ON THE LEGALITY OF GENE PATENTS

DIANNE NICOL*

[This article considers the legal and policy deliberations on gene patenting that have occurred since the issue came to the fore in the early 1990s. The analysis is contextualised with brief overviews of the science of genetics and genomics and the law of patents. Legislation, administrative guidelines and case law are analysed, focusing on the jurisdictions of Australia, the US and the UK. This article concludes that, despite ongoing legal and policy developments, clear guidance as to the legality of gene patents remains elusive. It is obviously desirable to have proper and certain gene patenting laws. In time, this is likely to happen. In the interim, it is argued that other mechanisms are also available for dealing with gene patents, negating the desirability of a radical overhaul of gene patenting laws.]

CONTENTS

I INTRODUCTION

All member states of the World Trade Organization ('WTO') are obliged to make patents available for all inventions in all fields of technology, provided that they fulfil the patent validity requirements of novelty, inventive step (or non-obviousness) and industrial applicability (or utility), as provided by art 27 of the

* BSc (Hons) (Manchester), LLB (Hons), LLM (Tas), PhD (Dalhousie); Senior Lecturer, Faculty of Law, University of Tasmania.

Agreement on Trade-Related Aspects of Intellectual Property Rights.[1] Article 29 of *TRIPS* identifies the disclosure requirements: member states must require that the invention be fully described, including the best method of performance.

These patentability and disclosure requirements encapsulate the core features of the patent bargain. The 20-year monopoly afforded to standard patents[2] around the world is only granted by states for inventions that are patentable and fully disclosed. The public is said to benefit from this bargain in two ways. First, the 20-year monopoly rewards innovation on the part of the patent holder. Second, full disclosure encourages others to innovate by inventing around live patents and by making use of the disclosed invention once the patent has expired.[3] However, the public benefit can easily be distorted if patent holders are overly rewarded with too great a monopoly for their innovation, or if there is insufficient disclosure of the invention leading to uncertainty as to its true nature and its best method of performance. Both could discourage or restrict innovation by others.

Problems may also arise if patent holders are inadequately rewarded for their innovation. This can happen if the patent monopoly is unduly restrictive, or if the validity of the patent is uncertain. In such situations, patent holders might be discouraged from making optimal use of a patent monopoly, and both patent holders and others may be discouraged from further innovation. Hence, it is essential that patent law set proper and certain boundaries on what is and is not patentable and that patents are only granted for inventions that meet the patentability and disclosure requirements.

Nowhere are the boundaries of patent law less certain than for genetic inventions. Over the last 14 or so years, these gene patents[4] have attracted more academic debate, policy discussion and calls for law reform than any other type of patent. From the Australian perspective, these policy and law reform issues were most recently canvassed by the Australian Law Reform Commission ('ALRC') in its inquiry into gene patenting and human health.[5] There is a growing body of jurisprudence considering the legality of gene patents in some

[1] *Marrakesh Agreement Establishing the World Trade Organization*, opened for signature 15 April 1994, 1867 UNTS 3, annex 1C (*Agreement on Trade-Related Aspects of Intellectual Property Rights*) (entered into force 1 January 1995) ('*TRIPS*').

[2] Some countries also have a lesser form of patent grant. In Australia, for example, innovation patents are granted for up to eight years: *Patents Act 1990* (Cth) ss 62, 68. A lower level of inventiveness is required for innovation patents than for standard patents: *Patents Act 1990* (Cth) ss 7(2)–(3) (inventive step requirements), 7(4)–(5) (innovative step requirements).

[3] Various theories have been postulated to justify patents, primarily focusing on economic rationales rather than the natural or moral rights of the inventor. Currently, the dominant paradigm is the incentive to innovate. For a full discussion, see Roberto Mazzoleni and Richard R Nelson, 'Economic Theories about the Benefits and Costs of Patents' (1998) 32 *Journal of Economic Issues* 1031. See also Lee Bendekgey and Diana Hamlet-Cox, 'Gene Patents and Innovation' (2002) 77 *Academic Medicine* 1373.

[4] The precise boundaries of the term 'gene patent' are also uncertain. In this article, the term is intended to encompass any patent that includes a claim to a deoxyribonucleic acid ('DNA') sequence.

[5] ALRC, *Genes and Ingenuity: Gene Patenting and Human Health*, Report No 99 (2004). The final report of the inquiry was tabled in federal Parliament in August 2004. The only other areas that have attracted similar levels of debate are software patents and business method patents.

jurisdictions, particularly in the US.[6] Alongside these developments, genetic technology continues to advance and gene patent applications continue to be filed in ever-increasing numbers.[7] A recent study by Kyle Jensen and Fiona Murray concluded that nearly 20 per cent of all human genes have been claimed in patents granted in the US, with some genes featuring in up to 20 separate patents.[8]

So many years into the gene patent debate, it is timely to reflect on how far we have come, to assess whether the legality of gene patenting is any clearer now than it was 14 years ago, to determine whether the lack of clarity in this area has produced any undesirable outcomes, and to consider whether anything needs to be done to better protect the public benefit. This article seeks to canvass these and related issues. In doing so, some of the key judicial decisions, legislation and policy statements will be analysed.

II THE HISTORICAL CONTEXT

A *Primer on Genetics and Genomics*

Any discussion regarding gene patenting must necessarily being with the science of genetics and genomics. Although the modern science is staggeringly complex and rapidly evolving, the core concepts are relatively simple. It is not necessary to go too far beyond these concepts to understand the legal issues that are being raised in the courts and in policy debates.

We should start with a mention of the unique structure of the DNA molecule. DNA is a complex chemical that is made up of a sequence of nucleotides, each of which contains one of the four bases: adenine, cytosine, guanine and thymine. In humans there are around three billion of these nucleotides arranged in precise order along our chromosomes.

One of the primary functions of DNA is as a source of the information necessary to produce all of the proteins required by a living organism.[9] The site on the DNA molecule that carries the information to produce a particular protein is the gene.[10] Each protein is produced by the same two-step process. In the first step,

6 It is interesting to note, however, that there has been hardly any discussion of such matters in the Australian courts.

7 The World Health Organization provides some useful data on the general rise in patents in biotechnology in World Health Organization, *Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries* (2005) 20.

8 Kyle Jensen and Fiona Murray, 'Intellectual Property Landscape of the Human Genome' (2005) 310 *Science* 239, 239. Over 75 per cent of these gene patents have only one patent owner, but the remainder have fragmented ownership. The authors report that the two genes with the most fragmented ownership have eight assignees for nine patents, and 12 assignees for 14 patents: at 240. Such fragmented ownership is likely to increase significantly the cost of access for downstream innovators. See also Birgit Verbeure, Gert Matthijs and Geertrui Van Overwalle, 'Analysing DNA Patents in relation with Diagnostic Genetic Testing' (12 October 2005) *European Journal of Human Genetics* 1 <http://www.nature.com/ejhg/journal/vaop/ncurrent/pdf/5201503a.pdf>.

9 This is also our hereditary information, and another function of DNA is to pass on this information to our descendants.

10 There is not a direct one-to-one correspondence of genes to proteins. In humans, for example, the latest estimates of the number of genes are as low as 20 000, yet there are far more proteins.

known as transcription, a precise copy of the information encoded in the gene is made within another complex molecule, messenger ribonucleic acid ('mRNA'). In the second step, called translation, groups of three nucleotides on the mRNA (known as codons) pair with a particular amino acid, and the amino acids are joined together to form strands known as polypeptides. The proteins formed by these polypeptides have to go through various conformational changes before they can perform their function.

It is generally the case that only a small portion of the protein is functional. As a result, it is possible to alter some of the amino acids without affecting their function. The group of related amino acid sequences that all perform the same function is sometimes referred to as a genus. This feature creates a dilemma for holders of patents claiming rights over such proteins. Unless the entire genus is claimed, small changes to non-functional parts can be made without infringing the patent. Hence, the goal of the patent holder is to obtain broad enough patents to cover the entire genus of functionally-equivalent proteins.[11]

There is some redundancy in the translation code, because there are 64 codons yet only 20 amino acids. Most amino acids are, therefore, complementary to more than one mRNA codon. This is known as degeneracy of the code. Hence, the same sequence of amino acids can be created from a number of different DNA sequences, also often referred to as a genus. The story is further complicated by the fact that there is not a straight transition from DNA to mRNA to protein, because not all of the DNA in the region of the gene codes for amino acids. The non-coding regions are removed following the transcription process.

There are various incentives for research aimed at understanding how these processes work. In humans, the primary focus is health care, which includes:

- identifying and testing for genetic diseases;
- producing synthetic therapeutic proteins to replace defective natural proteins;
- producing other small molecule drugs that interact with particular proteins; and
- developing therapies to rectify or replace defective genes.

In other species, the research effort is directed towards developing improvements to the food supply as well as therapeutics, and focuses on manipulating the genome by inserting foreign genes, activating and deactivating host genes and so on.

One of the greatest landmarks in this research effort was the discovery of how to splice and clone genes. The first gene splices were performed by Herbert Boyer and Stanley Cohen in 1973.[12] Gene splicing led to the development of recombinant DNA technology. By splicing short strands of DNA from one

Hence, a particular gene might carry the information to make several proteins. See International Human Genome Sequencing Consortium, 'Finishing the Euchromatic Sequence of the Human Genome' (2004) 431 *Nature* 931.

11 John Barton provides some useful scenarios which assist in further clarifying this issue: John H Barton, 'Changing Intellectual Property Issues in the Biotechnology Industry' (1999) 18 *Biotechnology Law Report* 3, 4.

12 See National Research Council, *Intellectual Property Rights and the Dissemination of Research Tools in Molecular Biology* (1997) 40–2.

species into the DNA from other more rapidly reproducing species, further research and the production of usable quantities of proteins coded for by those strands were both facilitated.

Towards the end of the 1980s, a plan was formulated to map and sequence the entire human genome. In 1990, the Human Genome Project was established for this purpose.[13] In part, the Project was facilitated by the development of a new technique, reverse transcription, whereby complementary DNA ('cDNA') copies of mRNA could be made.[14] Since mRNA is only transcribed from active genes within the DNA sequence, the cDNA produced by reverse transcription will also be a copy of those active genes. In general, however, the cDNA copy will not have precisely the same gene sequence as the original DNA that was used to transcribe the mRNA, known as genomic DNA ('gDNA'), because it contains only the coding components of the gDNA.

Short fragments of cDNA are known as expressed sequence tags ('ESTs'). These ESTs are derived from genes, as they are copied from mRNA. However, the identity of the genes, their location and their function are not known. ESTs can be powerful research tools, particularly as probes for the genes from which they are derived. The development of EST technology was therefore an important step in the progress of the research effort. It also signalled the start of the debate about gene patents. In 1992, the Human Genome Project was described as the biggest patenting issue in the US,[15] due to the large number of patents for ESTs in 1991 that were applied for by the National Institutes of Health ('NIH'), the biggest public sector research organisation in the US.[16]

In the new millennium, research into identifying, isolating and manipulating individual genes and understanding the basis of genetic disease continues. Vast monetary commitments have been made to international collaborative ventures focusing on whole genome research, such as the HapMap Project and the SNP Consortium,[17] and a host of other projects.

