In defence of gene patents

Emma Toumi

Date received (in revised form): 18th November, 2002

Emma Toumi
specialises in biotechnology and intellectual property and is a Patent Associate of McDermott, Will & Emery, an international law firm with nearly 1,000 attorneys. The intellectual property department is one of the largest in the world and has expertise in areas of biotechnology and pharmaceuticals.

Abstract

For two years the Nuffield Council of Bioethics has scrutinised the pros and cons of gene patenting in the healthcare industry. The Council recently published its findings, saying that too many patents have been granted on gene sequences and, in future, gene patents 'should be the exception rather than the rule'. The Council's recommendations even go as far as to propose the discontinuance of monopoly rights on existing gene patents for certain applications such as diagnostic tools. The consequences of curtailing patent rights could have a deleterious effect on the healthcare industry where patents are essential for recovering the investment made in drug discovery. Furthermore, it could lead to a 'dark age' where the human gene sequences responsible for disease are kept secret by a minority of the industry players. In its defence, the patent system is a very sophisticated, self-correcting system with safeguards to protect society from unwarranted monopolies. Its purpose is to put every scientific advance into the public domain with the trade-off of a time-limited monopoly awarded to the proprietor.

Keywords: *gene, patents, ethics, clearing house, patent pool*

THE IMPORTANCE OF GENE PATENTS IN THE HEALTHCARE INDUSTRY

The aim of the Nuffield Council on Bioethics' (NCB) discussion paper on 'The ethics of patenting DNA', published in July 2002, was to examine the issues relating to genetics and intellectual property, particularly those that concern human healthcare and research related to healthcare. The protection of intellectual property rights in the healthcare industry is an important issue since this industry relies heavily on patents to recover the investment made on drug discovery. Furthermore, for fledgling biotechnology companies, not likely to see a profit on their balance sheets for years, patents are essential for attracting the venture capital required to keep them afloat. Any changes to the system that would compromise intellectual property rights could seriously jeopardise these industries.

One of the greatest concerns for a pharmaceutical company is its product pipeline. Since it takes, on average, ten years for a drug to complete the regulatory process,[1] and only one in ten compounds reach the marketplace,[2] pharmaceutical companies require a constant stream of drugs at different stages of development in order to remain profitable. The investment necessary to bring a pharmaceutical product to market has been estimated as £350m.[1] The stream of drugs in the product pipeline ensures that the huge cost of drug development is paid for by a supply of patent-protected drugs which can make a healthy profit for a few years before the generic firms move in and undercut prices of drugs that are off-patent. However, there is trouble on the horizon: the volume of drugs in the product pipeline has diminished. The cause is the massive investment in the early 1990s in combinatorial chemistry as a tool for drug development. This technique has not paid the dividends expected. It was thought, by some, that the problems of drug discovery could be solved by creating massive libraries of potential drugs by high-speed and combinatorial chemistries. Scientists focused more on what could be made rather than what should be made,[2] with the result that now there is an alarming shortfall in the number of new drugs entering the market and pharmaceutical companies are undergoing a series of takeovers in order to replenish the shortfall in their product pipelines.

There is light at the end of the tunnel. The mapping of the human genome provides substantially more targets than

Dr Emma Toumi
McDermott, Will & Emery,
7 Bishopsgate,
London EC2N 3AR, UK

Tel: +44 (0) 20 7577 6900
Fax: +44 (0) 20 7577 6950
E-mail: etoumi@europe.mwe.com

Our children may well be able to exploit the genome with impunity

have been studied in all of pharmaceutical research to date. The greatest hurdle to mining this potential drug source is identifying the DNA regions responsible for disease, deciphering the proteins and creating potential antagonists. However, despite these obstacles there are more than a hundred drugs and vaccines derived from biotechnology for coronary heart disease, cancers, arthritis, hepatitis, diabetes and HIV.[2] Many of these drugs enjoy a period of patent protection because they are the expression products of gene patents. If a change in law were to result in the abolition of gene patents then there would be detrimental consequences on the product pipeline. Academic research would not be able provide new drugs based on genes at the same pace as industry. For a start it does not have the same resources. In 1998, the UK pharmaceutical industry spent £2.4bn on research and development whereas the British Government spent £800m.[3] Furthermore, although university research is essential to the basic research required in drug discovery, it does not have the infrastructure or resources required to take a drug through the efficacy and clinical trials needed to get it to market. The healthcare industry is an innovation engine on the road to drug discovery but it requires patents to fuel the process.

