

GENENTECH AND THE STOLEN GENE: PATENT LAW, AND PIONEER INVENTIONS

DR MATTHEW RIMMER*

Faculty of Law, The Australian National University

Abstract

This paper evaluates the litigation over the biotechnology patent dispute between the University of California and Genentech. First it outlines the scientific work behind the cloning of the human growth hormone, and looks at the patent office, and its treatment of biotechnological inventions. Second, it considers the court room dispute, and the legal case of the University of California and the biotechnology company in this dispute. Finally, it considers the implications of this dispute for policy reform in respect of patent law and biotechnology.

Introduction

The *Washington Post* article provides a melodramatic account of the origins of a major patent dispute between a public university and a private biotechnology firm:

The men with foreign accents trod carefully through desolate hallways. They weren't supposed to be there, but the University of California at San Francisco had something they wanted, and they knew just where to find it. It was an hour before midnight on New Year's Eve and nobody was around to see the deed unfold. The men took the elevator to a ninth-floor laboratory. They retrieved vials and beakers, hauled the material downstairs, put it in their car and raced south toward the offices of a tiny new company not far from the azure waters of San Francisco Bay.¹

This film noir account of a 'midnight raid' is disputed. The University of California at San Francisco claims credit for a major discovery that took place in 1978. A group of researchers - Peter Seeburg, John Shine, Howard Goodman - for the first time identified the DNA on human growth hormone. The DNA was patented by the University of California. Genentech was alleged to have

* Matthew Rimmer, BA (Hons)/ LLB (Hons) (ANU), PhD (UNSW), is a Lecturer at ACIPA, at the Faculty of Law in the Australian National University. The author is grateful to his informant Professor John Shine, Dr Kathy Bowrey for her comments on this paper, and Paul Clarke for his research assistance. This project has been supported by an Australian Research Council Discovery Grant to research 'Gene Patents in Australia: Options for Reform'.

¹ Gillis, J. '20 Years Later, Stolen Gene Haunts A Biotech Pioneer', *Washington Post*, 17 May 1999, p A01.

taken and used the University's actual DNA invention without permission. It was also accused of using the information in the University's patent to make and sell its drug called Protropin. However, Genentech denied that any such 'midnight raid' took place. It argued that its research into human growth hormone was independent of the work of the public university. The University of California brought legal action against Genentech for patent infringement. The litigation was finally resolved through a settlement in 1999.

The dispute between the University of California and Genentech points to a realignment in the culture and political economy of research. It highlights a shift in the way that researchers think of themselves, and interact with one another.² The litigation sheds light on a debate over the use of patents in the area of basic biological research. Eisenberg explores the potential negative impact of patent rights on scientific norms in the field of biotechnological research: 'By providing such broad exclusive rights, patent law may aggravate pre-existing conflict between scientific norms and the reward structure of science.'³ Her collaborator Rai supports this claim.⁴ Kieff is a naysayer who argues that intellectual property rights are consistent with the norms of science: 'It is not even clear that the pre-1980 basic biological research community had a prescriptive norm that specifically rejected patents, as distinct from other forms of intellectual property.'⁵ In reply, Rai comments:

My assertion that academic scientists did not seek patents before 1980 - a statement that is clearly supported by the data - is not a claim that scientists were, or are, altruistic and selfless human beings. The combination of descriptive and prescriptive norms that existed before 1980 encouraged vigorous competition. The prize, however, was not patents.⁶

Such arguments need to be grounded in historical and sociological work about the understanding of intellectual property by scientists at that time.

This article is part of a wider historical attempt to document and recall the origins of the biotechnology industry. The dispute between the University of California and Genentech is instructive about the origins of the biotechnology industry in the United States in the 1970's.

² Rabino, I. 'Ethical Debates In Genetic Engineering: U.S. Scientists' Attitudes on Patenting, Germ-Line Research, Food Labeling, and Agri-Biotech Issues', *Politics And The Life Sciences*, 1998, Vol. 17 (2), p 147-163.

³ Eisenberg, R. 'Proprietary Rights And The Norms Of Science In Biotechnology Research', *Yale Law Review*, 1987, Vol. 97, p 177.

⁴ Rai, A.K. 'Regulating Scientific Research: Intellectual Property Rights And The Norms Of Science', *Northwestern University Law Review*, 1999, Vol. 94, p 77.

⁵ Kieff, F.S. 'Facilitating Scientific Research: Intellectual Property Rights And The Norms Of Science - A Response To Rai And Eisenberg', *Northwestern University Law Review*, 2001, Vol. 95, p. 691.

⁶ Rai, A.K. 'Evolving Scientific Norms And Intellectual Property Rights: A Reply To Kieff', *Northwestern University Review*, 2001, Vol. 95, p. 707.

The Oral History Office of Bancroft Library at the University of California has been conducting interviews with scientists, entrepreneurs, and university administrators who were involved in the development and commercialisation of the life sciences.⁷ Drawing upon this work, Sally Smith Hughes has written a dazzling case study of the Cohen-Boyer patent in respect of recombinant DNA.⁸ She argues that the patent was a turning point in the commercialisation of molecular biology, and a harbinger of the social and ethical issues associated with biotechnology today. Stephen Hall made an early attempt to document the race to synthesize a human gene, focusing upon Genentech, Biogen, Eli Lilly and the University of California.⁹ The anthropologist Paul Rabinow has also told a number of stories about the history of biotechnology. He has written accounts of the polymerase chain reaction (PCR),¹⁰ the French genomics project,¹¹ and the Icelandic genomics project by Decode.¹² Similarly, the sociologist Alberto Cambrosio and his collaborators have written a history of scientific research into monoclonal antibodies.¹³ There is much to be learned from such historical case studies. Such memories will serve as an important antidote to the bullish predictions of venture capitalists about the biotechnology industry. One can only gain a sense of the future of genomics with a honest appreciation of its past.

Building upon this past work, this paper adopts a methodology of social history. It seeks to bring to life the real complexity and messiness of patent law, as it negotiates complex questions of patent ownership and infringement. This article focuses the litigation over the biotechnology patent dispute between the University of California and Genentech. It is supported by the analysis of the transcripts of a patent trial that is viewed as a landmark in biotechnological patent jurisprudence. It first considers the scientific norms and values regarding intellectual property in the biological sciences. It outlines the scientific work behind the cloning of the human growth hormone at the University of California, and the foundation of the first biotechnology company Genentech.

⁷ The Bancroft Library. *Bioscience and Biotechnology: Resources for Historical Research, 1999-2002*, <http://sunsite.berkeley.edu:2020/dynaweb/teiproj/oh/science/>

⁸ Smith Hughes, S. 'Making Dollars Out Of DNA: The First Major Project In Biotechnology And The Commercialization Of Molecular Biology, 1974-1980', *Isis*, 2001, Vol. 92, p. 541-578.

⁹ Hall, S. *Invisible Frontiers: The Race To Synthesize A Human Gene*. London: Sidgwick and Jackson, 1987.

¹⁰ Rabinow, P. *Making PCR: A Story of Biotechnology*. Chicago: The University of Chicago Press, 1996

¹¹ Rabinow, P. *French DNA: Trouble In Purgatory*. Chicago: The University of Chicago Press, 1998.

¹² Rabinow, P. 'Learning to Fly: A New Page in History', *GeneLetter*, 2000.

¹³ Cambrosio, A. and P. Keating. 'Monoclonal Antibodies: From Local to Extended Networks,' in A. Thackray, ed., *Private Science: Biotechnology and the Rise of the Molecular Sciences*. Philadelphia: Pennsylvania, 1998, p. 165-181.

It considers the involvement of public research institutions and the first private companies in the groundbreaking case of *Diamond v Chakrabarty*, in which the Supreme Court recognised that biotechnological inventions could be patentable subject matter.¹⁴ It then considers the court room dispute, and the legal case of the University of California and the biotechnology company in this dispute. It evaluates the jury decision in respect of patent validity and patent infringement, and examines the settlement between the University of California and Genentech. Finally it considers the implications of this dispute for policy reform in respect of patent law and biotechnology. In particular, this paper deals with the ongoing controversy over the patenting of genes, express sequence tags, and research tools. It highlights the inadequacies of the utility requirement in processing such applications in respect of biotechnology. It also considers the need for the development of conflict of interest policies in collaborations between the private sector and the public sector.