Following the completion of the Human Genome Project in 2003, research in the so-called post-genomic era focuses on matters such as:

- understanding the structure and function of the genome as a whole, and how gene coding and non-coding regions interact;
- understanding how mRNA works, and how exons and introns interact; and
- understanding how proteins acquire their structure and function.

[13] For a history of the Human Genome Project, see the National Human Genome Research Institute, *All about the Human Genome Project (HGP)* (2005) <http://www.genome.gov/10001772>.

[14] For a useful discussion of this technology, see Bendekgey and Hamlet-Cox, above n 3, 1373–5.

[15] Linda Maher, 'The Patent Environment: Domestic and European Community Frameworks for Biotechnology' (1992) 33 *Jurimetrics Journal* 67, 128.

[16] See, eg, Rebecca Eisenberg, 'Genes, Patents and Product Development' (1992) 257 *Science* 903.

[17] One of the lead funding agencies of both projects, the Wellcome Trust, describes these ventures as two global partnerships that are characterising variations in the human genome. It states that single nucleotide polymorphisms ('SNPs') are changes to single letters of the DNA code, which occur in about one in every 1000 nucleotides. The SNP Consortium is mapping these SNPs, whereas the HapMap Project is investigating the combinations of SNPs that are inherited together: Wellcome Trust, *The SNP Consortium and the International HapMap Project* (2005) <http://www.wellcome.ac.uk/doc_WTD003500.html>.

B *The Rise of the Biotechnology Industry*

A thriving biotechnology industry has emerged in parallel with these research developments, focusing on the advancement of new medicines, genetic tests and therapies in the medical sector and genetically-modified organisms in the agricultural sector. While each of these developments has attracted some controversy,[18] the public benefit from biotechnology has prevailed, with many governments looking to the industry for future economic growth.[19] However, much like the pharmaceutical industry, biotechnology is research intensive, failure rates are high and there is a long road from research to product development. Further, as with pharmaceutical companies, biotechnology firms place great reliance on their patent portfolios.

In the 1980s and 1990s, the early leaders in the medical biotechnology industry followed three main lines of research and development.[20] First, a number of companies were set up to produce therapeutic proteins by means of recombinant DNA technology. John Barton refers to this phase of the development of the industry as 'old', 'traditional' and 'first generation'.[21] Examples of old biotechnology companies include Genentech and Kirin-Amgen. Their products included recombinant insulin, erythropoietin ('EPO'), human growth factor, tissue plasminogen activator, tumour necrosis factor and various other proteins. As we shall see, the patents covering many of these products have been heavily litigated. Rebecca Eisenberg refers to this phase of gene patenting as 'patenting genes as drugs'.[22]

The second and third lines of research and development are what Barton referred to in 1999 as the 'new generation' of biotechnology.[23] During the 1990s, a number of companies had become specialised in hunting for specific disease-related genes, locating them within the human genome, isolating them, sequencing their codes and developing diagnostic tests. Perhaps the best example is Myriad Diagnostics, which for a number of years owned highly contentious

[18] In the medical sector, many of the complex ethical, legal and social issues arising from these developments were canvassed by the ALRC and the Australian Health Ethics Committee in their joint report entitled *Essentially Yours: The Protection of Human Genetic Information in Australia*, Report No 96 (2003). In the agricultural sector, see, eg, the recent US report of the Committee on Genetically Modified Pest-Protected Plants, Board on Agriculture and Natural Resources, National Research Council, *Genetically Modified Pest-Protected Plants: Science and Regulation* (2000), and the earlier Australian report of the House of Representatives Standing Committee on Industry, Science and Technology, Parliament of Australia, *Genetic Manipulation: The Threat or the Glory* (1992).

[19] For example, in Australia, the federal government has expressed strong support for the development of an Australian biotechnology industry: see Biotechnology Australia, *Australian Biotechnology: A National Strategy* (2000). See also Dianne Nicol and Jane Nielsen, 'The Australian Medical Biotechnology Industry and Access to Intellectual Property: Issues for Patent Law Development' (2001) 23 *Sydney Law Review* 347.

[20] At around the same time, Monsanto and other agricultural companies were developing techniques for genetically modifying crop species.

[21] Barton, 'Changing Intellectual Property Issues in the Biotechnology Industry', above n 11, 3.

[22] Rebecca S Eisenberg, 'Why the Gene Patenting Controversy Persists' (2002) 77 *Academic Medicine* 1381, 1381.

[23] Barton, 'Changing Intellectual Property Issues in the Biotechnology Industry', above n 11, 5–9.

patents relating to two genes linked to increased susceptibility to breast cancer (BRCA 1 and 2).[24] For Eisenberg, this phase is 'patenting genes as diagnostic products'.[25]

At around the same time, other companies including Celera Genomics, Incyte Genomics and Human Genome Sciences focused their research efforts on automated sequencing of large numbers of DNA fragments. Once again, the patent claims made by these companies have been highly controversial. For Eisenberg, these types of claims amount to 'patenting genes as research tools' and 'patenting genes as trivial advances', moving away from patenting end products towards patenting scientific information.[26]

The biotechnology industry is even more complex now than it was in the late 1990s. The industry has undergone massive expansion. Some companies, especially those in sequencing, have diversified while others have specialised. New industry sectors have developed, including genomics, bioinformatics, and gene chip technology, to name a few. Barton argues that patents owned by these companies, covering such subject matter as computer-based genomic information, databases and manipulating procedures, could create more serious encumbrances for medical research than patents on ESTs.[27] One of the dominant features of the industry is that innovation is cumulative: many small steps must be taken on the road to product development and many pathways intersect and overlap. Where each step or pathway is protected by a patent, the pace of innovation could be slowed, particularly when broad patent rights are granted to early innovators.[28]

The public sector has been heavily involved in the expansion of the biotechnology industry. This has occurred both indirectly through input of findings from the Human Genome Project, and directly through applied research, often in collaboration with industry partners. The result is the formation of a significant private industry around pre-product development research.[29] This is part of a

[24] In November 2004, Myriad Diagnostics sold its BRCA patents to the University of Utah Research Foundation, but it continues to hold exclusive licences to the patents: see Institut Curie, 'Breast and Ovarian Cancer Susceptibility Gene BRCA1: Another Victory for Opponents of Patents Held by Myriad Genetics: European Patent Office Rejects the Essential Points of BRCA1 Gene Patents' (Press Release, 31 January 2005) <http://www.curie.fr/upload/presse/myriadpatents310105.pdf>.

[25] Eisenberg, 'Why the Gene Patenting Controversy Persists', above n 22, 1382.

[26] Ibid 1383–5. See also Rebecca S Eisenberg, 'How Can You Patent Genes?' (2002) 2(3) *American Journal of Bioethics* 3.

[27] John H Barton, 'Patents, Genomics, Research and Diagnostics' (2002) 77 *Academic Medicine* 1339, 1339–40. He also adds SNPs to his list: at 1339.

[28] See especially Suzanne Scotchmer, 'Standing on the Shoulders of Giants: Cumulative Research and the Patent Law' (1991) 5(1) *Journal of Economic Perspectives* 29, 32–3. See also Michael A Heller and Rebecca S Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research' (1998) 280 *Science* 698; Rebecca S Eisenberg, 'Bargaining over the Transfer of Proprietary Research Tools: Is This Market Failing or Emerging?' in Rochelle Cooper Dreyfuss, Dianne Leenheer Zimmerman and Harry First (eds), *Expanding the Boundaries of Intellectual Property: Innovation Policy for the Knowledge Society* (2001).

[29] Rebecca S Eisenberg and Richard Nelson, 'Public vs Proprietary Science: A Fruitful Tension?' (2002) 77 *Academic Medicine* 1392. See also Don Chalmers and Dianne Nicol, 'Commercialisation of Biotechnology: Public Trust and Research' (2004) 6 *International Journal of Biotechnology* 116.

wider trend favouring science that has commercial applicability. One outcome is that the patent pathway has been pushed back further, right to the point of scientific discovery.

The success of this commercialisation drive is evinced by the fact that public sector organisations currently own a significant share of granted gene patents, at least in the US.[30] As noted above, debates about gene patenting began in earnest with the filing of EST patent applications by the NIH. The EST claims were ultimately rejected as they failed to satisfy the patentability requirements,[31] and were subsequently withdrawn. A change in policy meant that the NIH did not pursue the EST patent claims further, but this did not stop a number of companies from lodging large numbers of similar patent applications. The stated aim of the NIH in applying for the EST patents was to encourage product development.[32] However, they could just as easily have had the opposite effect by blocking later downstream research on genes and proteins and development of diagnostic tests, therapies and drugs. If nothing else, the NIH's actions demonstrated the need for detailed public discussion and clear official guidelines on gene patenting.[33]

III CHARACTERISING GENE PATENTS

A DNA sequence claimed in a patent may cover an entire gene or a shorter fragment of a gene, for example an EST, or even a sequence from a non-coding region of the genome. However, gene patents do not simply claim rights over the sequence information; they claim much more than this. Broadly speaking, there are four different types of patent claims:

- product claims, which give the patent holder rights to all uses of the patented product, whether they are known at the time of patenting or not, and whether they are claimed or not. These are the broadest types of patent claims. They are frequently used to protect chemical compounds. One of the crucial issues here is the legitimate extent of these claims: that is, whether or not it is permissible to claim the entire genus of products that function in the same way as the isolated product;
- process or method claims, which claim broad rights to all uses of a particular technology (recombinant DNA technology was protected in this way);

30 Jensen and Murray, above n 8, 240. The authors estimate that 28 per cent of patents that include claims to human genes are owned by public sector organisations, including governments, schools, universities, research institutions and hospitals. See also Frederick M Scherer, 'The Economics of Human Gene Patents' (2002) 77 *Academic Medicine* 1348, 1357–8.

31 See, eg, Eliot Marshall, 'Intellectual Property: Companies Rush to Patent DNA' (1997) 275 *Science* 780.

32 Bernadine Healy, 'Special Report on Gene Patenting' (1992) 327 *New England Journal of Medicine* 664, 665.

33 By 1992, such public discussions were already underway: a public meeting had been called by the Genome Patenting Working Group in the US, and the Patent and Trademark Office had given notice of public hearings and requested comments on patent protection for biotechnological inventions. See Genome Patenting Working Group, Committee on Life Sciences and Health, Federal Coordinating Council for Science, Engineering and Technology, Office of Science and Technology Policy, *Federally Funded Genome Research: Science and Technology Transfer Issues: Proceedings of a Public Meeting, May 21, 1992* (1992).