EPC provides a robust even-handed examination process for an invention regardless of the technology area

HOW CAN GENE PATENTS BE JUSTIFIED?

A patent is a legal means of appropriating new knowledge possessed by an individual by publishing to the world how to carry out the invention, on condition that, for a specified time, that individual would enjoy privileged rights. In the grand scheme of things this monopoly is relatively short. Since the maximum term of a patent is 20 years (although patents covering medicinal products, having obtained marketing authorisation, may be eligible for a supplementary protection certificate, thereby extending the term of the patent by a maximum of five years for the medicinal product covered by the basic patent), our children may well be able to exploit most of the genome with impunity. If the rights enjoyed by gene patents were curtailed, the consequences may be a 'dark age' for molecular biology where genes exploited by the healthcare industry for gene therapy or diagnostics were kept secret. A secret could be kept out of the public domain indefinitely. For example, in 1886 Dr John Pemberton formulated a recipe for Coca Cola that remains a secret to this day. If the sequences of genes were to become trade secrets, at the very least it would amount to a waste of resources in duplicated research or litigation over breaches of confidential information, and at worst it would impede the free circulation of scientific knowledge.

A second justification for gene patents is that obtaining a patent is not an easy process. It is subject to stringent examination. Not all applications for gene patents are granted. For an invention to be awarded a patent it must fulfil the strict requirements for patentability. The invention must be novel, possess an inventive step and be industrially applicable. Each patent application is judged on its own merits. The patent system has evolved over centuries into one with sufficient flexibility to accommodate advances in technology. The UK Patents Act 1977 and the European Patent Convention provide for a robust even-handed examination process for an invention, regardless of the technology area. This results in patents being granted (or rejected) in all technology areas applying the knowledge and standards of those skilled in that technology area at the appropriate time (ie not using hindsight) as a benchmark for determining whether an invention is truly 'inventive' under the patent rules. (Exclusions to patentability are discoveries, scientific theories, mathematical models, aesthetic creations, schemes, rules and methods for performing mental acts, playing games or doing business, programs for computers and presentations of information and

methods of medical treatment.[4]) When the regulations governing the grant of patents are applied correctly and those officers examining the applications are of an appropriate calibre for the area of technology then the system should move with advances in technology and become virtually self-correcting when once truly innovative and pioneering technology crosses over the threshold of being commonplace. In the past, a great deal of ingenuity was required to sequence the genes responsible for disease. The NCB paper acknowledges the great contribution and openly states that these early gene patents were justified.

The patent system is virtually self-correcting when once truly innovative technology crosses over the threshold of being commonplace

The scene of patenting and genomics changed forever as a result of the activities of Craig Venter[5] in the USA. When he was working for the National Institutes of Health (NIH) in the early 1990s, patent applications were lodged in respect of over 2,200 genetic applications about whose operation nothing was known at that time. This action enlivened an urgent national and international debate. In the end, the NIH decided not to proceed with the applications.[6] However, it provoked an active debate in Europe. Eventually, this resulted in the Biotechnology Directive. Although the Directive provides that the human body and its elements *in a natural state* are unpatentable[7] and that a mere DNA sequence without indication of function is not patentable,[8] it also provides that a patent may be granted for a gene if the gene in question *was produced by technical means*[9] (emphasis added).

A patent does not give a right of ownership

The patenting of genes is a highly emotive issue. Richard Land, President of the Christian Life Commission of the Southern Baptist Convention, declared that 'the patenting of human genetic material attempts to wrest ownership from God and commodifies human biological materials and, potentially human beings themselves'.[7] In an attempt to ward off ethical objections, various recitals were inserted into the final text of the Directive.[10] Recital 12 refers to the general principle 'that the ownership of human beings is excluded'. This recital was included after extensive lobbying by politicians concerned about slavery issues and is a reflection of how poorly understood the complicated issues of patent law and genetics are to many people. First, there are many laws in Europe to guard against slavery and exploitation. The patent system is the wrong forum to discuss issues of this nature. Secondly, the proprietor of a patent does not own a patented article once it has been sold to a consumer. For example, Mr Dyson does not own the Dyson vacuum cleaners in the cleaning cupboards of our homes. Andrew Sheard, at a recent meeting of the Human Genetics Commission,[3] showed enormous clarity by saying that 'a patent is a time-limited right to prevent someone else from profiting from your invention and selling it on, and does not give a right of ownership, but rather is analogous to copyright'.

