis* of his lack of technical knowledge in an article calling for broad reform in U.S. patent system).

²²⁷ *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156 (4th Cir. 1958).

²²⁸ *Id.* at 161–162.

²²⁹ *Id.* at 162–163.

²³⁰ *Id.* at 162 (emphasis added).

²³¹ *Id.* at 163.

²³² *Id.* at 164–165.

²³³ See, e.g., BLAUSTEIN, *supra* note 29; Edmund A. Godula, *Judge Learned Hand and the Concept of Invention*, 9 PAT., TRADEMARK, & COPYRIGHT J. RES. & EDUC. 159 (1965); Stephen H. Philbin, *Judge Learned Hand and the Law of Patents and Copyrights*, 60 HARV. L. REV. 394 (1947).

two years removed from a law practice on Wall Street that was entirely unrelated to issues of intellectual property. And—even more problematically—they almost surely did not recognize that the question of whether Adrenalin was product of nature went almost completely untouched by the litigants who presented evidence and arguments to young Judge Hand.

After 1958, Learned Hand's product-of-nature pronouncements from *Parke-Davis* have ascended in remarkable fashion from obscurity to conventional wisdom.²³⁴ Perhaps most significantly, in 2001, the USPTO used Hand's *Parke-Davis* opinion as a key source of authority for new "Utility Examination Guidelines" that were designed to create a systematic procedure for evaluating the growing number of applications for patents on genes.²³⁵ In publishing these "Guidelines," the USPTO acknowledged that critics had raised objections about the agency's expressed willingness to grant gene patents. The objections aired in 2001 mirror almost exactly the fundamental arguments made more recently by the plaintiffs in *Myriad*:

Several comments state[d] that a gene is not a new composition of matter because it exists in nature, and/or that an inventor who isolates a gene does not actually invent

or discover a patentable composition because the gene exists in nature. These comments urge the USPTO not to issue patents for genes on the ground that genes are products of nature.²³⁶

The USPTO flatly rejected these concerns and staked out the position that an "isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent . . . because that DNA molecule does not occur in isolated form in nature."²³⁷ The USPTO further asserted that "[p]atenting compositions or compounds isolated from nature follows well-established principles."²³⁸ As the chief example of the "well-established" practice of patenting isolated or purified products of nature, the USPTO authors pointed to "an early patent for *adrenaline*."²³⁹ But, in characterizing Takamine's patent in this way, James B. Littlewood's bureaucratic descendants betrayed a subtle—yet significant—misunderstanding of what was, in fact, patented in 1903: Littlewood clearly would have refused a patent on a purified or isolated version of the hormone "adrenaline"; instead, this veteran patent examiner was only willing to grant a patent on "Adrenalin" (capital *a*; no *e*) after he was cajoled to accept the proposition that this medical product was *not* just

234 The ascendancy of Hand's *Parke-Davis* opinion to legal conventional wisdom can be seen by its inclusion in various casebooks, hornbooks, and treatises. See, e.g., INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE 135–136 (Robert P. Merges, Peter S. Menell, & Mark A. Lemley eds., 4th ed. 2006) (casebook includes an edited version of Hand's *Parke-Davis* opinion focusing on the purified-products-of-nature discussion); IVER P. COOPER, BIOTECHNOLOGY AND THE LAW, §3.3 "Purified" Products of Nature (2010) (affirmatively quoting Hand's entire statement on the patentability of purified products of nature from *Parke-Davis*); STEPHEN M. MCJOHN, INTELLECTUAL PROPERTY, EXAMPLES & EXPLANATIONS 213 (3d ed. 2009) (quoting Hand in *Parke-Davis* to explain that "substances that occur in nature (genes, hormones, and other chemicals) . . . may be patentable subject matter if they are purified, isolated, or concentrated").

235 Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

236 *Id.* at 1093.

237 *Id.*

238 *Id.*

239 *Id.* (emphasis added).

an isolated or purified version of the naturally occurring hormone.

In 2001, the USPTO went on to quote Judge Hand's entire three-sentence proclamation from *Parke-Davis* on the patentability of "extracted product[s]" of nature as the definitive statement on the matter.²⁴⁰ The way in which the USPTO authors chose to introduce this pivotal quotation from Hand also warrants scrutiny: "In a decision finding the patent valid, the court explained that compounds isolated from nature are patentable."²⁴¹ This phrasing implies that the patentability of an isolated product of nature was at the center of the dispute between *Parke-Davis* and *Mulford*. But the hard historical truth is that the patentability of such natural products was tangential (at most) to the issues raised by the litigants in *Parke-Davis*.