- product-by-process claims, which cover products made by one specific process. Such claims would still cover all uses of those products, but only where the product is made using that process. These claims become important where the product is already known or where it would otherwise be excluded from patenting;[34] and
- use or purpose-bound claims, which cover specific disclosed uses of a product. Many have argued that gene patents should be restricted to use claims.[35]

In the 1980s, companies in the therapeutic protein area commonly made product-by-process claims to the protein made by means of recombinant DNA technology. Kirin-Amgen's EPO patent provides a good example of these types of claims. Kirin-Amgen's scientists discovered a way of using recombinant DNA technology to produce commercial quantities of EPO, an important and rare protein that plays a major role in regulating the rate of red blood cell formation. Kirin-Amgen successfully obtained patents that included product-by-process claims for EPO in a number of countries. The main claim in the Australian patent was for:

> A purified and isolated polypeptide having the primary structural conformation and one or more of the biological properties of naturally-occurring erythropoietin and characterised by being the product of procaryotic or eucaryotic expression of an exogenous DNA sequence.[36]

Interestingly, the wording of this claim is slightly different in other jurisdictions. In Kirin-Amgen's European patent, for example, the primary claim refers to expression in a 'host cell' rather than expression of an exogenous DNA sequence.[37] The importance of this distinction will become apparent later.[38] For now, it is sufficient to note that the key feature of this claim is that it is not restricted to a particular animal species or to a particular amino acid sequence. It is a classic genus claim, including all forms of EPO-type polypeptides produced by recombinant DNA technology, whatever their source. These claims are

[34] It should be noted that despite a tradition of allowing such claims in some jurisdictions, their legality is now questionable. See *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd* [2005] 1 All ER 667 ('*Kirin-Amgen*'). See below Part IV(D)(1).

[35] See, eg, Nuffield Council on Bioethics, *The Ethics of Patenting DNA: A Discussion Paper* (2002) 71 <http://www.nuffieldbioethics.org/fileLibrary/pdf/theethicsofpatentingdna.pdf>; Danish Council of Ethics, *Patenting Human Genes and Stem Cells* (2004) 101–2 <http://www.etiskraad.dk/graphics/03_udgivelser/engelske_publikationer/patenting_human_genes/patents04/patenting_human_genes.pdf>. For a detailed evaluation of the pros and cons of restricting gene patents to purpose-bound claims, see Sven J R Bostyn, *Patenting DNA Sequences (Polynucleotides) and Scope of Protection in the European Union: An Evaluation* (2004) 56–67 <http://www.ivir.nl/publications/bostyn/patentingdna.pdf>. On 26 October 2005, the European Parliament passed a resolution entitled *Patents for Biotechnology Inventions*, cl 5 of which calls on the European Patent Office to only grant patents in connection with concrete applications and to only allow purpose bound protection: <http://www.europarl.eu.int/omk/sipade3?TYPE-DOC=TA&REF=P6-TA-2005-0407&MODE=SIP&L=ENLSTDOC=N>.

[36] *Genetics Institute Inc v Kirin-Amgen Inc [No 3]* (1998) 156 ALR 30, 38 (Heerey J) ('*Genetics Institute*').

[37] *Kirin-Amgen* [2005] 1 All ER 667, 676 (Lord Hoffmann).

[38] See below Part IV(B).

obviously wider than the invention, and they have provided Kirin-Amgen with an extremely broad monopoly over the production of this important therapeutic protein.

In the 1990s, sequencing and diagnostics companies started to seek even broader product patents, extending beyond known therapeutic proteins to all uses of the disclosed sequence information. In effect, patents cast in these terms give the patent holder the exclusive right to control all uses of the gene sequence, including both its use as a tool for further upstream research and its use in commercial research and development of tests, therapies and drugs.[39]

A distinction has been drawn in the literature between the use of gene sequences as broadly-applicable research platforms that open up unchartered areas of investigation, much like recombinant DNA technology did, and their use as tools for more downstream research (for example, the use of a gene sequence for diagnostic testing for a particular disease).[40] Innovation is most likely to be inhibited if broad research platforms are not made widely available to follow-on researchers.[41] However, downstream tools could also have an inhibitory effect on innovation if access is denied or made difficult,[42] and they could have a profound effect on consumer access to health care.[43] For example, Myriad's suite of patents has effectively given it the exclusive right to conduct diagnostic testing relating to breast and ovarian cancers, and it has been actively enforcing its rights against public and private sector researchers using the BRCA genes as well as against laboratories offering BRCA tests in a number of countries.[44]

It should be noted that in Europe, the claims in some of Myriad's patents were declared invalid in a series of opposition proceedings in 2004 and 2005.[45] These

39 The Nuffield Council identifies four distinct applications of DNA sequence claims: diagnostic testing, research tools or methods, gene therapy or methods, or the production of therapeutic proteins to be used as medicines: Nuffield Council on Bioethics, above n 35, 47–8.

40 See especially Jorge A Goldstein and Elina Golod, 'Human Gene Patents' (2002) 77 *Academic Medicine* 1315, 1326–7; Arti K Rai, 'Genome Patents: A Case Study in Patenting Research Tools' (2002) 77 *Academic Medicine* 1368, 1369–70.

41 Heller and Eisenberg, above n 28.

42 See Rai, 'Genome Patents', above n 40, 1369–70, where she argues that there is, in fact, no bright line between broad research platforms and more downstream research tools.

43 This is illustrated by empirical studies on the impact of gene patent enforcement on the provision of diagnostic services and diagnostic research in the US: see especially Mildred K Cho et al, 'Effect of Patents and Licenses on the Provision of Clinical Genetic Testing Services' (2003) 5 *Journal of Molecular Diagnostics* 3; Jon F Merz et al, 'Diagnostic Testing Fails the Test' (2002) 415 *Nature* 577.

44 See Jordan Paradise, 'European Opposition to Exclusive Control over Predictive Breast Cancer Testing and the Inherent Implications for US Patent Law and Public Policy: A Case Study of the Myriad Genetics' BRCA Patent Controversy' (2004) 59 *Food and Drug Law Journal* 133.

45 Patent EP0699754 relating to BRCA1 was successfully opposed and was revoked on 11 November 2004, but is the subject of an appeal: European Patent Office, 'Public Opposition Hearing on "Myriad/Breast Cancer" Patent at the European Patent Office (17–19 May)' (Press Release, 13 May 2004) <http://www.european-patent-office.org/news/pressrel/2004_05_13_e.htm>. The main claims in Patent EP0705902, also relating to BRCA1, were revoked on 12 September 2005, but this decision is also the subject of an appeal. The patent had originally claimed a number of mutations in the BRCA1 gene and diagnostic methods for determining a predisposition to breast cancer. The patent is now limited to a gene probe for detecting a specific mutation: European Patent Office, 'European Patent on Mutations in Breast and Ovarian Cancer Susceptibility Gene Amended after Public Hearing' (Press Release, 25 January 2005) <http://www.european-patent-office.org/news/pressrel/2005_01_25_e.htm>. However, opposition to patent EP0785216 relating to BRCA2 was unsuccessful and the patent was allowed to be

decisions have important consequences for diagnostic service providers in Europe. However, the extent to which they actually clarify the law relating to gene patenting is less clear. The first decision in 2004 primarily rests on technical issues associated with Myriad's attempts to amend the claims made in the patent to extend their scope. Detailed reasons for the other decisions were not available at the time of writing. Consequently, they are not considered further in the analysis that follows.

Despite the highly controversial nature of Myriad's actions, it had at least disclosed mutant sequences and their function. Claims of such breadth become even more contentious when they are based solely on EST sequence information, without disclosure of the full gene sequence or its function. Two variants of EST claims are frequently referred to in the literature: 'comprising' claims and 'consisting of' claims. The word 'comprising' is recognised in patent law to mean 'including' or being 'open-ended'.[46] Hence, 'comprising' sequence claims are generally interpreted to include any subject matter that uses the disclosed sequence, even where those uses have not been disclosed.[47] On the other hand, claims using the words 'consisting of' are restricted to the sequence as claimed — they are 'closed'.[48]

The attraction for patent holders in making 'comprising' EST claims is that it means they have rights not only over the EST itself and its use as a research tool, but also the full gene sequence, the proteins for which it codes, diagnostic tests, and even gene therapies that may subsequently be developed — despite the fact that neither the full gene sequence nor its function is disclosed. Thus, these patent holders could demand licence fees from any downstream user of the EST sequence, even if the user never actually referred to the sequence information provided by the patent holder. This seems to be quite a windfall for someone who has acquired the EST sequence information entirely through automated processes. A 'consisting of' claim, on the other hand, would be restricted to the EST sequence itself and its use as a research tool. However, it is questionable whether a claim of this nature has sufficient usefulness to be patentable.

Even where a full gene sequence is disclosed and a function has been ascribed to the gene, it still may be too great a reward for the patent holder to claim rights to all uses of the sequence information. This is particularly the case when the sequence information is obtained by computerised sequencing technology and function is ascribed solely based on computerised screening for homology with other sequences. It is difficult to see how the analogy between DNA and other chemical substances can be sustained in such an environment.[49]

maintained in its amended form. The patent now relates to use of a particular mutation in BRCA2 for diagnosing predisposition to breast cancer in Ashkenazi-Jewish women: European Patent Office, 'Patent on "Breast Cancer Gene 2" Patent Maintained in Amended Form after Public Hearing' (Press Release, 29 June 2005) <http://www.european-patent-office.org/news/pressrel/2005_06_29_e.htm>.

46 See Goldstein and Golod, above n 40, 1319.

47 *Genentech Inc v Chiron Corp*, 112 F 3d 495, 501 (Rich J) (Fed Cir, 1997).

48 Goldstein and Golod, above n 40, 1319.

49 The distinction between the 'bricks and mortar' world of traditional patent law and the intangible world of the information economy is extensively discussed in Eisenberg, 'How Can You Patent

IV THE LAW: WHAT EXACTLY CAN BE PATENTED?

A *Patent Law Primer*

Although *TRIPS* prescribes the patentability and disclosure requirements that must be included in the patent laws of all WTO member states, there is considerable variability between countries — both in the substantive law relating to patentability and disclosure of gene-related inventions, and in the procedural law prescribing the mechanisms for obtaining and maintaining patents. Some of the key aspects of obtaining a valid patent are described below, and the main points of difference between the three key jurisdictions of Australia, the US and the UK are highlighted.[50]

1 *The Invention Requirement*

Patents can only be claimed for inventions: there must be appropriate subject matter. Section 6 of the *Statute of Monopolies 1623*, 23 Jac 1, c 3 provided the first elucidation of the requirements for a valid patent, specifying that there should be a 'manner of new manufacture'. Some jurisdictions, including Australia, still retain this terminology.[51]

Despite the antiquity of the 'manner of manufacture' test, recent reports considering reform of Australian patent law recognise that this requirement has served its purpose well and should remain as the touchstone of patentability.[52] In the leading Australian case interpreting s 6, *National Research Development Corp v Commissioner of Patents*,[53] the High Court set out the key requirements that were to be satisfied:

> For a process to fall within the limits of patentability which the context of the *Statute of Monopolies* has supplied, it must be one that offers some advantage which is material in the sense that the process belongs to a useful art as distinct from a fine art, that its value to the country is in the field of economic endeavour.[54]

US patent law uses similar but not identical language, providing that: 'Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor …'[55]

The case law interpreting the 'manner of manufacture' test in Australia and the equivalent 'composition of matter' test in the US recognises a range of exceptions for material that is considered to be unpatentable because it fails to satisfy

Genes?', above n 26. See also Mark Sagoff et al, 'Open Peer Commentary' (2002) 2(3) *American Journal of Bioethics* 12.