Any person can oppose the grant of a patent

The NCB discussion paper recognises the special nature of DNA but concludes that the exclusive rights on gene patents are defensible if the patent fulfils the requirements for patentability because patents promote research and development of new medicines and vaccines. However, the NCB paper expresses concern over granting patents for DNA sequences that have been identified and characterised only by current technology, ie *in silico* analysis of the DNA sequence and comparisons by computer simulation with other identified sequences, because this routine procedure lacks inventiveness. Patent applications of this nature would not be granted by the European Patent Office (EPO) which sets a high threshold for inventiveness. Furthermore, in order to prevent unwarranted monopolies from entering the patent register, the EPO has a nine month opposition period where any person can oppose the grant of a patent. In 2001, the EPO granted three patents on the *BRCA1* gene, the first known gene with a role in familial breast and ovarian cancer, to Myriad Genetics, a US

This NCB recommendation may breach the European convention on Human Rights

company. In one joint opposition, filed on 28th August 2002, Genetic Societies and Cancer Research Institutes from 11 European countries have filed opposition against the third patent on *BRCA1*. Oppositions against the first and second patents were filed in October 2001 and February 2002 respectively.[11] The NCB paper states that the EPO's approach was appropriate but condemned the patentability requirements set by the USPTO. The USPTO recently re-evaluated guidelines for granting biotechnology patents.[12] The new guidelines focus on the utility (usefulness) requirement of the patent statute creating a higher barrier for the biotechnology industry in demonstrating the function and use of gene-based inventions by requiring the disclosure of at least one specific, substantial and credible utility. The NCB paper welcomes these new guidelines, which came into force 18 months ago, but it recommends that the impact of these guidelines be monitored.

CURTAILING THE PROPRIETARY RIGHTS OF EXISTING GENE PATENTS

Compulsory licences

One of the most disturbing recommendations of the NCB paper is the granting of compulsory licences on existing gene patents. The NCB stated that it did not support the wholesale and indiscriminate use of compulsory licensing. However, with respect to diagnostic tests, based on genetic information where the enjoyment of exclusive rights was not in the public interest, it recommended that those seeking to use the diagnostic tool or develop an alternative should seek a compulsory licence from the relevant authorities if they are refused a licence from the owner of the patent. This may be difficult in practice since, firstly, there are thousands of gene and partial gene patents, some of which overlap, and, secondly, by what criteria do you decide that the enjoyment of exclusive rights of a human gene is not in the 'public interest'? This recommendation may also breach the European Convention on Human Rights (ECHR). Article 1 of the First Protocol of the ECHR provides that every natural or legal person is entitled to the peaceful enjoyment of his possessions. It says that no one shall be deprived of their possessions except in the public interest and subject to the conditions provided for by law and by the general principles of international law. It would be down to the UK courts to decide whether interference with property rights is justified in the public interest. The public interest may well lie heavily in favour of the advancement of science and the development of new drugs by the healthcare industry that requires the incentive of patents to recoup investment.

A working solution to the difficulties of gene patents used in diagnostics was discussed at a recent workshop by the Organization for Economic Co-operation and Development (OECD) on 'Genetic inventions, intellectual property rights and licensing practices'.[13] During the workshop the problems facing the biochip industry were discussed. Biochips are sensors that contain arrays of immobilised oligonucleotides (in the order of 10,000–100,000 elements), each representing a gene or gene sequence. They are revolutionising the way pharmaceutical scientists conduct drug discovery because they provide a diagnostic tool that monitors the expression of thousands of genes. However, biochips could be plagued by royalty stacking problems where royalties need to be paid to many entities because they are protected by gene patents.