Shaping Life in the Lab: The Boom in Genetic Engineering¹⁵

Stanley Cohen of Stanford University and Herb Boyer of the University of California, San Francisco, were responsible for the development of recombinant DNA.¹⁶ This invention made it possible to recombine and clone DNA, thus providing basic scientists with a simple and precise method for studying the structure and function of genes of higher and lower organisms. Sally Smith Hughes comments that the Cohen-Boyer patents were a catalyst for an attitudinal shift among scientists, research institutions and entrepreneurs: 'The patent and its two companions of 1984 and 1988 were instruments in the transformation of perceptions and policy regarding commercial activity in academia.'¹⁷

The reputation of the University of California for recombinant DNA technology attracted a number of international post-doctoral researchers - including Peter Seeburg from the Federal Republic of Germany, and John Shine from Australia. A collaborative team of scientists worked on growth hormone at the University of California. Peter Seeburg was the conceptual driver, the individual with the vision of really wanting to isolate the growth hormone DNA sequences. John Shine was involved very much in a lot of the cloning and joining together of the DNA molecules, and especially in the sequencing of the DNA, the determining the sort of sequence of those strings on a bead. Howard Goodman was the head of the laboratory. He had quite a major role

¹⁴ *Diamond v Chakrabarty* (1980) 447 US 303

¹⁵ The title is taken from a Time Magazine article in 1980 about Herb Boyer and the public listing of Genentech.

¹⁶ For a discussion of the patenting of the Boyer-Cohen patent, see Smith Hughes, S. 'Making Dollars Out Of DNA: The First Major Project In Biotechnology And The Commercialization Of Molecular Biology, 1974-1980', *Isis*, 2001, Vol. 92, p. 541-578.

¹⁷ Smith Hughes, S. 'Making Dollars Out Of DNA: The First Major Project In Biotechnology And The Commercialization Of Molecular Biology, 1974-1980', *Isis*, 2001, Vol. 92, p. 573-574.

in developing a lot of the chemical reactions using those enzymes that join DNA together. Dr John Baxter was involved in a lot of the knowledge about the biology and the clinical use of growth hormone. A post-doctoral fellow in that laboratory Joe Martial was involved in helping to extract RNA from pituitary genes in sort of preliminary experiments leading up to the cloning experiments.

The research was of great scientific, medical, and commercial importance. Human growth hormone is a very important and vital hormone of the body. It is prescribed for children that do not achieve their natural height without human growth hormone. Human growth hormone is also useful in other research. It has been used in the areas of arthritis, and cystic fibrosis, as well as in treatments for cardiovascular disease, lung disease, heart disease, and healing patients with wounds.

The researchers at the University of California were naïve about the commercial implications of such research. Shine comments: 'Biologists were not familiar with industry because of the significant time difference between a fundamental biological discovery and its commercial application. So you were not really exposed to questions of intellectual property. It was just something totally foreign to your psyche.'¹⁸ Such a statement helps resolve an ongoing debate about the scientific norms at work in the biotechnology community in the 1970's. Nonetheless the discovery was reported to the University of California patent office.

With the cloning of the insulin gene and other technologies that were happening at the time, the University of California gained an awareness of the issues related to patents. So their patent attorneys and lawyers would work with the scientists extensively to get them to file patents, and explain the inventions. Shine recalls that such initial exchanges were an 'administrative burden'.¹⁹ He said that the biologists were 'frustrated' because they had to provide fundamental explanations of their research, which written up in pedantic ways by patent attorneys.²⁰ The problem was that the prior art field at that time had very few biological patents - there were mainly patents dealing chemicals. In hindsight, Shine recognises that the University of California were particularly fortunate to have the services of a patent attorney called Lawrence Greenley.²¹ He understood the technology reasonably well, and was able to write very good patent specifications for the time. The researchers gave them the information that they had discovered - the sequence of human growth hormone DNA, the transfer vector, and all of the necessary intellectual property information that was required to file a patent application.

There was disagreement within the Goodman laboratory over the determination of authorship and inventorship for the purposes of patent law. There was tension between the head of the laboratory, and the post-doctoral students. In particular, Seeburg felt aggrieved about Goodman claiming credit for the scientific research:

What shattered me was when we told Howard that we had expression of growth hormone. The next thing we knew, they had called in patent lawyers from the university and patented the [expression] between Goodman, Rutter, and Baxter, putting themselves on as inventors, and they hadn't even known about it [until] we had told them.²²

Shine discussed the matter of authorship and inventorship with greater tact and diplomacy. He recognised the difficulties of assigning such credit in a collective enterprise of scientific research.²³ One of the other inventors, Baxter, argued that Howard Goodman deserved credit because he had set up one of the best laboratories in the world to use this technology. In the end, three inventors were named on the patent application; and another two collaborators - Baxter and Martial - were entitled to a share of royalties under the agreement.

Seeburg and his laboratory head, Goodman, evidently had a falling out, and Seeburg could continue his research on the hormone expression process only at night and without support from Goodman. Denied a position by the university, Seeburg went to work for Genentech.

Genentech

Genentech, Inc. was founded in 1976 by venture capitalist Robert Swanson and biochemist Herb Boyer.²⁴ Swanson recognised the commercial value of recombinant DNA technology and held a meeting with Boyer. Swanson and Boyer borrowed \$500 and started a company to create bacteria factories to make medical products for people. Its first commercial contract was with Boyer's laboratory to clone the insulin gene with various cloning vectors. Genentech gave a grant in effect to the University of California, and that funded some of the initial research in this whole area.

Swanson of Genentech and his counsel Thomas Kiley sought to educate scientists and researchers about the value of patents and intellectual property protection. The entrepreneur said in an interview:

It's been clear for a long time that patents were critical for commercial development. It was really a critical part of this process to get scientists to understand that. It was somewhat in conflict with this idea that we were going to publish, and that was critical to getting the very best scientists and having them and the company be recognized for the quality of their research. So we developed this idea that we are going to publish our work because we think we get more benefit from doing that than we lose by telling our competitors what we're

¹⁸ Shine, J. 'Interview with the Author', Sydney, 23 April 2001.

¹⁹ Ibid.

²⁰ Ibid.

²¹ Ibid.

²² Hall, S. *Invisible Frontiers: The Race To Synthesize A Human Gene*. London: Sidgwick and Jackson, 1987, p. 280.

²³ Id, p. 205.

²⁴ Oral histories by Robert Swanson and Herbert Boyer can be found at the Bancroft Library, <http://www.lib.berkeley.edu/BANC/Biotech/>

*doing. But we're going to patent it beforehand.*²⁵

Swanson argued that scientific communication was not substantially delayed by the patenting process. He argued that any time delays would be minimal because patent attorneys were sympathetic to the concerns of scientists to publish as soon as possible.

There was intense competition to clone the insulin gene. Boyer decided that it would not be possible in the foreseeable future to clone or isolate the insulin gene itself. He collaborated with chemists from the City of Hope Medical Centre in Los Angeles to chemically synthesize insulin.²⁶ By contrast, Howard Goodman's laboratory sought to use enzymatic mechanisms to clone the insulin gene. It was able to clone the insulin gene long before their rivals were able to chemically synthesize it. However, Boyer and Genentech were well set up to commercially exploit the insulin gene and that technology. They had the ability to manipulate the sequence of that gene in a certain way, so as to programme bacteria to express it, and make large amounts of the functional protein. Genentech desperately needed the intellectual property over the insulin gene. They sought to license the technology from the University of California.

Genentech made a number of attractive offers to researchers in Goodman's laboratory. The lawyer for the University of California, Gerald Dodson, stresses that Genentech was keen to recruit the researchers at the University of California:

*Robert Swanson would attend wine and cheese parties at the University Lab on Friday afternoons to try and convince them to join Genentech and see what was going on. There were sailboat rides in the San Francisco Bay with Swanson and Tom Perkins, another venture capitalist to recruit these men. Genentech was real anxious to get these inventors from the University of California over to Genentech.*²⁷

The aggressive recruitment drive of Genentech can be explained by the acute labour shortage in the burgeoning field of biotechnology.²⁸ Of course this situation had changed by the 1980s. It was then possible to secure personnel with experience in the biotechnology industry by raiding other companies and increasing numbers of graduates sought employment in the industry.

²⁵ Swanson, R, 'An oral history conducted by Sally Smith Hughes', Bioscience and Biotechnology Archives and Oral Histories, Bancroft Library, 1996-1997, http://sunsite.berkeley.edu:2020/dynaweb/teiproj/oh/science/swanson/@Generic_BookView

²⁶ This agreement between the City of Hope Medical Research Centre and Genentech has since ended in acrimony in a contractual dispute.

²⁷ *The Regents of the University Of California v Genentech* (1999) No. C90-2232 CAL, trial transcripts.

²⁸ Kenney, M. 'Biotechnology And A New Economic Space', *Private Science: Biotechnology and the Rise of the Molecular Sciences*. Philadelphia: University of Pennsylvania Press, 1998, p. 137.