50 While other jurisdictions could have been considered, it was never intended that this article should be a comprehensive treatise on comparative patent law. Further, Australia, the US and the UK were chosen as these are the major marketplaces for the Australian biotechnology industry and are the sites of major gene patent battlefields.

51 See, eg, *Patents Act 1990* (Cth) s 18(1) and the definition of invention in sch 1.

52 See, eg, ALRC, above n 5, [6.20]–[6.30].

53 (1959) 102 CLR 252 ('*NRDC*').

54 Ibid 253 (Dixon CJ, Kitto and Windeyer JJ).

55 *Patents Act*, 35 USC §101 (1952).

this test. In the seminal US Supreme Court case of *Diamond v Chakrabarty*, Burger CJ, delivering the majority judgment, noted that laws of nature, physical phenomena and abstract ideas are not patentable.[56]

Under UK patent law, the concept of invention is not defined. Section 1(1) of the *Patents Act 1977* (UK) c 37[57] provides that a patent may only be granted for an invention that satisfies the patentability requirements. A list of matters that are not inventions for the purposes of the Act are provided in s 1(2):

> (2) anything which consists of —
>
> (a) a discovery, scientific theory or mathematical method;
>
> (b) a literary, dramatic, musical or artistic work or any other aesthetic creation whatsoever;
>
> (c) a scheme, rule or method for performing a mental act, playing a game or doing business, or a program for a computer;
>
> (d) the presentation of information;
>
> but … only to the extent that a patent or application for a patent relates to that thing as such.

There has been extensive debate as to the interpretation of the wording of s 1(2) and equivalent provisions in other European jurisdictions, although the law now appears settled. Clearly, the listed matters themselves will be excluded from patenting, but the phrases 'only to the extent that' and 'relates to that thing as such' indicate that the excluded material can, nevertheless, be used as the substratum of a patentable claim embracing the excluded material.[58] Furthermore, things excluded from patentability through s 1(2) can contribute to the 'inventive step' requirement to make the invention patentable.[59]

2 *Exclusions*

Outside of the limitations on patenting imposed by the invention, patentability and disclosure requirements, *TRIPS* allows certain things to be expressly excluded from patent law in member states:

> Article 27.2: Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.
>
> Article 27.3: Members may also exclude from patentability:
>
> (a) diagnostic, therapeutic and surgical methods for the treatment of humans or animals;

56 447 US 303, 309 (1980) ('*Chakrabarty*').

57 The UK, together with most other European states, is a signatory to the *Convention on the Grant of European Patents*, opened for signature 5 October 1973, 1065 UNTS 254 (entered into force 7 October 1977) ('*European Patent Convention*'), which prescribes the requirements for the patent laws of all signatory states. Hence, European patent law is significantly more harmonised than most other states.

58 See, eg, the English Court of Appeal decision in *Genentech Inc's Patent* [1989] RPC 147, 194 (Purchas LJ) ('*Genentech*').

59 Ibid.

> (b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. …

The exclusions are not mandatory, but they provide a complete codification as to what can legitimately be excluded by member states. They are based on the exclusions under the *European Patent Convention* and in the legislation of its signatory states.[60] For present purposes, the key *TRIPS* exclusions are those in arts 27.2 and 27.3(a). These exclusions are not expressly included in US or Australian legislation. Furthermore, recent Australian judicial decisions have confirmed that there is no case law supporting exclusion of diagnostic, therapeutic and surgical methods.[61] However, the case law relating to a public policy or morality exclusion is less clear. Section 6 of the *Statute of Monopolies 1623*, 23 Jac 1, c 3 stated that certain matters are not to be considered manners of new manufacture, including those that are 'generally inconvenient'. The Australian Federal Court has confirmed that s 6 has been incorporated in its entirety into the *Patents Act 1990* (Cth).[62] Whether this allows consideration of moral or public policy considerations, however, is a moot point.[63]

There is one universally-accepted exclusion that could be said to be so obvious that it goes without saying: that human beings cannot be patented. In Australia, s 18(2) of the *Patents Act 1990* (Cth) expressly excludes human beings, and adds that the biological processes for their generation are also not patentable inventions. However, it is doubtful that the exclusion of human beings would extend far enough to prohibit human gene sequences.

3 *The Novelty and Inventive Step Requirements*

Logically, patents are only available for new inventions. However, the mere fact that something is in existence prior to a patent being filed is not enough to destroy novelty: an enabling disclosure is required. Generally, patent law requires that challenges to novelty are made on the basis that prior art information (what has gone on before in the field — including what is generally known and what is written) disclosing all of the features of the invention has been made publicly available. Australian law requires that this prior art information exist in a single document, or in the doing of a single act, or in two or more related documents or acts.[64]

Inventive step (non-obviousness in US law) also requires an analysis of the prior art. The question is whether the teachings from the prior art make the invention obvious to an ordinary person skilled in the field. In Australia, for example, the question to be addressed is whether the invention would have been obvious to a person skilled in the relevant art, having regard to the common

[60] See, eg, *Patents Act 1977* (UK) c 37, ss 1(3) (the art 27.2 exclusion where the French words '*ordre public*' are replaced by the words 'public policy'), 4(2) (the art 27.3(b) exclusion).

[61] See, eg, *Bristol-Myers Squibb v F H Faulding & Co Ltd* (2000) 97 FCR 524.

[62] Ibid. See also *Rescare Ltd v Anaesthetic Supplies Pty Ltd* (1992) 111 ALR 205; rev'd (1994) 50 FCR 1.

[63] Miranda Forsyth, 'Biotechnology, Patents and Public Policy: A Proposal for Reform in Australia' (2000) 11 *Australian Intellectual Property Journal* 202, 215–18.

[64] *Patents Act 1990* (Cth) s 7(1), sch 1 (definitions of 'prior art information' and 'prior art base').

general knowledge (what was generally known and used in the field) and prior art information that the skilled person could reasonably be expected to have ascertained, understood and regarded as relevant.[65]

4 *The Utility Requirement*

Utility (industrial applicability in European law) requires that the invention has some commercial value. In Australia, this requirement is in part dealt with through the 'manner of manufacture' test in the *Patents Act 1990* (Cth) s 18(1)(a), as interpreted in *NRDC*. There is also a usefulness ground,[66] but this is not examined prior to grant, and it requires only that the invention does what it was intended to do and that the end in itself is useful. Commercial practicality or viability is not a necessary requirement, except that if a particular result is claimed, that result must be achievable.[67] In the US, on the other hand, the test is much more stringent, requiring evidence of specific, substantial and credible utility.[68]

5 *Patent Scope and Disclosure Requirements*

Patents have two components: the specification, which describes the invention, and the claims, which mark out the boundaries of the patent. The scope of patent claims is determined by the wording used. However, the patent is not necessarily limited to the literal wording of the claims. Australian and European courts apply a purposive construction when interpreting the claims.[69] In the US, the doctrine of equivalents performs a similar function.[70] There are still strict limits on the breadth of claims and the extent to which the precise language used in the claims can be further broadened through the rules of interpretation.

Disclosure requirements prescribe that the invention must be fully disclosed in the specification, including the best method of performance. Failure to do so means that the patent may be invalid. The language of disclosure varies between jurisdictions. In the US, there is a written description requirement.[71] In Australia, the requirements are referred to as sufficiency, clarity (lack of ambiguity) and fair basing.[72] In the UK, the language of sufficiency is used.[73]

65 *Patents Act 1990* (Cth) ss 7(2), (3).

66 *Patents Act 1990* (Cth) s 18(1)(c).

67 *Rehm v Websters Security Systems* (1988) 81 ALR 79, 96 (Gummow J); *Rescare Ltd v Anaesthetic Supplies Pty Ltd* (1992) 111 ALR 205, 231 (Gummow J).

68 *Brenner v Manson*, 383 US 519 (1966). More recent developments on the law relating to utility are discussed below in Part IV(D).

69 In Australia, see especially *Populin v HB Nominees Pty Ltd* (1982) 41 ALR 471; *Flexible Steel Lacing Co v Beltreco Ltd* (2000) 49 IPR 331. In the UK, see *Catnic Components Ltd v Hill & Smith Ltd* [1982] RPC 183; *Kirin-Amgen* [2005] 1 All ER 667.

70 *Graver Tank & Manufacturing Co Inc v Linde Air Products Co*, 339 US 605 (1950). Problems with the US doctrine were highlighted in *Festo Corp v Shoketsu Kinzoku Kogyo Kabushiki Co Ltd*, 234 F 3d 558 (Fed Cir, 2000).

71 *Patents Act*, 35 USC §112 (1952).

72 *Patents Act 1990* (Cth) s 40.

73 *Patents Act 1977* (UK) c 37, s 14.

B *Do Genes Cross the Invention Threshold?*

As previously noted, *TRIPS* prescribes that patents shall be available for any *inventions*. Patent laws recognise that discoveries are not inventions, either expressly (in Europe) or through statutory interpretation.[74] However, the task of distinguishing between discoveries and inventions is not at all straightforward, particularly when the subject matter is derived from the natural world. Intuitively, products of nature, including naturally-occurring genes, proteins and living organisms would seem to fall clearly under the discovery label. But even though such discoveries might not be patentable, patents can be claimed for methods embracing discoveries, or for products of discoveries, provided that they fulfil the other patenting requirements.[75] So, for example, even if the identification of a naturally-occurring gene is classified as a discovery, the utilisation of that knowledge to make a synthetic gene and gene products could still be characterised as a patentable invention.

A turning point for patenting in this area came in 1980 with the US Supreme Court decision in *Chakrabarty*, which allowed a patent for a bacterium that had been modified so that it could break down hydrocarbons. The patent application included a number of claims including a claim to the bacterium itself. This particular claim was rejected by the patent examiner on the basis that micro-organisms are products of nature and that, as living things, they are not patentable subject matter.

Burger CJ held that the task in this case was a narrow one of statutory construction and that the question was whether the bacterium was a manufacture or composition of matter. His Honour referred to the words of Thomas Jefferson, author of the first US *Patent Act* in 1793, who said that 'ingenuity should receive liberal encouragement',[76] and to the Committee reports accompanying the 1952 Act indicating an intention that patentable subject matter include 'anything under the sun that is made by man.'[77] Burger CJ concluded that a broad construction of the legislation was supported both by this legislative history and also by the express words of the statute, particularly the word 'any'. In this light, his Honour held that Chakrabarty's micro-organism plainly qualified, as he had

> produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork but his own; accordingly it is patentable subject matter under §101.[78]

74 See, eg, *Lane-Fox v Kensington & Knightsbridge Electric Lighting Co Ltd* [1892] 3 Ch 424.

75 In Australia, in *Rank Hovis McDougall Ltd's Application* (1976) 46 AOJP 3915 the Assistant Commissioner of Patents granted a patent for a new strain of micro-organism that could be used in a process for the production of an edible protein. The process itself was patentable, however, a patent was refused for the original micro-organism because it was naturally occurring. See also IP Australia, *Australian Patent Office Manual of Practice and Procedure* (2005) vol 2 [8.2.2], [8.2.5.3], [8.2.14] <http://www.ipaustralia.gov.au/resources/manuals_patents2.shtml>.