Biochips could be plagued with royalty stacking problems

Two seemingly similar, but fundamentally different, 'group' solutions have been proposed to overcome the royalty stacking problems in the biochip industry. The first would be based on a clearing house system and the second would be a privately created patent pool. The genetic material patent clearing house would be to genetic material and patents what Phonographic Performance Limited (PPL) and other collecting

societies are to the music industry. The first owner of copyright in a recording of music is the record company who arranged for the recording to be made. The record company often licenses the public performance of the sound recording to PPL which in turn will issue a standard licence to establishments wishing to play the music publicly (eg pubs or bars). In a similar way a biochip manufacturer could apply to a gene patent clearing house for one licence covering many gene patents. The second approach of patent pooling has worked well in the USA for companies holding patents thought essential to certain DVD formats.[14] These companies were careful to stay the right side of the US antitrust laws and companies in Europe would also have to be careful not to breach the European competition laws. Similarly the US Department of Justice approved the structure of a patent pool relating to the MPEG-2 video technology.[14] These patent pools license one or more of their patents to the pool, then split the resulting royalties among the parties – a similar model could potentially benefit the biochip industry.

US companies exploiting patent pools are careful to stay the right side of the antitrust lows

Limiting the scope of product patents in relation to DNA sequences

The NCB paper recommends that the scope of gene patents be limited to the products referred to in the patent claims. The recommendation would curtail 'reach through' patents, a phenomenon commonly seen in the drug industry. An example of a reach through patent was Pfizer's patent for the active ingredient of Viagra®. The patent for the use of Viagra® to treat male impotence (European Patent No. 0702555) was held to be invalid by the UK courts for being obvious. But generic firms have not been able to make copies of this lucrative drug because the active chemical in Viagra® is still protected by another patent previously filed for another medical use. The original patent granted for the chemical ingredient in Viagra® prevents third parties from making, using, offering for sale, selling or importing this chemical during the term of the patent, even for a brand new use, without the permission of the patent owners on the underlying active chemical ingredient. A patentee is required to disclose only one use, ie to teach others how to use the invention in at least one way. The patentee is not required to disclose all possible uses or even the best method of using the invention. However, by making the invention public knowledge the patent system promotes the subsequent discovery of other uses. This is one of the great benefits of the current patent system. When patents for genes are treated as chemicals, progress is promoted because a new chemical is made available as a basis for future research. Other inventors who develop new and inventive methods of using the gene have the opportunity to obtain a patent on these new uses.

Patent claims stake out a fence around a field of invention

PATENTS IN PRACTICE

The NCB paper expresses concern that patents restrict research. In the UK the research exemption allows academics and research bodies to use the knowledge published in patents without fear of infringement. The OECD studies[13] examined the situation throughout the world and confirmed that patents on research tools are rarely enforced, and that in general firms do not pursue public research bodies for infringement. Also, while researchers sometimes avoid pursuing particular areas of research due to broad blocking patents or where multiple licences are required, most of the time firms do find working solutions.

In practice, the claims of a patent stake out a fence around a field of invention. Every product or process falling within the fence infringes the patent but everything falling outside is open for exploitation by other parties. One benefit of a patent is that third parties are motivated to invent or design around the invention to exploit the knowledge 'legitimately'. A recent example, relating to gene patents, was

heard in the UK Court of Appeal in *Kirin Amgen v TKT* (31st July, 2002).[15] The subject of Amgen's patent was the production of erythropoietin using standard genetic engineering techniques. The Amgen patent described isolating the erythropoietin gene and reinserting it into a host cell in order to manufacture it. TKT manufactured erythropoietin by a different method involving activation of a cell's endogenous erythropoietin gene. This gene activation technique was not available, nor was it contemplated, at the time the Amgen patent was filed and it was held by the Court of Appeal to be a method of erythropoietin production which did not infringe the Amgen patent. This is an excellent example of new technology being developed spurred on by the existence of a patent.

New technology is spurred on by the existence of a patent

When it is not possible to design around a patent, inventors have often found a working solution. For example, Rosgen, the British licensee of two important breast cancer tests, decided in 2000 not to charge royalties to the National Health Service.[16] Rather than inhibit the use of the test by public sector doctors, Rosgen aimed to recoup lost profits by offering a private sector service.