By contrast, the patentability of isolated products of nature *was* at the center of the lengthy patent application process for Adrenalin. And, during this process, no one—including Takamine and his attorneys—ever disputed the basic principle laid out in *Ex parte Latimer*: isolated or purified products of nature should not be

patented. Indeed, a quick foray into a counter-factual past should reinforce a major point: if—if!—the patentability of isolated products of nature had been litigated before Judge Hand in *Parke-Davis*, the plaintiffs likely would have been estopped from broadly arguing that "extracted [natural] product[s] without change" could be patented. After all, Takamine's attorneys had consistently acknowledged during patent prosecution that *Latimer* provided "the official interpretation of the doctrine involved."²⁴²

In 2010, District Court Judge Robert W. Sweet emerged from his reading of *Parke-Davis* to label Hand's pronouncements on the patentability of purified products of nature as unreliable "dicta."²⁴³ Another recent commentator on *Parke-Davis* has suggested that "[o]ne could argue endlessly over the extent to which Judge Hand's discussion [of purification and patentability] constitutes dicta."²⁴⁴ Such endless argumentation might be possible (and perhaps even entertaining) in the absence of detailed historical investigation. But after examining the full trial record in historical context, I would go so far as to call Hand's pronouncements

²⁴⁰ *Id.*

²⁴¹ *Id.*

²⁴² *Knight Bros. (for Takamine) to Commissioner of Patents, Amendment*, Sept. 25, 1902 (filed Sept. 26, 1902), Transcript of Record, *supra* note 32, at 886 (Takamine's attorneys never wavered from this position in their subsequent communications with the Patent Office).

²⁴³ *Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office (Myriad)*, 702 F. Supp. 2d 181, 225–226 (S.D.N.Y. 2010), *as amended* (Apr. 5, 2010), *aff'd in part, rev'd in part*, ___ F.3d ___, 2011 WL 3211513 (Fed. Cir. 2011).

²⁴⁴ Feldman, *supra* note 28, at 1396.

“dicta on adrenaline.” Or should it be “dicta on Adrenalin[®]”?²⁴⁵

If the U.S. Supreme Court agrees to consider *Myriad*, the justices should not turn to *Parke-Davis* for sage guidance from a judicial genius. Instead, they need to grapple with a difficult question that arises from this old case: Has the time come to reverse the trajectory of historical inertia that began with a small—almost inadvertent—shove in the wrong direction, a century ago, from an inexperienced and under-informed district court judge? Perhaps the answer to this question should be “yes,” given that “[t]he settled expectations of the inventing community”²⁴⁶ rest upon such fundamentally flawed judicial dicta. Instead, for wisdom on the patentability issues at stake in *Myriad*, the Court could turn to the ration-

ale offered by Benton J. Hall in 1889 for refusing a patent on the core of a pine needle.²⁴⁷ Indeed, Learned Hand himself almost surely would have been forced to follow *Ex parte Latimer* in 1911—if the patentability of an isolated or purified product of nature had been at issue in *Parke-Davis v. Mulford*, which (for the last time) it was not.

Alternatively, the Supreme Court might determine that the scientific, social, and economic benefits of allowing patents on human genes (and other such isolated products of nature) have been so salutary that the policy should be continued. This would not change the historical reality that Learned Hand misstated the law in 1911; we would, however, need to reclassify the young judge’s error as a lucky mistake.

²⁴⁵ This history is, at least partially, a cautionary tale about the dangers and disadvantages of allowing a trademark that is so similar to a generic term. If, for example, the trademark for Parke-Davis’s product had been “Sanguetine” (Eli Lilly’s name for a early competing product, see *supra*, p. 385) rather than “Adrenalin,” it seems likely that subsequent confusion about the meaning of *Parke-Davis v. Mulford* might have been significantly diminished.

There was, in fact, considerable contemporaneous controversy in the medical community about what to call the hormone from the adrenal gland and the medical product(s) derived from it. American medical scientists were sufficiently concerned about the potential for confusion between “Adrenalin” and “adrenaline” that they actively turned toward the use of a different generic term (“epinephrine(e)”). See, Philip Mills Jones, *The Active Principle of the Adrenal Gland: What Name Shall Be Given to It?* [editorial], 2 CAL. ST. J. MED. 178 (1904); *The Name “Epinephrin” versus the Name “Adrenalin”* [editorial], 56 JAMA 901 (1911); *Proprietary versus Unprotected Names: The Question of Term to Be Applied to the Active Principle of the Suprarenal Gland*, 56 JAMA 910 (1911) (contains extensive extracts from correspondence with various physicians and Parke-Davis on the topic). This naming difficulty has also received some historical attention. See, Horace W. Davenport, *Ephinephrin(e)*, 25 PHYSIOLOGIST 76 (1982); E. M. Tansey, *What’s in a Name? Henry Dale and Adrenaline*, 1906, 39 MED. HIST. 459 (1995) (primarily focused on British context for controversy).

²⁴⁶ Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office (*Myriad*), __ F.3d __, 2011 WL 3211513 (Fed. Cir. 2011) (quoting Moore’s concurrence).

²⁴⁷ *Ex parte Latimer*, 1889 DEC. COMM’R PAT. 123 (1889).