76 447 US 303, 308 (1980).

77 Ibid 309.

78 Ibid 310.

The decision in *Chakrabarty* has been widely accepted as correctly stating the law, both in the US and other jurisdictions.[79] The holding in *Chakrabarty* has been interpreted expansively by the US Patent and Trademark Office ('USPTO') and courts, facilitating the patenting of a wide range of biotechnological inventions. The only requirement to bring material that has been isolated or purified under the umbrella of patentable subject matter would seem to be that it offers some material advantage in utility over the naturally-occurring material.[80]

In Australia, there is no court decision that explicitly considers whether gene sequences are inventions or discoveries.[81] However, this issue was considered by the Deputy Commissioner of Patents in *Kirin-Amgen Inc v Board of Regents of University of Washington*[82] in opposition proceedings against Kirin-Amgen's EPO patent. The Deputy Commissioner accepted that a claim directed to naturally-occurring DNA would likely be claiming no more than a discovery per se and not be a manner of manufacture. However, it was sufficient that the patent claimed a purified and isolated sequence. It was held that these claims did not extend to the naturally-occurring chromosome, or any other naturally-occurring entity. But by being directed to a purified and isolated DNA sequence, they claimed 'an artificially created state of affairs', even though the sequence itself was claimed.

Similarly, a Patent Office fact sheet on the patenting of biotechnology inventions provides the following guidance:

> although standard patents can be obtained for biological material such as microorganisms, nucleic acids, peptides and organelles, this material is only patentable if it has been isolated from its natural environment, or has been synthetically or recombinantly produced. For example, DNA or genes in the human body are not patentable, however, a DNA or gene sequence which has been isolated from the human may be patentable.
>
> Patent specifications must also describe a specific use for biological material. For example, if the invention relates to a gene, the specification must disclose a specific use for the gene such as its use in the diagnosis or treatment of a specific disease or its use in a specific enzymatic reaction or industrial process.[83]

The law on this matter awaits definitive judicial pronouncement in Australia.

[79] See, eg, Jeffrey L Ihnen, 'Patenting Biotechnology: A Practical Approach' (1985) 11 *Rutgers Computer and Technology Law Journal* 407, 409.

[80] This distinction is illustrated by a 1993 case in which an anonymous applicant unsuccessfully attempted to obtain a patent for a DNA sequence produced by normal cells. See the discussion of this case in Goldstein and Golod, above n 40, 1316.

[81] *Chakrabarty* was referred to with approval by the Australian High Court in *Grain Pool of Western Australia v Commonwealth* (2000) 202 CLR 479, 502 (Gleeson CJ, Gaudron, McHugh, Gummow, Hayne and Callinan JJ), 532 (Kirby J). See also Matthew Rimmer, 'Franklin Barley: Patent Law and Plant Breeders' Rights' (2003) 10(4) *E Law — Murdoch University Electronic Journal of Law* [12] <http://www.murdoch.edu.au/elaw/issues/v10n4/rimmer104.html>.

[82] (1995) 33 IPR 557. The later court decision in the same case did not consider this issue: see *Genetics Institute* (1998) 156 ALR 30. For further discussion of this and other Patent Office decisions of similar vintage, see Charles Lawson and Catherine Pickering, 'Patenting Genetic Materials — Failing to Reflect the Value of Variation in DNA, RNA and Amino Acids' (2000) 11 *Australian Intellectual Property Journal* 69.

[83] IP Australia, *Australian Patents for Biological Inventions* (2005) 2 <http://www.ipaustralia.gov.au/pdfs/patents/specific/biotech.pdf>.

In analysing the situation in Europe, we must recall two features of European patent law: discoveries are explicitly excluded, but they can form the substratum of valid claims. On this basis, gene sequences might be excluded from patenting if they are classified as being discoveries.[84] But if some sort of practical application — which need not of itself be novel or non-obvious — is claimed, this will be patentable.

In the case of *Genentech*, the English Court of Appeal concluded that the mere identification of the gene sequence for human tissue plasminogen activator protein was a discovery, but that methods embracing the sequence could be patentable (provided that they were clearly identified and defined), and that inventive step could reside in the production of the sequence itself.[85] Thus, the Court held that a DNA sequence itself is a discovery, but the incorporation of the DNA sequence into an expression vector could have been patentable if the production of the sequence was not obvious. The Court was divided, however, on the issue of obviousness.

The implications of the *Genentech* interpretation are illustrated in a more recent case involving Kirin-Amgen's UK patent for EPO.[86] In this particular case, Kirin-Amgen was pursuing a number of parties for infringing its EPO patent, including the TKT group, which had found a mechanism to activate the EPO gene in situ in a human cell. This is different from what Kirin-Amgen was doing: they had taken the EPO gene from a human cell and introduced it into the cell of another mammal (a hamster) via a bacterial vector, using standard recombinant procedures. Recombinant DNA technology was also utilised by TKT, but the gene sequence expressing EPO was not itself recombined.

Recalling that Kirin-Amgen's European claim referred to expression in a 'host cell', Kirin-Amgen attempted to argue that this claim covered any DNA sequence that caused EPO to be expressed, whether exogenous or endogenous, provided that some form of recombinant DNA technology had been applied to the cell. In effect, this argument would have required a finding by the House of Lords that Kirin-Amgen had exclusive rights to the EPO DNA sequence, whether in recombinant or natural form, or that it had exclusive rights to all industrial uses of the EPO sequence (or at least the application utilised by the TKT group). The House of Lords refused to accept either interpretation. On the question of Kirin-Amgen's claim to the EPO sequence, Lord Hoffmann followed *Genentech*, holding that the gene sequence information itself was not an invention, but merely a discovery regarding information about the natural world.[87] For his Lordship, Kirin-Amgen's invention was a way of making EPO, not the DNA sequence coding for EPO itself, and although the sequence information lay at the heart of the invention, it was not the invention. Hence, while the patent as claimed might have covered recombinant DNA processes that involved taking a

[84] We will come back to this crucial point again shortly. See also Bostyn, above n 35, 12–16.

[85] The patent was held to be invalid by all three judges, but for different reasons. It appears that Mustill LJ was even somewhat reluctant to accept the proposition that methods embracing discoveries are patentable: [1989] RPC 147, 268–9.

[86] *Kirin-Amgen* [2005] 1 All ER 667.

[87] Ibid 691.

sequence from one cell and placing it in another cell where it would express EPO, it did not cover any conceivable use of the EPO DNA sequence unless that use fell within the legitimate scope of the invention as claimed. We shall see that the House of Lords did not accept that the TKT group's use came within the scope of the claims, and further concluded that some of the claims in the patent were actually invalid.

To give a full picture of UK law on this point, the *Directive on the Legal Protection of Biotechnological Inventions*[88] also needs to be considered. The Directive is an annexure to the *European Patent Convention*, provided for the purpose of assisting examiners, courts and applicants for biotechnology patents in determining the validity of those patents. In art 5, the Directive states:

> 1 The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.
>
> 2 An element isolated from the human body or otherwise produced by means of a technical process, *including the sequence or partial sequence of a gene*, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.[89]

As a necessary consequence of art 5(2), it seems that gene sequence claims can be made in Europe. However, if they are to be enforceable they must be strictly limited to the isolated sequence in order to comply with art 5(1). It has been argued that these two provisions are conflicting. As the Danish Council of Ethics states: 'You cannot simultaneously forbid patents on the human body or elements thereof and then permit a sequence or partial sequence of a human gene, albeit isolated from the human body, to be patented.'[90]

Nevertheless, it does appear that if patent holders can find ways to restrict their claims to isolated DNA sequences, such claims should not be invalidated by art 5(1). How, then, can art 5(2) be reconciled with the *Genentech* and *Kirin-Amgen* decisions?[91] Lord Hoffmann himself provided an answer to this question, conceding that Kirin-Amgen could have made a claim: 'including any DNA

[88] *Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the Legal Protection of Biotechnological Inventions* [1998] OJ L 213/13 ('*Biotechnology Directive*'). See also Commission of the European Communities, *Report of the Commission to the European Parliament and the Council: Development and Implications of Patent Law in the Field of Biotechnology and Genetic Engineering* (2002) <http://www.europa.eu.int/eur-lex/en/com/rpt/2002/com2002_0545en01.pdf>; Commission of the European Communities, *Report of the Commission to the Council and the European Parliament: Development and Implications of Patent Law in the Field of Biotechnology and Genetic Engineering* (2005) ('*European Commission Second Report*') <http://www.europa.eu.int/comm/internal_market/en/indprop/invent/com_2005_312final_en.pdf>.

[89] (Emphasis added).

[90] Danish Council of Ethics, above n 35, 24. Cf *Kingdom of the Netherlands v European Parliament and Council of the European Union* (C-377/98) [2001] ECR I-7079, I-7106–9 (Advocate General Jacobs). See also Bostyn, above n 35, 40–4.

[91] It should be noted that although *Kirin-Amgen* was heard after the *Biotechnology Directive* was finalised, it was decided under old law.

sequence, whether exogenous or endogenous, which expresses EPO in consequence of the application to the cell of any form of DNA recombinant technology.'[92]

His Lordship added that whether the specification would have been sufficient to support it is another matter. The problem for Kirin-Amgen was that because it did not make this claim, it needed to argue that the sequence information was the invention itself, rather than merely being *included* in the patent as claimed.

In the US to date, there is no evidence that the courts will interpret sequence claims with quite the same stringency as the House of Lords in like cases. The lack of relevant case law in Australia makes it difficult to predict how Australian courts might interpret like claims.

In summary, it is generally recognised that claims including DNA sequences that have been isolated from their natural environment can satisfy the invention threshold, but that naturally-occurring sequences are discoveries. However, this distinction could be regarded as purely semantic, having no real practical application. This is because a claim made over an isolated sequence could be argued to extend to include other industrial uses of the naturally-occurring sequence as well (for example, endogenous activation by means of a technical process). As a result of the UK decisions, it appears that gene sequence patent holders will bear the heavy onus of showing how their claims are limited to the isolated sequence. If patent holders fail in discharging this onus, their sequence claims will be invalid.

C *Is It Permissible to Exclude Genes from Patenting?*

1 Ordre Public *or Morality*

So far, this article has focused primarily on the impact of gene patents on innovation. However, the debate about gene patenting goes much deeper than this, particularly in the areas of ethics and social policy. Objections to gene patenting range from the belief that there is something fundamentally unethical or immoral about gene patenting per se, because genes are part of the common heritage of humankind, through to concerns that genetic research, particularly research involving human genetic material, should not be commodified, and concerns about the impact of gene patenting on access to health care. Each of these concerns has merit, and none should be dismissed lightly. However, an in-depth discussion regarding the ethics and social policy of gene patents extends beyond the scope of this article. The point here is to examine the legality of gene patents and this requires some analysis of the extent to which it is possible to consider ethics and social policy within the current legal framework or within a suitably reformed framework. On the question of law reform, it should be noted that there have been a number of public inquiries and reviews on these issues around the world, none of which have resulted in recommendations to exclude genes from patenting on social or ethical grounds.[93]

[92] *Kirin-Amgen* [2005] 1 All ER 667, 692.