On a larger scale, the international community is making concerted efforts to prevent patented drugs for treating HIV from being beyond the reach of the poorest nations crippled by AIDS. There are now cocktails of drugs for treating HIV that appear to delay the onset of AIDS indefinitely. However, many of these drugs are protected by patents that make them too expensive for these nations to treat those afflicted. The Doha Declaration, made at the World Trade Organization meeting in November 2001, stated that a solution to the crisis will be found by the end of 2002. The solution will probably take the form of allowing governments of the least developed nations, which have no pharmaceutical industry of their own, to grant compulsory licences to import cheap generic drugs.[17]

Doha Declaration

CONCLUSIONS

The NCB paper has been a valuable exercise and it is important to continue discussions between lawyers, ethicists, scientists and patent experts. The very complicated nature of patent law and molecular biology means that experts are needed to identify the exact nature of the technical, scientific and legal problems involved. However, the NCB paper failed to provide any solid data to support its claims. A writer for the *Financial Times*[18] said that

> one of the most surprising aspects of the Nuffield Council's report is that, after two years' work, it failed to quantify reliably the number of patents that assert rights over DNA sequences – beyond saying 'many thousands' had been granted. Patent offices are failing to collate or release information that would be useful for formulating policy.

A second criticism is that many of its recommendations appear to be unworkable, in particular its recommendation on imposing compulsory licences on existing gene patents without giving insight into the criteria by which this would be exercised.

Perhaps things are best left alone. An in-depth examination of the patent system may show that it is a self-correcting system that will give reward only to inventors deserving a time-limited monopoly for pushing back the frontiers of science. However, it is important to continue these discussions even though we may not achieve a coherent policy on gene patents until after they have all expired.

References

1. Haycock, P. (2001), 'The importance of patents in biotechnology', *World Patent and Trade Mark News*, June, pp. 1–2.
2. Manly, C. J. (2001), 'Discovery technologies and the issues facing drug discovery', *Curr. Drug Discovery*, September, pp. 9–10.
3. Sheard, A. (2002), 'An industry perspective' (URL: http://www.hgc.gov.uk/business_meetings_12february.htm).

4. Article 52 European Patent Convention.
5. Kelves, D. J. (2001), 'Patenting life: A historical overview of law, interests and ethics' (URL: http://www.yale.edu/law/ltw/papers/ltw-kevles.pdf).
6. Kirby, J. M. (2001), 'Intellectual property and the human genome' (URL: http://www.unesco.org/ethics/en/vivant/IP_Human_Genom_Kirby_En.rtf).
7. Article 5(1) of the Directive of the European Parliament and of the Council of 6th July, 1998, on the legal protection of biotechnology inventions.
8. Article 5(3) of the Directive of the European Parliament and of the Council of 6th July, 1998, on the legal protection of biotechnology inventions.
9. Article 5(2) of the Directive of the European Parliament and of the Council of 6th July, 1998, on the legal protection of biotechnology inventions.
10. Crespi, S. (1995), 'Biotechnology patenting: The wicked animal must defend itself', *Europ. Int. Prop. Rev.*, Vol. 9, pp. 431–441.
11. Halley, D. and Matthijs, G. (2002), 'European-wide opposition against the breast cancer patents', Swiss Society of Medical Genetics (URL: http://www.ssgm.ch/sections/News/brca1_(eng).htm).
12. United States, *Federal Register*, No. 66(4), 5th January, 2001, pp. 1092–1111.
13. OECD (2002), 'Genetic inventions, intellectual property rights and licensing practices' (URL: http://www.oecd.org/pdf/M00031000/M00031448.pdf).
14. Mueller, L. (2001), 'Patent pools: should the biotech industry jump in?', I-Street (URL: http://www.i-street.com/magazinearchive/yr2001/mn12/patent.asp).
15. *Kirin Amgen v Transkaryotic System*, 31st July, 2002 (URL: http://www.courtservice.gov.uk/judgments/judg_home.htm).
16. *Independent* (2000), 'Patenting genes can be the best way to help us' (URL: http://www.independent.co.uk/story.jsp?story=41414).
17. Toumi, E. (2002), 'TRIPS & compulsory licensing: A path to affordable medicines?, *ERA News*, Vol. 122, pp. 12–14.
18. *Financial Times* (2002), 'Genes off pat', *Financial Times* (US edition), 31st July, p. 12.