At Genentech, Seeburg worked with a postdoctoral researcher named David Goeddel and others to replicate and extend the human growth hormone work, aiming to get a complete sequence that could be put in bacteria for mass production. The work at Genentech, however, was frustrated by poor source tissue and many failures.

On New Year's eve on the 31st of December 1978, it was alleged that two employees of the fledgling biotechnology firm, Genentech, Seeburg and Alex Ullrich, went to the University of California in the dead of night, and took samples from the research material that they had left there. The University of California demanded the return of the human growth hormone. The biotechnology firm Genentech refused. According to Seeburg, the material removed from Goodman's laboratory was used to complete the Genentech human growth hormone project by himself and Goeddel. Seeburg testified under oath that he and Goeddel made a secret agreement to conceal the use of the University of California DNA material in their Genentech developmental research.

In 1979, Seeburg and his colleagues at Genentech published the results of the Genentech project in a paper in the journal *Nature*.²⁹ In 1979, Genentech filed its own patent application and named as inventors on the patent, Goeddel and Herb Heyneker. This application later yielded a patent. Genentech publicly claimed the production of human growth hormone for the first time in bacteria using its own DNA. The patent was issued in 1982. In 1985, Genentech received approval from the Food and Drug Administration for its drug, and began selling the human growth hormone drug, Protropin. It acquired a range of patents in respect of human growth hormone.³⁰

In the wake of its patent applications, Genentech offered its stock to public investors on 14 October 1980. The stock at its initial public offering underwent the most dramatic escalation in value in Wall Street history - the offering of one million shares of stock at \$35 per share climbed to \$89 a share within the first twenty minutes of trading.³¹ This excitement was reflected in an article in *Time Magazine*, which featured Herb Boyer on the cover, with the headline: 'Shaping Life In The Lab: The Boom In Genetic Engineering.'³² By the end of the day, the company had raised \$36 million and was valued at \$532 million - a sign of investors' enthusiasm for biotechnology at the time.

²⁹ Goeddel DV, Heyneker HL, Hozumi T, Arentzen R, Itakura K, Yansura DG, Ross MJ, Miozzari G, Crea R, and Seeburg PH. 'Direct Expression in Escherichia coli of a DNA Sequence Coding for Human Growth Hormone', *Nature*, 1979, Vol. 281, p. 544-548.

³⁰ Goeddel, et al. United States Patent 4,634,677; Plasmid capable of expressing human growth hormone (6/1/1987) United States Patent 4,658,021 Methionyl human growth hormone (14/4/1987); United States Patent 4,898,830. Human growth hormone DNA (6/2/1990)

³¹ Rifkin, J. *The Biotech Century*. New York: JP Tarcher, 1998, p 43.

³² Bancroft Library, <http://bancroft.berkeley.edu/Exhibits/Biotech/25.html>

The Patent Office

As a result of the research carried out by public institutions and fledgling biotechnology companies, the United States Patent and Trade Mark Office (PTO) was forced to consider whether genetic engineering techniques were patentable subject matter.

In 1978, Alvin Tatenholz was the examiner at the PTO who handled all of the biotechnology applications – including the one for human growth hormone by the University of California. He informed the applicants that he was not going to take up the case for examination. Tatenholz thought that the subject matter that was involved here, which included a cloning vector, could have been affected by a case on the patenting of genetic engineering before the Supreme Court of the United States.

Ananda Chakrabarty, a microbiologist then at the General Electric Company, had used genetic engineering techniques to create a novel bacterium that presumably had never before existed in nature.³³ Because Chakrabarty's bacterium showed promise in breaking down crude oil, its lucrative potential for cleaning up oil spills or remediating toxic waste led him to file for what is known as a utility patent in 1972.

After much legal dispute in the lower courts, the Supreme Court of the United States finally considered whether genetic engineering techniques were patentable. It is worth revisiting the submissions of three friends of the court – the University of California, Genentech, and the People's Business Commission.

The University of California intervened in the case of *Diamond v Chakrabarty*. Counsel Edward Irons and Mary Sears stressed that the case was relevant to academic research on insulin and human growth hormone:

*Relevant inventions made at the University likewise entail the insertion of man-made plasmids containing genes from other organisms into a host microorganism. For example, the University's inventions involve the preparation and insertion into a strain of E.coli of plasmids containing mammalian genes which express various proteins such as insulin and growth hormone, in great demand for therapeutic purposes.*³⁴

Daniel Kevles stressed that the University of California 'was no more alive than other universities to the hopes of revenues from biotechnology, only more immediately interested, by virtue of the activities on its San Francisco campus'.³⁵ This statement was echoed and generalised

in a single amicus brief filed on behalf of a number of peak organisations in respect of biochemistry and molecular biology.

Genentech also intervened in the *Diamond v Chakrabarty* case as an amicus curiae. Swanson reflected:

*This case, which didn't have a lot of commercial relevance, had a great deal of relevance to the biotechnology industry in terms of drug development. We felt that we needed to participate and we did, and fortunately the court made the right decision.*³⁶

Counsel Thomas Kiley emphasized that the Court's decision would have a profound impact on the question of whether investments in research expenditures and recombinant DNA technology should be made in view of the character of patent protection available.³⁷ He encouraged the Court to 'confirm the patentability of micro-organisms and both encourage a beneficent science and ensure that broad and forward looking incentives remain for those who would pull the next technology'.³⁸ Such an intervention demonstrates how Genentech was at the vanguard of legal innovation in respect of biotechnological inventions.

Both the University of California and Genentech were united in the belief that biotechnological inventions should be patentable. By contrast, Jeremy Rifkin and the Peoples Business Commission contended that the Congress of the United States never intended that living organisms, whether modified through genetic engineering or not, be patentable.³⁹ They claimed that the technology of genetic engineering was not in the public interest, and should not be unduly encouraged by giving unwarranted economic incentive to corporations in the field of genetic research and development through the vehicle of awarding potentially lucrative patents on living organisms.

In *Diamond v Chakrabarty*, the Supreme Court of United States held by a majority of five to four that genetically engineered organisms are either a manner of manufacture or a composition of matter and are therefore patentable.⁴⁰ It regarded the matter as one of narrow statutory interpretation. The court also said that it lacked the competence to address arguments about the ethics of genetic engineering and recommends that they be addressed to Congress and the President, as the balancing of competing values and interests was more a matter of high policy for resolution within the legislative process. The Supreme Court stated that 'anything under the sun made by man' is patentable subject matter. This

the Molecular Sciences. Philadelphia: University of Pennsylvania Press, 1998, p 68.

³³ Swanson, R. 'An Oral History Conducted by Sally Smith Hughes', Bioscience and Biotechnology Archives and Oral Histories, Bancroft Library, 1996-1997, http://sunsite.berkeley.edu:2020/dynaweb/teiproj/oh/science/swanson/@Generic_BookView

³⁷ Amicus Curiae Brief of Genentech Inc.

³⁸ Amicus Curiae Brief of Genentech Inc.

³⁹ Amicus Curiae Brief of the People's Business Commission.

⁴⁰ *Diamond v Chakrabarty* (1980) 447 US 303

³³ For interviews with the inventors see D Kevles, 'A History of Patenting Life in the United States with Comparative Attention to Canada and Europe', European Group on Ethics in Science And New Technologies To The European Commission, 12 January 2002.

³⁴ Amicus Curiae Brief of the Regents of the University of California.

³⁵ Kevles, D. 'Diamond v Chakrabarty and Beyond', *Private Science: Biotechnology and the Rise of*

has been followed like a mantra by the PTO and the courts for the following decades.

The real beneficiary of this decision was the patent office bureaucracy. The lack of a rule or clear status about the patentability of biotechnological inventions created administrative difficulties. Rational ordering in law is the preferred model for positive law that eschews morality as a basis of decision making at the outset.

Shortly after the decision in *Diamond v Chakrabarty*, the patent office took up the examination of the patent number 4,363,877. It informed the applicants that the claims were allowed, and that they had to pay an issue fee. The Patent Office re-examined the patent on six different times. It considered any additional prior art that was not considered in the original examination, to ensure that the claims of the patent were valid over that of additional prior art. The first re-examination proceeding was initiated by the University of California. The remaining five re-examination proceedings were requested by Genentech. The Patent Office concluded that claims 6, 7, and 8 of the 4,363,877 patent were valid over more than 300 additional prior art references cited in those six proceedings.