[93] See, eg, ALRC, above n 5, [7.81]. The ALRC concluded that it is better to regulate research activities directly than to address ethical and social concerns by excluding the subject matter,

Courts and Patent Offices have generally expressed reluctance to engage in public policy and morality debates unless they are specifically enjoined to do so. The US Supreme Court in *Chakrabarty* was asked to consider the policy arguments, particularly the potential hazards of the technology. In response, Burger CJ stated:

> We are without competence to entertain these arguments — either to brush them aside as fantasies generated by fear of the unknown, or to act on them. The choice we are urged to make is a matter of high policy for resolution within the legislative process after the kind of investigation, examination, and study that legislative bodies can provide and courts cannot.[94]

In a similar vein, Finkelstein J in the Australian case of *Bristol-Myers Squibb v F H Faulding & Co Ltd* stated that: 'Judges should not be called upon to resolve moral questions and, speaking generally, legal principles are not to be ascertained by reference to standards of ethics or morality.'[95] Thus, even though the general inconvenience exclusion is incorporated into the *Patents Act 1990* (Cth) following s 6 of the *Statute of Monopolies 1623*, 23 Jac 1, c 3, and despite suggestions that this provision could be interpreted to require consideration of public policy or moral issues,[96] it seems unlikely that unless directed, the courts or the Patent Office would be willing to enter into such debates. The situation is different in Europe and a number of other jurisdictions,[97] where patent offices and judges are required to consider these matters. The *ordre public* or morality exclusion has been considered by the European patent authorities in a series of biotechnology patent decisions, two of which are considered below.

In *Plant Genetic Systems*,[98] the patent claimed processes and plants involving genetic modification for the production of an enzyme capable of neutralising or inactivating a herbicide. The Board of Appeals of the European Patent Office held that the concept of *ordre public* covers the protection of public security and the physical integrity of individuals as part of society, encompassing also the protection of the environment. As such, inventions should be excluded where their exploitation is likely to breach public peace or social order (for example an act of terrorism) or seriously prejudice the environment. The Board said that

and further that the social and ethical concerns that are raised by the use or exploitation of patented inventions are better addressed by specific measures to facilitate use: at [7.84]–[7.88]. The Nuffield Council, while recommending that patents asserting rights over DNA sequences should be the 'exception rather than the norm', saw that the avenues for achieving this end were by discouraging the granting of certain patents and rigorously applying the patent criteria, rather than by exclusion: Nuffield Council on Bioethics, above n 35, xi–xii. Similarly, the Danish Council of Ethics recommended that it should not be possible to award broad gene patents but that, despite the special status of genes, it should continue to be possible to obtain gene patents in future: Danish Council of Ethics, above n 35, 100–1.

94 *Chakrabarty*, 447 US 303, 316–17 (1980).

95 (2000) 97 FCR 524, 559–60.

96 There is some authority for this proposition. See, eg, *Joos v Commissioner of Patents* (1972) 126 CLR 611, 623, in which Barwick CJ held that if we were to have an exclusion for methods of medical treatment, it would be on ethical grounds, through general inconvenience. Forsyth, above n 63, 209–11 also makes a strong case for the introduction of public policy considerations using general inconvenience.

97 Including, in the Australasian region, Japan, Hong Kong, Thailand, and the Philippines.

98 [1995] EPOR 357.

serious prejudice to the environment must be sufficiently substantiated at the time the decision is made about whether or not to grant or revoke the patent. In this case, arguments were based on the possibility of some undesired effect in the future, but this was not sufficient to substantiate revocation. The Board held that morality relates to the belief that some behaviour is right and acceptable while other behaviour is wrong, based on the accepted norms of conduct of a particular culture. On analysis, the Board determined that with regard to the morality issue: 'plant biotechnology per se cannot be regarded as being more contrary to morality than traditional selective breeding'.[99]

Howard Florey/Relaxin[100] involved a patent application by the Howard Florey Institute in Australia, concerning the molecular cloning and characterisation of a gene sequence coding for human relaxin. Relaxin is a hormone secreted by pregnant women. Green members of the European Parliament opposed the patent and urged the Opposition Division of the European Patent Office to accept their argument that the patent was contrary to the immorality provision. They argued that the patent was an affront to human dignity, on the basis that the isolation of the gene requires tissue to be taken from pregnant women; that it amounted to a modern form of slavery, on the basis that it involves dismemberment of women and their piecemeal sale; and that the patenting of human genes equates to the patenting of human life, which is intrinsically immoral.

The Opposition Division indicated that the function of this provision is to ensure that patents are not granted for inventions that would universally be regarded as outrageous. As such, it is only invoked in rare and extreme cases. The Opposition Division was not persuaded that this was such a case, holding that:

- use of donated ovarian tissue to extract the gene was no more immoral than use of donated blood as a source of life saving substances. Further the isolation procedure need not be repeated as the gene, once sequenced, can be chemically synthesised;
- ownership of the patent is not akin to slavery because it does not give the owner any right whatsoever to individual human beings, but merely the right to exclude for a limited period of time third parties from commercially using the patented invention.
- DNA is not life, rather a chemical substance that carries genetic information. The Division saw no moral distinction in principle between patenting human genes on the one hand, and other human substances on the other.

Article 6 of the *Biotechnology Directive* reproduces the *ordre public* or morality exclusion and provides, in para 2, a narrow list of the types of inventions that shall be considered unpatentable:

(a) processes for cloning human beings;
(b) processes for modifying the germ line genetic identity of human beings;
(c) uses of human embryos for industrial or commercial purposes;

[99] Ibid 369 (Examiners Kinkeldey, Galligani and Moser).
[100] [1995] EPOR 541.

(d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.

Given the decided cases and the wording of the *Biotechnology Directive*, it would appear that the *ordre public* or morality exclusion is considerably limited in scope. There may well be some specific cases that succeed, based on arguments that serious prejudice to the environment could result from the exploitation of the invention or that the invention is likely to cause serious risks to human life or health. However, these cases must be thought of as most rare.

In conclusion, therefore, the legality of gene patenting does not appear to have been compromised in any substantive way by public policy and morality arguments to date. Moreover, law reform proposals do not provide a strong foundation on which to build such arguments in the future.

2 *Diagnostic, Therapeutic and Surgical Methods*

A provision for the exclusion of gene patents of this nature might exclude methods of clinical diagnosis of genetic conditions, but would not exclude diagnostic products, test kits, reagents and the like. Hence, it is likely to be of limited value, and in Australia the ALRC was not convinced that there was sufficient justification to recommend amendment of the *Patents Act 1990* (Cth) in this respect.[101]

D *How Do Genes Fulfil the Standard Patent Requirements?*

1 *Novelty*

Because patent law requires that challenges to novelty are made on the basis that prior art information disclosing all of the features of the invention has been made publicly available, the isolation and characterisation of a gene outside of its natural environment will make it novel.[102] The rationale for this conclusion is that, prior to this, the gene sequence information was not publicly available. While there will always be disputes between competitors as to who was the first to disclose an invention and whether follow-on inventions satisfy the novelty requirement, until recently novelty had not engendered the same level of debate as inventive step and utility.

However, the House of Lords decision in *Kirin-Amgen* raises an important novelty issue. In that case, the House of Lords accepted the European Patent Office practice that product-by-process claims could not be made unless the product itself was new, being different from any existing product in the state of the art, and that this difference could not be described in chemical or physical terms.[103] One of Kirin-Amgen's claims was to 'a polypeptide product of the expression … of a DNA sequence'.[104] The Lords did not accept that this was

[101] ALRC, above n 5, ch 21. Even in Europe, where such method patents are excluded, the exclusion is limited to methods performed on the human body, which would not exclude genetic testing carried out on bodily samples removed from the body: see Bostyn, above n 35, 77–9.

[102] See Bostyn, above n 35, 17–18, 44–6.

[103] *Kirin Amgen* [2005] 1 All ER 667, 694 (Lord Hoffmann).

[104] Ibid 676.

sufficiently different from naturally-occurring EPO, or that the different method of manufacturing was sufficient to make it new. Consequently, the claim was held to be invalid on the ground of anticipation.[105]

2 *Inventive Step*

Arguably, the techniques used to isolate and characterise genes are now so routine that very little inventive ingenuity is required to describe a new gene. In particular, the use of computer technology has dramatically improved the ease and speed of gene identification. However, in the US, the inventive step requirement has been interpreted liberally for gene sequences. The focus is placed on the invention itself rather than the techniques for its production. This means that the focus of inquiry for gene patents is whether the gene sequence is obvious, not whether the method used to obtain it was obvious to try.

The US courts have accepted that the degeneracy of the genetic code means that until the claimed molecules are actually isolated and purified, it would have been highly unlikely that a person skilled in the area could have contemplated what was obtained. In *Re Bell*,[106] for example, DNA and RNA sequences coding for human insulin-like growth factors ('hIGF') were claimed. The prior art provided a reference to amino acid sequences for certain hIGF, and a patent disclosing the general method for isolating a gene when the amino acid sequence was known. The Court of Appeals held that the degeneracy of the genetic code meant that there are vast numbers of DNA sequences that might code for a specific protein (in this example, the estimate given was 10^{36}). Therefore, it was concluded that prior disclosure of amino acid sequences and general sequencing methods did not render the claimed sequences obvious. Similar findings were made in *Re Deuel*, although the Court did recognise that the situation might be different where a protein is of a sufficiently small size and simplicity that only a small number of DNA sequences will code for it.[107]

In Europe, on the other hand, the focus is on whether the isolation of the gene was obvious. The test is whether the technique used to obtain the sequence information was 'obvious to try'.[108] Dillon LJ in *Genentech* provided some early guidance as to the interpretation of the inventive step test to gene patents in the UK. His Lordship held that on the facts of this case, it was obvious to the person skilled in the art to set out to produce human tissue plasminogen activator by recombinant DNA technology. Whether the person skilled in the art actually had the ability to perform the task was irrelevant. Consequently, he concluded that there was nothing by way of inventive step to support the claims in the patent.[109]

Since *Genentech*, other decisions in Europe have confirmed that a recombinant DNA sequence will be obvious if it can be shown that all the techniques needed

105 Ibid 696.
106 991 F 2d 781, 1529 (Lourie J) (Fed Cir, 1993).
107 51 F 3d 1552 (Fed Cir, 1995).
108 UK Patent Office, *Examination Guidelines for Patent Applications relating to Biotechnological Inventions in the UK Patent Office* (2005) 9–10 <http://www.patent.gov.uk/patent/reference/biotechguide/biotech.pdf>.
109 *Genentech* [1989] RPC 147, 235.

to produce it were well known.[110] Hence, *in silico* gene identification or 'data mining' by computerised matching of unknown human gene sequences to homologous animal gene sequences would be obvious.[111] As the UK Patent Office states:

> a sequence may be shown to lack inventive step and that is where an earlier disclosure points to the inevitability of arriving at a particular sequence even though the actual structure of the sequence is not determined until sometime later.[112]

While the courts in Australia have not been given the opportunity to address this issue with respect to gene sequence patents, recent High Court authority suggests that the US approach would be favoured in Australia. In *Aktiebolaget Hässle v Alphapharm Pty Ltd*, the High Court rejected the notion that obviousness is determined by considering whether or not something is obvious to try, instead affirming that the relevant inquiry is whether the invention itself is obvious.[113] The Court based its decision on the precise wording of the *Patents Act 1990* (Cth) s 7(2): 'whether an invention would have been obvious'.