The Patent Office granted a patent in respect of 'recombinant DNA transfer vectors containing codons for human somato-mammotropin and for human growth hormone'. The named inventors included Howard Goodman, John Shine, and Peter Seeburg. The assignee was the Regents of the University of California. The patent was issued on the 14th December 1982. The scientists published the results in *Nature*.⁴¹

20 Years Later, Stolen Gene Haunts a Biotech Pioneer⁴²

The University of California filed patent infringement suits against the biotechnology company, Genentech, in 1990 and 1997. John Shine affirmed:

*It was a very important test case because it demonstrated that industry had to respect fundamental core patents. I appreciate that there are a lot of bad patents out there which have been used to stop developments. There is a lot of trivial stuff. In this case, the patent went back to the patent office, and was re-examined half a dozen times. They asked all sorts of questions. And clearly it was a very strong fundamental patent. The company made a policy decision that they were going to fight it. Fortunately, it was eventually settled.*⁴³

⁴¹ Seeburg, P., Shine, J., Martial, A., Ivarie, R., Morris, J., Ullrich, A., Baxter, J. and Goodman, H. 'Synthesis of Growth Hormone by Bacteria', *Nature*, 1978, Vol. 276, p. 795-798.

⁴² Title comes from the article, Gillis, J. '20 Years Later, Stolen Gene Haunts A Biotech Pioneer', *Washington Post*, 17 May 1999, p A01.

⁴³ Shine, J. 'Interview with the Author', Sydney, 23 April 2001.

A jury trial was held in the U.S. District Court for the Northern District of California beginning in April, 1999. In June 1999, the jury was unable to reach a verdict on the infringement issue. A second trial was scheduled to begin in January 2000. However, a settlement was reached between the parties which ended the legal proceedings.

Litigation

Since its inception, Genentech has used litigation as part of its business strategy. It has been involved in patent litigation in the United States,⁴⁴ the United Kingdom,⁴⁵ and Australia.⁴⁶ In an interview, Swanson comments upon the reputation of Genentech for being an aggressive enforcer of its intellectual property:

*One aspect of it we haven't talked about was that because we were the first to produce human hormones in microorganisms, we got some very broad patent protection. We decided to use that to protect our early products, but then we licensed it broadly for anything beyond that. It was a very inexpensive license, and we donated those royalties to the Genentech Foundation, which now invests in biomedical research and other things in the local northern California area. The idea was that you needed to protect your own products - that was critical. But you didn't want to stop the development of the science; otherwise you'd block everybody out of the business. I think you do need to be aggressive. I think Tom Kiley has the analogy. He says it's sort of like you've planted the seed, and you've raised the crops, and someone else comes and steals the corn. Well, you know, that isn't right. [laughter] So you have to stop them from doing that. We've had some battles, but only when somebody was trying to steal our corn.*⁴⁷

⁴⁴ Liao, S.A. 'Resolving The Dilemmas Between The Patent Law and Biotechnology: An Analysis Of Three Recent Biotechnology Patent Cases', *Computer And High Technology Law Journal*, 1995, Vol. 11, p 229.

⁴⁵ Sherman, B. 'Genentech and another v Wellcome Foundation Ltd: A Step Backward in Protecting Biotechnological Inventions', *International Review Of Industrial Property And Copyright Law*, 1990, Vol. 21 (1), p 76.

⁴⁶ *Genentech Inc v Eli Lilly and Company* [1988] APO 9 (24 March 1988); *Genentech Inc v The Wellcome Foundation Limited* [1988] APO 15 (16 May 1988); 11 IPR 401; 1988 AIPC 90-493; *Genentech Inc. v Amrad Corporation Limited* [1994] APO 17 (22 February 1994); 29 IPR 218; *Genentech Inc and Central Sydney Area Health Service v Celtrix Pharmaceuticals Incorporated* [1993] APO 39 (19 May 1993); 26 IPR 629 and [1995] APO 60 (19 October 1995); 34 IPR 162; *Genentech Inc v Human Genome Sciences Inc* [2000] APO 22 (17 March 2000) and APO 33 (27 April 2000).

⁴⁷ Swanson, R. 'An Oral History Conducted by Sally Smith Hughes', Bioscience and Biotechnology Archives and Oral Histories, Bancroft Library, 1996-1997, http://sunsite.berkeley.edu:2020/dynaweb/teiproj/oh/science/swanson/@Generic__BookView

Five law suits arose out of various research arrangements involving the University of California, Genentech and the pharmaceutical company, Eli Lilly.⁴⁸ These arrangements related to recombinant DNA technology and its use in the production of human growth hormone. These law suits were eventually consolidated.

Genentech was locked into litigation against the University of California. It became entrenched in a position that it was going to defend the case, no matter what. Genentech engaged in a Fabian legal strategy. It sought to delay and stall, hoping to exhaust the resources and the will of the University of California in a long-drawn out battle. Genentech engaged in forum-shopping, looking for a jurisdiction which would best suit their case. There was much debate whether the litigation should be heard in the District Court of California or the District Court of Indiana. Genentech filed multiple suits. As a result, there was much discussion of the consolidation of the litigation. Genentech also sought to expand the case to include allegations that the University of California and Eli Lilly had violated anti-trust and state law. In particular, they alleged that the parties had engaged in anti-competitive licensing and fraud.

In response, the University of California sought protection under the Eleventh Amendment, which provided: 'The judicial power of the United States shall not be construed to extend to any suit in law or equity commenced or prosecuted against one of the United States by Citizens of another state, or by citizens or subjects of any foreign state.' It was successful at first in this motion before the District Court.⁴⁹

Although they displayed great procedural and tactical finesse, the tactics of Genentech were ultimately unsuccessful. The case was heard in the District Court of California. The parties involved were whittled down. Genentech reached a settlement with Eli Lilly, the pharmaceutical company who had licensed the patent of the University of California.⁵⁰ The various law suits were consolidated.⁵¹ The issues were narrowed down to patent validity and infringement.⁵² Other matters that Genentech had introduced into the case were dismissed for want of evidence. Furthermore, the Federal Court of Appeals ruled that the University of California was not allowed to hide under the shield of the eleventh amendment.⁵³

⁴⁸ *The Regents of the University of California v Genentech* (1990) C-90-2232; *The Regents of California v Eli Lilly* (1991) C-90-0373; *Genentech v Eli Lilly and the Regents of the University of California* (1990) 90-1678C; *Eli Lilly v Genentech* (1987) 87-0219C; and *Genentech v Eli Lilly* (1988) 88-1463-C.

⁴⁹ *Genentech v The Regents of the University of California* (1996) 939 F Supp 639

⁵⁰ Genentech. 'Genentech and Lilly Reach Settlement', Press Release, Press Release, South San Francisco, California, 5 January 1995.

⁵¹ *In Re The Regents Of The University of California* (1992) 964 F 2d 1128

⁵² *In Re Recombinant DNA Technology Patent and Contract Litigation* (1994) 874 F Supp 904.

⁵³ *Genentech v The Regents of the University of California* (1998) 143 F 3d 1446

The effect of such tactical manoeuvring and operations was to stretch out the litigation for ten years before it came to trial. The matter was like the law suits in Charles Dickens' *Bleak House*. This litigation demonstrates that procedural law is just as important as substantive law in litigation over biotechnology patents. There is a need to analyse civil litigation as well as substantive issues over the validity and infringement of patents.

Trial

The University of California was represented by Gerald Dodson, a partner in the Palo Alto office of Morrison & Foerster and a member of the firm's Litigation Department. The lawyer argued that the patent application over the human growth hormone by the University of California was valid. He stressed that this invention was a pioneering invention. Dodson summed up a range of evidence from expert witnesses to support this contention:

*The invention was a major scientific achievement. Dr Shine testified that the whole recombinant DNA revolution was just beginning. Mr Burchfiel testified that in deciding whether something is a pioneering invention, if it opens new fields of research, it's entitled to a broad range of equivalents. And Dr Flavell said the UC '877 patent was the first to provide codons for human growth hormone which allowed an entire industry to open up. And Dr Heyneker pointed out the important nature of the pioneering institution at the University of California at the time.*⁵⁴

The argument taps into a wider debate about patent law and 'pioneer inventions'.⁵⁵ The definition of 'pioneer inventions' remains vague and imprecise. There are a number of cases that mention the concept.⁵⁶ However, there is not a specific category of inventions that can be identified. The term 'pioneer invention' is used as a shorthand to describe an invention that is very significant, one that opens new fields of research or endeavour or one that permits new industries to be founded.⁵⁷

Under the doctrine of 'pioneer inventions', the courts may grant a broader scope of protection to patents covering revolutionary technological advances. They will construe the claims of 'pioneer inventions' much more broadly than other patents, allowing the claims to encompass a broader range of 'equivalents' during an infringement determination. Conversely, improvement patents in a crowded art are only entitled to a very narrow range of equivalents.