The leniency of the US test has been subject to intensive criticism, both within the US,[114] and internationally,[115] because it essentially means that *any* invention disclosing a gene sequence will satisfy the inventive step requirement, and that gene patents are per se non-obvious. Ultimately legislative reform may be necessary in the US and Australia (depending on how the inventive step test is applied in that country), but in the interim it is highly desirable for patent examiners to be provided with new administrative guidelines requiring them to look more closely at the level of inventive ingenuity involved in solving the technical problem.[116]

3 *Utility*

The EST patent applications filed by the NIH in the US in 1991 led to a flurry of statements as to the utility of partial sequences and sequences of unknown function. The common trend that has emerged around the world is that raw sequence data is not generally considered to be patentable, because it fails to satisfy the utility requirement. In the US, new utility guidelines published in 2001 confirm that specific, substantial and credible utility of the claimed invention must be demonstrated in the application.[117] In summary, these requirements will only be satisfied where the applicant shows that the utility is

110 For a review of the relevant case law, see UK Patent Office, above n 108, 9–10.
111 Ibid 2–3.
112 Ibid 7.
113 (2002) 212 CLR 411, 429 (Gleeson CJ, Gaudron, Gummow and Hayne JJ).
114 See, eg, Stephen A Merrill, Richard C Levin and Mark B Myers (eds), *A Patent System for the 21st Century* (2004) 92 <http://www.nap.edu/html/patentsystem/0309089107.pdf>.
115 See, eg, Nuffield Council on Bioethics, above n 35, 30.
116 Similarly, in the US, the National Research Council recommended that the USPTO and the Federal Circuit should abandon the so-called 'per se' rule announced in *Re Bell* and *Re Deuel* that prevents consideration of the technical difficulty faced in obtaining pre-existing gene sequences and consider the approach in other industrialised countries: Merrill, Levin and Myers, above n 114, 95.
117 *Utility Examination Guidelines*, 66 Fed Reg 1092, 1095 (2001).

specific to the claimed subject matter, which has a 'real world' application that is credible to a person of ordinary skill in the art. This requirement will be met for gene sequence patents if the function of the sequence is disclosed. Hence, as a general rule, it would seem to be most unlikely that EST patent claims could fulfil the US utility requirement.

Article 5(3) of the *Biotechnology Directive* requires that industrial applicability for gene patents is disclosed in the patent application. The extent to which this provision actually imposes more stringent obligations than the usual industrial applicability requirement in European patent law remains open to debate.[118] The Australian Patent Office similarly considers that patentable sequences must have a definite industrial use.[119] However, there is no express requirement for specific, substantial and credible utility to be demonstrated by the applicant for a patent. A review of Australian patent law in 2000 recommended that the 'manner of manufacture' test should be retained, but that the Patent Office should adopt the examination practice of requiring specific, substantial and credible utility.[120] Subsequently, the ALRC recommended that these requirements should be expressly incorporated into the *Patents Act 1990* (Cth).[121]

These developments in the law relating to utility would seem to alleviate concerns that EST patents could be granted for speculative use as mere research tools. Indeed, there has been some suggestion in the literature that the EST patenting debate became a dead issue following the publication of the US guidelines.[122] However, until recently, it was still unclear exactly how much utility would need to be disclosed for an EST to be patentable.[123] For example, Barton has suggested that it may be possible for the utility requirement to be satisfied for 'consisting of' claims if the EST can be used to fish out the full gene sequence and to make the protein.[124]

The recent US Court of Appeals decision in *Re Fisher*,[125] which involved claims to five ESTs isolated from maize leaves, has provided some much-needed clarification. The patent claimed various different uses of the ESTs, including as molecular markers for mapping the entire maize genome. The Court considered the specific and substantial components of the utility requirement. The majority held that specific utility requires a use that is 'not so vague as to be meaning-

118 See Bostyn, above n 35, 53–5.

119 IP Australia, above n 83, 2.

120 Intellectual Property and Competition Review Committee, *Review of Intellectual Property Legislation under the Competition Principles Agreement* (2000) 151–4.

121 See ALRC, above n 5, Recommendation 6-3. Article 17(9)(13) of the Australia–US Free Trade Agreement also requires that both parties adopt this test. Whilst the Patent Office states that it already requires that this test be satisfied, there is little guidance as to how this achieved: ALRC, above n 5, 148.

122 See, eg, John A Robertson, 'Sequence Patents Are Not the Issue' (2002) 2(3) *American Journal of Bioethics* 22.

123 The Nuffield Council, for example, expresses concern that the 'credibility' test may be set too low if all that is required is 'theoretical possibility': Nuffield Council on Bioethics, above n 35, 31.

124 Barton, 'Changing Intellectual Property Issues in the Biotechnology Industry', above n 11, 7.

125 421 F 3d 1365 (Fed Cir, 2005). As noted in the decision, the real party in interest is Monsanto Technology LLC, owned by the Monsanto Company.

less'[126] and that provides 'a well-defined and particular benefit to the public'.[127] Substantial utility requires that the claimed invention 'has a significant and presently available benefit to the public',[128] and 'not that it may prove useful at some future date after further research'.[129] The majority concluded that the claimed ESTs were 'no more than research intermediaries that might help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes'[130] and that all of the asserted uses 'represent merely hypothetical possibilities'.[131] As such, for the majority, the claimed ESTs were fundamentally different from other patentable research tools, such as microscopes.[132] This decision lends support to the view that, as a general rule, it will be extremely difficult to overcome the utility hurdle for EST claims in the US.

E *What Can Be Claimed and How Much Must Be Disclosed?*

There are many instances where the claims made in a patent are much broader than what is actually described in the specification. Take the following examples:

- where a gene sequence has been described in one species of animal or plant, but claimed for many;
- where one DNA sequence for making a particular protein is described but claims are made to the genus of DNA sequences that could produce that protein, as well as to the genus of amino acid sequences that perform the same function; and
- where all uses of the sequence are claimed, even uses that are unknown or unanticipated at the time of the patent application.

In Australia, the breadth of patent claims for biotechnology inventions was considered in *Genetics Institute*.[133] Heerey J held that the claim to the product of procaryotic or eucaryotic expression of an exogenous DNA sequence was permissibly wide because the DNA sequence for EPO was a principle of general application and, therefore, it was acceptable for the claim to be made in correspondingly general terms. In coming to this conclusion, Heerey J cited with approval Lord Hoffmann's judgment in *Biogen Inc v Medeva plc*.[134] The principle of general application test stems from case law relating to patents claiming classes of chemicals, in which broad claims to the entire class have been allowed provided that a beneficial property common to the class is dis-

126 Ibid 1371 (Michel CJ).
127 Ibid.
128 Ibid.
129 Ibid.
130 Ibid 1373.
131 Ibid.
132 On the other hand, Rader J, in his minority judgment, saw no clear distinction between ESTs and microscopes, because both 'supply information about molecular structure' and both 'advance research and bring scientists closer to unlocking the secrets of the corn genome to provide better food production for the hungry world': ibid 1380.
133 (1998) 156 ALR 30.
134 [1997] RPC 1, 48–9, cited ibid 143–5.

closed. Although there have been no other opportunities to consider this issue in the Australian courts, the *Genetics Institute* decision signals that as a general rule, broad claims to gene sequences and their products may be accepted when the full sequence and a method of isolating it is disclosed.

The *Kirin-Amgen* decision in the UK contrasts with the Australian decision in *Genetics Institute*, even though it deals with the exact same invention. It is necessary to recall two matters. First, Lord Hoffmann concluded that the patent covered a way of making EPO, and not the sequence information coding for EPO, which he held was a discovery. Second, the main claim in the European patent referred to expression in a 'host cell'. Based on general principles of construction, his Lordship concluded that this required the presence of a 'guest', which did not include endogenous expression as applied by TKT, and hence there was no infringement.[135] It is interesting to note that the TKT technology would not have come within the scope of the Australian patent because the primary claim in Australia was limited to expression of an exogenous DNA sequence. In the UK decision, having reached the conclusion that the TKT process was not covered by Kirin-Amgen's claims, Lord Hoffmann did not need to rule on the issue of sufficiency of disclosure. However, he intimated that because the invention was the method of making EPO and not the sequence itself, the facts did not support the exercise of the principle of general application. In his Lordship's view, Kirin-Amgen had not disclosed in general terms all possible ways of making EPO using recombinant DNA technology.[136]

Whether the principle of general application test will provide adequate guidance in dealing with disclosure and scope of claim issues in all gene patent cases in the UK and Australia remains to be seen.[137] The case law on disclosure and scope of claims is much richer in the US, where there is clear evidence of the judiciary's reluctance to uphold broad patent claims. There have been a number of important cases on this point, three of which will be considered.

In *Amgen Inc v Chugai Pharmaceutical Co Ltd*,[138] the Federal Circuit held that Amgen could not claim all EPO gene analogues, bearing in mind that EPO has 165 amino acids, and that over a million analogues could be made by the substitution of just three amino acids. The Court held that there must be enabling disclosure of other DNA analogues before claims can be made to the DNA coding for any polypeptide having similar properties to EPO, stating that:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials and to describe how to obtain it … Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of

[135] *Kirin-Amgen* [2005] 1 All ER 667, 688.
[136] Ibid 697–9.
[137] Support for this test is provided in Bostyn, above n 35, 31–5.
[138] 927 F 2d 1200 (Fed Cir, 1991) ('*Amgen*').

> preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property.[139]

In *Regents of the University of California v Eli Lilly & Co*,[140] the Court of Appeals further clarified two points on the written description requirements in the US. First, the Court held that in order to claim a DNA sequence there must be written description of the sequence itself. Second, claims to generic sequences such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA' without more were not adequate written descriptions of the genus as they did not distinguish the claimed genus from others, except by function. The written description must define structural features common to the genus that distinguishes it from others.