⁵⁴ *The Regents of the University Of California v Genentech* (1999) No. C90-2232 CAL, p. 4758.

⁵⁵ Thomas, J. 'The Question Concerning Patent Law And Pioneer Inventions', *Berkeley Technology Law Journal*, 1995, Vol. 10 (1), <http://www.law.berkeley.edu/journals/btlj/articles/vol10.html>

⁵⁶ Burchfield, K. *Biotechnology And The Federal Circuit*. Washington DC: The Bureau Of National Affairs Inc, 1995.

⁵⁷ *The Regents of the University Of California v Genentech* (1999) No. C90-2232 CAL, p. 1390.

In this case, Genentech disputed the characterisation of the research into human growth hormone as a 'pioneer invention'. The lawyers protested that there was no forewarning that the University of California was going to make such a claim in court.⁵⁸ Genentech hedged that there was no separate class of 'pioneer inventions'. Furthermore it argued that the '877 patent created no new industry. There is a danger, though, that such arguments rebound back on Genentech. As Swanson testified, the company had sought broad patent protection for its own revolutionary research.

Should groundbreaking research be rewarded with broad patents? Scholars are divided about the use of 'pioneer inventions'. Oddi has proposed the grant of a 'revolutionary patent' for pioneer inventions.⁵⁹ In contrast, Merges and Nelson have argued that patent law should favour improvement innovations over pioneer inventions: 'Without extensively reducing the pioneer's incentives, the law should attempt at the margin to favor a competitive environment for improvements, rather than an environment dominated by the pioneer firm.'⁶⁰ For his part, Thomas does not attempt to choose between these competing views. He calls for a better philosophical and historical framework for an understanding of 'pioneer inventions'.⁶¹

Gerald Dodson relied upon the evidence of Seeburg and a number of documents to support his case in relation to patent infringement. He emphasizes that in 1979, UC warned Genentech about the unauthorized use of the UC's invention. There was a series of correspondence back and forth between university officials and Genentech about the University trying to get its DNA back. There is a piece of correspondence, for example, where Swanson, the president Genentech, tells the University officials,

*What are you worrying about? That's in a patent application of the university's. Your rights are protected. Don't worry about it.*⁶²

Furthermore, Gerald Dodson highlights an admission by Genentech to the Food and Drug Administration that the DNA was identical. He also stresses the confidential memoranda of Genentech's general course in which he said that there was use of university materials in the human growth hormone project.

In the trial, Genentech's strategy was to make small concessions to win the argument. Kidd recognised that

⁵⁸ *The Regents of the University Of California v Genentech* (1999) No. C90-2232 CAL, p. 1500.

⁵⁹ Oddi, A. 'Beyond Obviousness: Invention Protection In The Twenty-First Century', *American Law Review*, 1989, Vol. 38, p. 1097.

⁶⁰ Merges, R. and Nelson, R. 'On The Complex Economics Of Patent Scope', *Columbia Law Review*, 1990, Vol. 90, p. 839.

⁶¹ Thomas, J. 'The Question Concerning Patent Law And Pioneer Inventions', *Berkeley Technology Law Journal*, 1995, Vol. 10 (1), <http://www.law.berkeley.edu/journals/btlj/articles/vol10.html>

⁶² *The Regents of the University Of California v Genentech* (1999) No. C90-2232 CAL, trial transcripts.

the University deserved its '877 patent. He conceded that Goodman, Shine, and Seeburg had isolated 24 to 191, the 3 prime region. He acknowledged that the University deserved the recognition for what it did. However, Kidd attacked the breadth of the patent made by the University of California. In his closing argument, Kidd sought to attack several of the key claims. He maintained that the university was not deserving of three claims – claim 6, claim 7 and claim 8. Kidd stressed that there were important differences between the transfer vector of the University of California, and the manufacturing expression vector of Genentech.

In his closing argument, Kidd contested the claim of patent infringement, and mounted a ferocious attack upon the credibility of Peter Seeburg as a witness. This is understandable given that he had offered such damaging evidence against Genentech. Kidd alleged that the scientist had tarnished the reputation of a number of Genentech scientists by changing his story. He instead relied upon the evidence of a number of Genentech scientists -Goeddel, Heyneker, Yelverton and Ross. They argued that the evidence showed that Genentech not only used its own independent work, but left a clear trail in a number of laboratory notebooks – which he called the 'four magic lab-books'. Kidd claimed that the evidence of the other Genentech scientists should be preferred to that of Peter Seeburg.

Jury

The jury upheld the validity of the patent issued to the University of California. It rejected Genentech's claim that the 1982 patent was invalid on the grounds that the publicly released patent did not contain enough information to allow a scientist of 'ordinary skill' to use it. United States District Judge Charles Legge found that that verdict would be binding in a retrial of the infringement issue.

However, the jury did not deliver a unanimous verdict on the side of the University of California in relation to the other main issue. The jurors voted 8-1 in favor of the University's claim of patent infringement, but were unable to resolve the impasse in six days of deliberations. The federal court jury was deadlocked on a suit by the University of California accusing Genentech of stealing a patented DNA molecule and using it to develop a top-selling human growth hormone.⁶³

Juror Sarah Mau of Union City said she threw out Seeburg's testimony, because 'if he lied once, what makes us think he's not lying now?'⁶⁴ But she said she voted to find patent infringement, based on other evidence. Foreman Ron Losch, a San Francisco attorney, also voted in the university's favour. He said the lone holdout juror was not convinced that Genentech's chemical product was the equivalent of the university's patented biological material, on the basis of testimony that chemistry is unpredictable.

⁶³ Egelko, B. 'Hung jury relief for Genentech', AP Writer, *The Reporter.com*, 3 June 1999, <<http://www.thereporter.com>>.

⁶⁴ *Ibid.*

Dodson, the university's lawyer, said he was disappointed by the hung jury but felt that the partial verdict 'puts beyond any question the validity of this patent'.⁶⁵ Stephanie Ashe from Genentech's communications office noted that the result 'shows that obviously we presented a strong case'.⁶⁶ Furthermore, she speculates, 'The jury was not misled by the sensational testimony by some of (the university's) witnesses'.⁶⁷ Kidd, Genentech's lawyer noted that the deadlock 'shows that the university did not prove its case on infringement'.⁶⁸

The decision raised some disquiet about whether juries are competent to resolve patent cases, especially in software and biotechnology fields. One solution is to let the judge adjudicate such matters and limit the responsibilities of the jury. Another is to adopt a scientific expert to advise the court. A more radical option is for a court to convene a hot tub of scientific experts to reach consensus.

Settlement

In the end, the University of California and Genentech, Inc. agreed to a proposed settlement of the patent infringement lawsuits relating to Genentech's human growth hormone products.⁶⁹

Under the terms of the settlement agreement, Genentech agreed to pay the University of California \$150 million and make a contribution in the amount of \$50 million toward construction of the first biological sciences research building at Mission Bay, a new 43-acre research and teaching campus of the University of California, San Francisco. The building would bear a name proposed by Genentech and acceptable to the University of California.

Both parties agreed that this settlement was not an admission that Genentech infringed University of California's patent or used the genetic material in question.

Commenting on the proposed agreement, University of California President Richard Atkinson said:

*The proposed settlement underscores the value that research at the University of California contributes to advancing science, spawning new industries and improving people's lives. The University and Genentech have continued cooperative research relations throughout this patent dispute. Now that this issue is behind us, we look forward to accelerating our scientific collaborations.*⁷⁰

The chairman and chief executive officer of Genentech Arthur Levinson said: 'Genentech has decided to put this matter behind us and avoid the distraction and uncertainty

⁶⁵ Ibid.

⁶⁶ Ibid.

⁶⁷ Ibid.

⁶⁸ Ibid.

⁶⁹ Genentech. 'University of California and Genentech Settle Patent Infringement Lawsuits', Genentech Press Release, San Francisco And South San Francisco, California, 19 November 1999.

⁷⁰ Ibid.

of another jury trial covering complex patent issues that are based on events that took place nearly twenty years ago.⁷¹

Dodson claimed that the settlement of the litigation over the patent for human growth hormone would result in greater royalties for universities.⁷² The lawyer said that the lawsuit 'raised the bar for royalty rates on fundamental patents'.⁷³ In the past, he explained:

*Pharmaceutical companies had thought of these fundamental patents as 'dog food.' They had not recognized the value. And we haven't, in the past, had the courts recognize these patents either.*⁷⁴

Dodson recounts that royalty rates paid by outside companies for university- licensed technology in the biotech field were previously 'in the range of 1 or 2%'.⁷⁵ He predicted that after the Genentech litigation the universities would be able to ask for up to 'about 6 or 7%'.⁷⁶ However, some credit, too, must go to the universities themselves for persisting with the case.

The settlement gave heart to other research institutions with grievances against Genentech. The City Of Hope National Medical Center filed a law suit in 1999, complaining that the company had deprived the hospital of royalties it deserved for work that helped lay the foundation for the biotechnology industry.⁷⁷ Under a contract signed in 1976, it agreed to pay the City of Hope to synthesize the gene for human insulin.⁷⁸ The gene was put into bacteria, which produced the insulin. Human insulin, which Genentech licensed to Eli Lilly and Company Eli Lilly, became the first drug produced by genetic engineering.

Under the contract, Genentech gained ownership of all patents on the techniques developed by City of Hope in exchange for a 2 per cent royalty.⁷⁹ City of Hope, however, contended that Genentech owed it \$457 million in royalties and interest arising from more than 20 deals in which Genentech licensed the patents to other

⁷¹ Ibid.

⁷² 'Out-Licensing Brings Schools Profits, Big Legal Bills', National Law Journal, 8 March 2001.

⁷³ Ibid.

⁷⁴ Ibid.

⁷⁵ Ibid.

⁷⁶ Ibid.

⁷⁷ Genentech. 'Genentech Announces Verdict In Contract Dispute', Press Release, South San Francisco, California, 10 June 2002, <http://www.gene.com/gene/news/detail.jsp?detail=5127&No=1>

⁷⁸ Tansey, B. 'Genentech In Limbo: Potential Cost Of Punitive Damages Weighs Heavily On Biotech Firm', *San Francisco Chronicle*, 12 June 2002, <http://www.sfgate.com/cgi-bin/article.cgi?file=/chronicle/archive/2002/06/12/BU168518.DTL&type=business>

⁷⁹ Pollack, A. 'A Jury Orders Genentech To Pay \$300 Million In Royalties', *The New York Times*, 11 June 2002, <http://www.nytimes.com/2002/06/11/business/11DRUG.html>

companies, to produce alpha interferon, a hepatitis and cancer drug. In its suit, filed in 1999, the hospital also contended that Genentech had hidden the licensing deals.

The first trial resulted in a deadlocked jury, 7-5 in Genentech's favour, after six days of deliberation in October 2001. In the retrial, the case was submitted to the jury on the 16th May 2002 after a six-week trial in the Los Angeles County Superior Court. The jury deliberated for 17 days before announcing the verdict. In the second trial, the Los Angeles County Superior Court jury voted to award the City of Hope approximately \$300 million in additional royalties for breach of a 1976 agreement.⁸⁰ The Vice President of Intellectual Property at Genentech, Sean Johnston, reflected: 'We are disappointed by the verdict. Genentech does not intend to address the issue of appeal until all proceedings in the trial court are concluded.'⁸¹

The Gene Wars: Science, Politics and the Human Genome⁸²

The litigation between the University of California and Genentech has been a prelude to a wider policy debate about the patenting of genes and gene sequences. As Shine observes:

As the technology of DNA cloning became much more standard, we went through a period not long ago where people would clone a sequence of the human genome and try to claim a patent. The United States patent office declared that this was ridiculous. It was only possible to obtain a patent if one had truly developed some novel, new way of using something.⁸³

The United States Patent Office has been deluged with patent applications over genes and genetic sequences. It recognizes that many people in the biotechnology community are concerned with the possible impact of patents granted for DNA-related inventions on research and innovation in biomedical research and technology. The United States Patent office is of the view that new areas of technology do not create the need for a whole new specialized patent law. It has put into place utility examination guidelines, which provide that a claimed invention must have utility that is specific, substantial, and credible. However, the litigation over the patents for

⁸⁰ *City of Hope National Medical Center, Arthur Riggs and Keiichi Itakura v Genentech* (2002) BC215 152.

⁸¹ Genentech. 'Genentech Announces Verdict In Contract Dispute', Press Release, South San Francisco, California, 10 June 2002, <http://www.gene.com/gene/news/detail.jsp?detail=5127&No=1>

⁸² Title taken from the book, Cook-Deegan, R. *The Gene Wars: Science, Politics And The Human Genome*. New York and London: WW Norton & Company, 1994.

⁸³ Shine, J. 'Interview with the Author', Sydney, 23 April 2001.

human growth hormone raises doubts about the efficacy of such policy interventions. It highlights the difficulties in finding legislative, judicial or industry reforms to resolve these complex scientific, legal, and social problems.

Gene Patents

In fierce competition with biotechnology, genomics, and pharmaceutical companies, Genentech has filed patent applications in respect of genes, gene sequences, and proteins. In the 2001 annual report, Arthur Levinson comments:

Genentech is strongly positioned to capitalize on our understanding of the human genome, as we have had a concerted effort for the past five years in the genomics and bioinformatics areas. We have already filed patent applications on more than 1,200 full-length DNA sequences and are continuing our work to understand the underlying biology and therapeutic potential of these genes and the proteins they express.⁸⁴

Levinson observed, in the same 2001 report, that Genentech held more than 4,000 patents worldwide and had another 3,600 pending. He observed: 'One of the challenges of working at the leading edge of research is protecting intellectual property.'⁸⁵ If, as Clarisa Long argues, patent law is a 'signalling mechanism',⁸⁶ it is worthwhile analysing the patent portfolio of Genentech, and determine what signals the company is sending out to its potential shareholders and corporate rivals.

The Senior Vice President of Research at Genentech, Dennis Henner, charts the historical development of the law governing patentability of inventions arising out of genome research.⁸⁷ He mentions a number of important turning points - including the case of *Diamond v. Chakrabarty*,⁸⁸ the overruling of the decision of *In re Durden*⁸⁹ via the *Biotechnological Process Patent Amendments Act 1995* (US), and the utility guidelines issued by the United States Patent and Trademark Office.⁹⁰ In light of such developments, Henner claims:

We also tend to discount the fears of a land rush of patent application filings coming out of genomics research. If the PTO is doing its job correctly, patents will be granted only in those situations where they are warranted, and the

⁸⁴ Genentech, *Annual Report 2001*, http://www.gene.com/gene/ir/financials/annual-reports/2001/2_3_letter.htm

⁸⁵ Ibid.

⁸⁶ Long, C. 'Patent Signals', *The University Of Chicago Law Review*, 2002, Vol. 69 (2), p. 625.

⁸⁷ Henner, D. 'Statement of the Genentech Senior Vice President Of Research', United States Judiciary Subcommittee On Courts And Intellectual Property, 13 July 2000, <http://www.bio.org/laws/comments071200.html>

⁸⁸ *Diamond v. Chakrabarty* (1980) 447 U.S. 303

⁸⁹ *In re Durden* (1985) 763 F.2d 1406

⁹⁰ United States Patent And Trademark Office. 'Utility Examination Guidelines', *Federal Register*, 2001, Vol. 66 (4), p. 1092.

*rights under those patents will be limited to the contributions of the inventor. Likewise, a gene patent – properly examined – should not enable its owner to prevent parties from doing research, such as sequencing or studying a portion of the genome of an organism.*⁹¹

Henner concludes that the rules in patent law regarding the patenting of genes and gene sequences does not need to be revisited: 'The proper focus for discussions on 'gene patenting' is not on the question of whether patents should be granted on 'genes' but rather on the question of when it is appropriate to grant such rights.'⁹²

Genentech made the striking concession that patent protection should not extend to express sequence tags (ESTs). It was conscious of public concern about the subject - such as that voiced by the Human Genome Organisation.⁹³ Henner approved of the position of the United States Patent and Trade Mark Office to stringently review express sequence tags in light of the new utility guidelines:

*The PTO has indicated that certain 'first generation' EST filings are the most likely to receive the hardest review. The PTO has also indicated that a 'second generation' of filings that disclose full sequences of genes will receive a more rigorous evaluation for compliance with utility, written description and enablement. We believe this is the proper course for the PTO to follow.*⁹⁴

Such statement represents an incredible reversal of opinion. A senior patent counsel at Genentech, Max Hensley, encouraged Reid Adler of the National Institutes of Health was encouraged to apply for a patent in respect of Craig Venter's express sequence tags.⁹⁵ As is well known, the Patent and Trademark Office rejected the patent application in respect of ESTs on all several grounds - non-obviousness, novelty, utility, and written description.⁹⁶ Interestingly, corporate counsel for Genentech, Thomas Kiley, was critical of the NIH proposal to patent ESTs: 'The NIH proposal for patents is only an extreme example of a widespread practice in

biotechnology that seeks to control not discoveries themselves but the means of making discoveries.'⁹⁷ The episode demonstrates - yet again - what an important role Genentech played in pushing the boundaries of patent law. In this case, the company was not only the instigator of patent reform, but also at the same time its critic.

Furthermore, Genentech sought to appease its critics by making the declaration that it would not sue academic researchers in respect of research use of genomics information. It was sensitive to the criticism of commentators such as Michael Heller and Rebecca Eisenberg who complained about the difficulties that biomedical researchers faced in obtaining access to research tools.⁹⁸ Henner denied that the firm was at all interested in charging royalties in respect of research tools:

*I note that patents on research tools used to discover genes are not especially valuable in our view, and we do not make a priority out of pursuing patent protection for most of the research tools that Genentech scientists invent. We do not believe that enforcing patents on research tools represents sound policy, as it tends to discourage the open research environment that we believe is so important to scientific advancement and the biotechnology industry.*⁹⁹

Eisenberg cites a couple of famous examples of proprietary research tools have been widely distributed under licence agreements that permit subsequent research to go forward while preserving a return for the patent owner - such as the Cohen-Boyer patent on recombinant DNA technologies,¹⁰⁰ and the Hoffman-La Roche patent in respect of the polymerase chain reaction.¹⁰¹ She observes, though, that the transaction costs involved in exchange of research tools remains high because the diverse institutions involved in the exchange of research tools have been unable to agree upon

⁹¹ Henner, D. 'Statement of the Genentech Senior Vice President Of Research', United States Judiciary Subcommittee On Courts And Intellectual Property, 13 July 2000, <http://www.bio.org/laws/comments071200.html>

⁹² Ibid.

⁹³ The Human Genome Organisation, 'HUGO Statement On The Patenting Of Gene Sequences', 1995, <http://www.hugo-international.org/hugo/patent.htm>

⁹⁴ Henner, D. 'Statement of the Genentech Senior Vice President Of Research', United States Judiciary Subcommittee On Courts And Intellectual Property, 13 July 2000, <http://www.bio.org/laws/comments071200.html>

⁹⁵ Cook-Deegan, R. *The Gene Wars: Science, Politics And The Human Genome*. New York and London: WW Norton & Company, 1994, p 316-317; and Davies, K. *The Sequence: Inside The Race For The Human Genome*. London: Weidenfeld & Nicholson, 2001.

⁹⁶ Id, p 317.

⁹⁷ Id, p 321.

⁹⁸ Heller, M. and Eisenberg, R. 'Can Patents Deter Innovation? The Anticommons In Biomedical Research', *Science*, 1 May 1998, Vol. 280, p. 698; and Eisenberg, R. 'Bargaining over the Transfer of Proprietary Research Tools: Is This Market Failing or Emerging?' in R. Dreyfuss, H. First, and D. Zimmerman, eds., *Expanding the Bounds of Intellectual Property: Innovation Policy for the Knowledge Society*, Oxford: Oxford University Press, 2001.

⁹⁹ Henner, D. 'Statement of the Genentech Senior Vice President Of Research', United States Judiciary Subcommittee On Courts And Intellectual Property, 13 July 2000, <http://www.bio.org/laws/comments071200.html>

¹⁰⁰ Smith Hughes, S. 'Making Dollars Out Of DNA: The First Major Project In Biotechnology And The Commercialization Of Molecular Biology, 1974-1980', *Isis*, 2001, Vol. 92, p. 541-578.

¹⁰¹ Heller, M. and Eisenberg, R. 'Can Patents Deter Innovation? The Anticommons In Biomedical Research', *Science*, 1 May 1998, Vol. 280, p. 698; and Rabinow, P. *Making PCR: A Story of Biotechnology*. Chicago: The University of Chicago Press, 1996.

standardized contract language, or even agree a definition of 'research tools'.¹⁰² It should be remembered that Genentech was eager to gain an exclusive licence in respect of the Cohen-Boyer patent. So the company might well be working with a very narrow definition of a 'research tool'.

Much to the frustration and exasperation of Genentech, the outright critics of gene patents remain vocal that it is unethical to patent life forms. Jeremy Rifkin has been a persistent critic of gene patents. He has been undaunted that his arguments as an amicus curiae in the *Diamond v Chakrabarty* decision have gone unheeded. Rifkin renewed his attack upon gene patents in his books *The Biotech Century*,¹⁰³ and book *The Age Of Access*.¹⁰⁴ He has also campaigned heavily on the subject in the media and in policy debates.¹⁰⁵ Despite the objections of biotechnology companies like Genentech, the ethical question of whether the patenting of genes and gene sequences should be allowed under patent law will remain open to debate.

Utility Guidelines

In the wake of the human genome project, and thousands of applications for patent protection over genes and gene sequences, the United States Patent and Trade Mark Office has issued guidelines in respect of the application of the utility criteria.¹⁰⁶ Todd Dickinson detailed the administrative reforms to Congress.¹⁰⁷ The new utility guidelines required patent applicants to explicitly identify, unless already well-established, a specific, substantial and credible utility for all inventions. In effect, it raised the bar to ensure that patent applicants demonstrate a 'real world' utility. As a result, the PTO hoped that hundreds of genomic patent applications would be rejected, particularly those that only disclose theoretical utilities. The PTO vigorously responded to various criticisms of the

guidelines in its public consultation process.¹⁰⁸ It dismissed a host of objections to the patenting of genes and gene sequences.

The chief executive officer of Genentech, Levinson, supported the guidelines on utility that have been issued by the PTO:

*Patents are the lifeblood of the biotech industry and are crucial to spurring innovation and incenting companies to make the necessary significant investments to bring drugs to market. We support the PTO's guideline on utility, which creates an appropriately higher bar for biotechnology companies in requiring demonstration of biological function and use. We believe that this is the surest way to provide important incentives for the further pursuit of new innovative therapies by the biotechnology industry and to reward those that are successful in that pursuit.*¹⁰⁹

Henner also affirmed the administrative guidelines on utility, praising the PTO for its impressive job in promulgating guidelines that accurately reflected the current state of the law governing specific utility and written description.¹¹⁰ However, he also expressed some concerns about the application of these guidelines as part of the PTO's notice and comment process - in particular about the scientific assumptions used by the PTO in their training materials.¹¹¹ However, the company was confident that the guidelines and the training examples ultimately would be consistent with the law and reflect a proper perspective on scientific assumptions. It did not support legislative action to alter the standards of utility, enablement or written description in the name of genome research. However, there have been some reservations about administrative guidelines by the PTO amongst the biotechnology industry.¹¹²

¹⁰² Eisenberg, R. 'Bargaining over the Transfer of Proprietary Research Tools: Is This Market Failing or Emerging?' in R. Dreyfuss, H. First, and D. Zimmerman, eds., *Expanding the Bounds of Intellectual Property: Innovation Policy for the Knowledge Society*, Oxford: Oxford University Press, 2001.

¹⁰³ Rifkin, J. *The Biotech Century*. New York: JP Tarcher, 1998.

¹⁰⁴ Rifkin, J. *The Age Of Access: The New Culture Of Hypercapitalism Where All Of Life Is A Paid-For Experience*. New York: JP Tarcher, 2001.

¹⁰⁵ Zeregam B. 'Keep your genes on: Gene patenting will have dangerous repercussions for the biotech century, warns the economist Jeremy Rifkin', *Red Herring*, April 1999.

¹⁰⁶ USPTO. 'Revised Interim Utility Examination Guidelines' in the *Federal Register* on December 21, 1999 (Volume 64, Number 244), <http://www.uspto.gov/web/offices/com/sol/notices/utilexmguide.pdf>

¹⁰⁷ Dickinson, T. 'Statement On Patenting of Genes and Other Genomic Inventions', Subcommittee On Courts and Intellectual Property, House of Representatives, 13 July 2000, <http://www.uspto.gov/web/offices/ac/ahrpa/opa/bulletin/genomicpat.pdf>

¹⁰⁸ USPTO. 'Revised Interim Utility Examination Guidelines' in the *Federal Register* on December 21, 1999 (Volume 64, Number 244), <http://www.uspto.gov/web/offices/com/sol/notices/utilexmguide.pdf>

¹⁰⁹ Levinson, A. 'Genentech CEO Says Amgen/TKT Trial Outcome Not A Bellwether For Biotech - Broader Issue of Gene Patents Addressed at Congressional Hearings This Week', Genentech Press Release, San Francisco And South San Francisco, California, 13 July 2000, <http://www.gene.com/gene/news/detail.jsp?detail=4624&No=9>

¹¹⁰ Henner, D. 'Statement of the Genentech Senior Vice President Of Research', United States Judiciary Subcommittee On Courts And Intellectual Property, 13 July 2000, <http://www.bio.org/laws/comments071200.html>

¹¹¹ Genentech submission to the Patent and Trade Mark Office. http://www.uspto.gov/web/offices/com/sol/comments/utilit_ywd/genentech.pdf

¹¹² Kass, L. and Nitabach, M. 'A Roadmap For Biotechnology Patents? Federal Circuit Precedent And The PTO's New Examination Guidelines', *A/PLA Quarterly Journal*, 2002, Vol. 30, p. 233; and Smith, M.B. 'An End To Gene Patents? The Human Genome Project

The litigation between the University of California and Genentech has some important implications in respect of the utility guidelines. The lawyer Dodson said that his university clients wanted a wide perimeter in which to protect inventions whose potential for use was uncertain.¹¹³ He believed that the utility guidelines of the PTO were too restrictive and could hit universities with a devastating economic blow. In the Genentech case, for example, he had successfully argued that the university's early-stage research was worthy of patent protection, despite Genentech's claim that the university's patent was insignificant. Dodson observes: 'The patent system should be allowed to work, and it makes more sense to give people patents for inventions that have utility, even if the utility may not seem significant at the time of application. That has historically been the way the patent system has worked.'¹¹⁴

The litigation between the University of California and Genentech indicates that disputes over the patenting of genes and gene sequences will not be resolved swiftly or easily in the courts. Long-drawn out battles between research institutions, biotechnology companies, and government are to be anticipated. Dodson would rather the court system make these decisions instead of patent examiners:

*Bring a lawsuit and let the court decide if something has utility. The court could give a small damage award if they thought the utility was small. To the extent that people have received patents on inventions or devices perceived as having insignificant or de minimus utility, the system will remedy that.*¹¹⁵

Dodson maintains that the characterisation of the utility directives as guidelines, rather than rules, is ultimately a meaningless distinction. He observes, 'They will spill over into court challenges.'¹¹⁶ As Timothy Meigs observes: 'Because of the discrepancies between the utility guidelines and the relevant case law, this area of biotechnology patent law will likely remain unsettled until these issues have been addressed by the Board of Patent Appeals and Interferences and by the Federal Circuit.'¹¹⁷ The question of the utility of genomic research will eventually need to be dealt with by Congress.

Intellectual Property Management

The litigation between the University of California and Genentech has been represented as a case of

Versus The United States Patent And Trade Mark Office's 1999 Utility Guidelines', *University Of Colorado Law Review*, 2002, Vol. 73, p. 747.

¹¹³ Slind For, V. 'Both Sides Now: MoFo IP Partners Kate Murashige and Gerald Dodson Diverge on the PTO's New Guidelines for Biotech Patents', IP Worldwide, 14 June 2001.

¹¹⁴ Ibid.

¹¹⁵ Ibid.

¹¹⁶ Ibid.

¹¹⁷ Meigs, J.T. 'Biotechnology Patent Prosecution In View Of PTO's Utility Examination Guidelines', *Journal Of The Patent And Trademark Office Society*, 2001, Vol. 83, p. 451.

commercialism corrupting science. One journalist noted: 'The first round in a legal battle concerning the patent rights to a synthetic human growth hormone has just been completed, and the details of the conflict are an instructive illustration of how the push for huge profits from research in molecular biology may be corrupting the practice of basic science by both industrial and academic researchers.'¹¹⁸ Such concerns about the privatisation of biological science were seemingly confirmed by the litigation over human growth hormone and insulin. The litigation has important implications about collaboration between the public sector and the private sector. As Tom Abate comments:

*But no matter which side prevails in court, some damage has already been done. The trial has lifted the white frock of science, and revealed beneath it the all-too-familiar outlines of avarice, ambition, and duplicity.*¹¹⁹

The case raises important questions about ethics, corporate governance, conflict of interest, and transparency.

The conduct of the biotechnology company Genentech came under intense scrutiny. As Stephen Hall observes:

*Charges of conflict of interest were aired openly; suspicions of greed, of using knowledge obtained by publicly funded research for private gain, were whispered about as well. Boyer argues that he and Bob Swanson took great pains to negotiate a fair and equitable relationship with UCSF; but not everyone shares that view.*¹²⁰

In response, Genentech sought to deflect such criticism by attacking the conduct of Seeburg. The narrative told by the company was one of scientific fraud.¹²¹ This had serious repercussions outside the court. After the settlement of the suit between Genentech and the University of California, the Max Planck Society censured Seeburg for publishing data in a 1979 paper that he said was false.¹²² The committee concluded that 'a falsified description in a publication cannot be tolerated, no matter it dates back 20 years'.¹²³ Arguably, Seeburg became the scapegoat of the controversy. However, the ethical issues at stake in this case are systemic, and transcend the behaviour of any one researcher. Tough, searching questions needed to be asked of both academia and industry about conflict of interest policies.

¹¹⁸ Science Week. 'Academia vs. Industry: A US\$1 Billion Hormone Patent Battle', Science Week, <http://scienceweek.com>, 11 June 1999.

¹¹⁹ Abate, T. 'Showdown In Court Over Human Growth Hormone', *San Francisco Chronicle*, 3 May 1999.

¹²⁰ Hall, S. *Invisible Frontiers: The Race To Synthesize A Human Gene*. London: Sidgwick and Jackson, 1987, p. 150.

¹²¹ For a discussion of scientific fraud, see: La Follette, M. *Stealing Into Print: Fraud, Plagiarism and Misconduct In Scientific Publishing*. University of California Press, 1992.

¹²² Hagmann, M. 'Researcher Rebuked For 20-Year Misconduct', *Science Now*, 13 December 1999.

¹²³ Ibid.

However, this parable has not been heeded by the private sector and the public sector. Empirical evidence suggests that academia-industry ties are still largely unregulated. In a cross-sectional survey and content analysis study, Mildred Cho and her collaborators reviewed the policies at major biomedical research institutions in the United States between 1998 and 2000.¹²⁴ The researchers found that most conflict of interest policies of major institutions in the United States lack specificity about the kinds of relationships with industry that are permitted or prohibited. They concluded that the wide variation in management of conflicts of interest among institutions may cause unnecessary confusion among potential industry partners. Cho concluded that 'it would be to the long-term benefit of faculty, institutions, and companies to develop clear and specific policies based on agreed-on principles that protect universities' primary missions of education, research, and dissemination of knowledge.'¹²⁵

There is need for greater government regulations on conflict of interest in respect of collaborations between the private sector and the public sector. Rebecca Eisenberg and Arti Rai comment that universities are poor guardians of intellectual property because the immediate gain to be realised from patenting may outweigh the more distant possibility of gain from a university wide regime of collective self-restraint:

Universities face a very significant collective action problem, and traditional norms of open exchange may no longer be sufficiently robust to address this problem. The obstacle to relying solely on universities is particularly large because the primary remaining adherents to open science norms, individual research scientists, do not necessarily make the ultimate decisions about university patenting.¹²⁶

The authors conclude argue that funding agencies should have greater discretion in imposing restrictions on patenting by the recipients of government funding: 'We believe that the time is ripe to alter the Bayh-Dole Act to give funding agencies more latitude in guiding patenting and licensing activities of their grantees.'¹²⁷

Conclusion

The litigation between the University of California and Genentech represents a seismic shift in scientific and institutional attitudes to the patenting of biological inventions. The case highlighted the potential of the commercialisation of academic research in the life sciences. It also raised the ethical fears and anxieties

about the norms of the science being corrupted by commerce and business. The law suit shows that public research institutions would benefit from broad patent protection in respect of pioneer inventions and ground-breaking research. Such bargaining power would be a necessary safeguard in dealings with commercial entities. The conflict also shows the need for procedural reforms in patent litigation. There is a need to ensure that the time and expense of patent litigation is minimised. It would be of assistance if trained judges and juries with expert knowledge could preside over patent cases. The dispute between the University of California and Genentech foreshadows the wider debate over the patenting of genes, express sequence tags, and research tools. It demonstrates that the administrative guidelines on utility issued by the United States Patent and Trade Mark Office will not prove to be a conclusive solution. The litigation indicates the demand for better intellectual property management in collaborations between the public sector and the private sector. In particular, there is a need for the development of proper precautionary conflict of interest policies.

¹²⁴ Cho, M., Shohara, R., Schissel, A. and Rennie, D. 'Policies On Faculty Conflicts Of Interest At US Universities', *Journal Of The American Medical Association*, 2000, Vol. 284 (17), p. 2203-2208.

¹²⁵ Id, at 2208.

¹²⁶ Rai, A. and Eisenberg, R. 'The Public And The Private In Biopharmaceutical Research', Conference on the Public Domain, the Center for the Public Domain, Duke University, 9-11 November 2001.

¹²⁷ Ibid.