New written description guidelines were released in 2001, confirming the decision in *Eli Lilly* that describing a method for isolating a sequence is insufficient and that the complete sequence or other identifying features must be disclosed.[141] Furthermore, if a full sequence is disclosed for one species of a DNA sequence, patent rights are only allowed over that sequence. A genus of DNA sequences can only be claimed if there is sufficient description of a representative number of species. However, the guidelines do state that genus claims may be made where there is a written description of a representative number of species and other functional characteristics and there is a known or disclosed correlation between function and structure.[142]

In the 2004 case of *Re Wallach*,[143] the Court of Appeals appeared willing to relax somewhat the stringent disclosure requirements prescribed in *Amgen*, *Eli Lilly* and like cases. The Court held that the state of the art has developed to such an extent that 'the complete amino acid sequence of a protein may put one in possession of the genus of DNA sequences encoding it'[144]. Hence, provided that the amino acid sequence of the protein was disclosed, the genus of DNA sequences coding for it could also be claimed. In explaining the reason for this conclusion, the Court noted that conversion back and forth between an amino acid sequence and the DNA sequences encoding it is now routine. This satisfied the requirement for there to be a relationship between structure and function known to those ordinarily skilled in the art. Nevertheless, the Court held that Wallach's application did not meet the written description requirement because only the partial structure of the protein was disclosed.

139 Ibid 1206 (Lourie J).

140 119 F 3d 1559 (Fed Cir, 1997) ('*Eli Lilly*').

141 *Guidelines for Examination of Patent Applications under the 35 USC 112, ¶ 1, 'Written Description' Requirement*, 66 Fed Reg 1099 (2001). Merrill, Levin and Myers, above n 114, 94, note that *Eli Lilly* could also have an impact on inventive step: 'By narrowing the scope of some gene patents to the actual sequence disclosed it is possible that *Eli Lilly* might inherently prevent patents on some technologically obvious genes for which *Bell* would otherwise permit a patent.' The passage goes on to say, however, that this is not an adequate solution to the problems associated with the current inventive step test in the US.

142 *Guidelines for Examination of Patent Applications under the 35 USC 112, ¶ 1, 'Written Description' Requirement*, 66 Fed Reg 1099, 1106 (2001). See also *Enzo Biochem Inc v Gen-Probe Inc*, 296 F 3d 1316 (Fed Cir, 2002).

143 378 F 3d 1330 (Fed Cir, 2004).

144 Ibid 1333 (Lourie J).

Together, the developing body of case law and administrative guidelines have done much to clarify the written description requirement as it relates to gene patents in the US, placing sensible limitations on the scope of such claims. It clearly indicates that EST patents with comprising claims are likely to be invalid. However, the law in this area remains more uncertain in other jurisdictions.

V CONCLUSION: PROPER AND CERTAIN GENE PATENTING?

This analysis has shown that, despite the growing body of jurisprudence in this area, clear guidance as to the legality of gene patents remains elusive. There is still ambiguity and uncertainty, particularly with regard to the ambit of the inventive step, utility and disclosure tests and the distinction between inventions and discoveries. Consequently, would it be best simply to exclude genes from patenting? Although there continue to be calls in the academic commentary for this,[145] there is little support for it in the policy and law reform debates, and it is probably not within the realms of possibility that such an exclusion will be recognised at this time. Admittedly, though, the House of Lords decision in *Kirin-Amgen* has reopened the debate in that jurisdiction.[146] On this question of whether or not claims over gene sequences should be patentable in Australia, the ALRC has pointed out that:

> Whatever the merits of that argument, the Inquiry was faced with the fact that since the 1980s — in Australia and internationally — large numbers of patents have been granted on genetic sequences, provided they have been isolated from their natural state and otherwise satisfy the statutory requirements for patentability. The Inquiry ultimately concluded that if there had been a time to recommend that gene sequences should not be patentable, that time had long since passed. Rather, it was preferable to focus on reforms that would make the system work better.[147]

This is not to say that all is well with gene patent law. As stated at the start of this article, and as widely acknowledged in gene patent debates, patent law should set proper and certain boundaries on what is and what is not patentable.[148] In particular:

- the novelty, inventive step and utility requirements must be set at a suitably high standard to ensure on the one hand that true inventors are appropriately rewarded for their inventive ingenuity and on the other hand that others are not given too great a reward for trivial or routine improvements over the prior art; and
- gene patents should be of an appropriate breadth. If patents are too broad, then a single patent holder may have too great a control over a whole area of

[145] See, eg, Luigi Palombi, 'The Impact of *TRIPS* on the Validity of the European *Biotechnology Directive*' (2005) 2 *Journal of International Biotechnology Law* 62.

[146] R Stephen Crespi, 'Erythropoietin in the UK: A Setback for Gene Patents?' (2005) 23 *Nature Biotechnology* 367.

[147] ALRC, above n 5, 13.

[148] On the importance of granting high quality patents, see Organisation for Economic Co-operation and Development, *Patents and Innovation: Trends and Policy Challenges* (2004) 28–9.

research, but if they are too narrow a patent thicket could more likely arise, requiring multiple licences to be entered into to ensure the freedom to operate.

Does it matter that after all these years there is still uncertainty with regard to these matters? Significant steps have been taken in clarifying the law, both through judicial decisions and through legislative and administrative guidelines, particularly with regard to the utility and the disclosure requirements. The majority decision in *Re Fisher* is particularly important, and would seem to finally put to rest concerns about the legality of EST patents.[149] The inventive step requirement remains problematic in the US and Australia, and steps need to be taken to adopt a more stringent test, akin to that used in Europe. The introduction of use- or purpose-bound restrictions on claiming also warrants further scrutiny.[150] But further legislative reform is not necessarily the best option at this stage. For the most part, the gene patents that have been discussed in this article were issued in the 1980s and 1990s at the start of the biotechnology revolution, and many were overly broad. But this tends to be the case in any new area of technology. As more patents are granted in a new field, their scope necessarily decreases in order to satisfy the patentability criteria.[151] On this basis, the European Commission has recently concluded that: 'it may be questionable whether attempting to further refine the scope of protection of gene sequence patents in the light of divergences between national legislations will have any significant effect on actors in the field.'[152]

Examination practices should also be of a sufficiently high standard to ensure that only valid patents are issued, or appropriate administrative structures should be put in place to facilitate challenges to questionable patents. Examination practices are improving as patent offices are becoming more familiar with this new area of technology. Recently, Melanie Howlett and Andrew Christie undertook comparative studies relating to examination of EST patents in patent offices in the US, Europe, Japan and Australia. The authors sought examination of six hypothetical sequence claims by the four patent offices. They found that although the approach taken to examination differs slightly between offices, the results are essentially the same in all jurisdictions studied: EST patents will generally fail to fulfil the essential patenting requirements and hence will be rejected if no indication of specific function is provided or if the sequence claimed shows no unexpected effect, is obtained by conventional methods and has high homology with known DNA sequence.[153] They concluded that fears

149 However, it seems likely that this decision will be appealed, and it may be that the minority decision of Rader J is preferred.

150 See above n 35.

151 See Commission of the European Communities, *European Commission Second Report*, above n 88, 4.

152 Ibid 5.

153 Melanie J Howlett and Andrew F Christie, 'An Analysis of the Approach of the European, Japanese and United States Patent Offices to Patenting Partial DNA Sequences (ESTs)' (2003) 34 *International Review of Industrial Property and Copyright* 581, 601–2; Melanie J Howlett and Andrew F Christie, 'An Analysis of the Approaches of the Trilateral and Australian Patent Offices to Patenting Partial DNA Sequences (ESTs)' (2004) 15 *Australian Intellectual Property Journal* 156, 171–2.

held by the scientific community of a flood of granted EST patents for probes with no useful functions were not matched by patent examination practices.

In contrast to the Howlett and Christie study, however, an analysis of the scope and claims of other gene patents granted in the US suggests that examiners may be allowing claims that do not fulfil the legal requirements.[154] In this study, the authors excluded EST patents, focusing instead on complete sequences and other patents covering human genetic material, including mutations and diagnostic methods utilising the material. They examined 74 relevant patents on human genetic material, with a total of 1167 claims, and found that 38 per cent of claims were problematic, with utility and disclosure problems being found most frequently. They concluded that something needed to be done about the number of patents being granted 'that arguably do not measure up to the federal patent law'.[155] There has been some criticism of this study.[156] Nevertheless, it does suggest that we should be cautious in concluding that all is well with examination practices.

Does it matter that patent offices might issue some bad patents that do not fulfil the legal patenting requirements? Mark Lemley presents a persuasive case as to why it would be irrational to pay increased attention to validity and to put increased resources into the assessment of patent applications.[157] He argues that a massive increase in resources would be required to ensure validity of issued patents and that challenging the validity of questionable patents in court is more efficient.[158] However, Lemley's views are not universally shared.[159] There are legitimate fears that improper laws and bad patents will impact negatively on innovation. If access to the technology claimed in a key foundational patent is restricted, or if there are simply too many overlapping patent rights in a particular area, innovation can be blocked, delayed or deterred. However, a series of empirical studies on the impact of patents and patent licensing strategies in the biotechnology industry in various countries suggests that these fears do not appear to be eventuating at present.[160] Rather, the industry is finding solutions to

154 Jordan Paradise, Lori Andrews and Timothy Holbrook, 'Patents on Human Genes: An Analysis of Scope and Claims' (2005) 307 *Science* 1566, 1566–7. See also Merrill, Levin and Myers, above n 114, 47–9 for other examples.

155 Paradise, Andrews and Holbrook, 'Patents on Human Genes', above n 154, 1566–7.

156 Kate H Murashige, 'Problems in Patenting Human Genes' (2005) 308 *Science* 1868; Joseph J Rolla, 'Problems in Patenting Human Genes' (2005) 308 *Science* 1869. See also Jordan Paradise, Lori Andrews and Timothy Holbrook, 'Response' (2005) 308 *Science* 1869.

157 Mark A Lemley, 'Rational Ignorance at the Patent Office' (2001) 95 *Northwestern University Law Review* 1495.

158 Ibid 1531–2.

159 See, eg, Arti K Rai, 'Engaging Facts and Policy: A Multi-Institutional Approach to Patent System Reform' (2003) 103 *Columbia Law Review* 1035, 1080–4.

160 John P Walsh, Ashish Arora and Wesley M Cohen, 'Effects of Research Tool Patenting and Licensing on Biomedical Innovation' in Wesley M Cohen and Stephen A Merrill (eds), *Patents in the Knowledge-Based Economy* (2003) 285, 331. See also John P Walsh, Ashish Arora and Wesley M Cohen, 'Working Through the Patent Problem' (2003) 299 *Science* 1021; Joseph Straus, Henrik Holzapfel and Matthias Lindenmeir, *Empirical Survey on 'Genetic Inventions and Patent Law'* (2002); Dianne Nicol and Jane Nielsen, 'Patents and Medical Biotechnology: An Empirical Analysis of Issues Facing the Australian Industry' (Occasional Paper No 6, Centre for Law and Genetics, 2003) 57 <http://www.ipria.org/publications/pubfliers/BiotechReport Final.pdf>; Dianne Nicol and Jane Nielsen, 'Australian Medical Biotechnology: Navigating a Complex Patent Landscape' [2005] *European Intellectual Property Review* 313, 316; Intellectual

avoid these theoretical problems. The studies consistently report that one of the features of the industry is vigorous licensing activity. In particular, patents claiming foundational research tools, including gene patents, tend to be non-exclusively licensed. Other strategies include inventing around patented inventions, ignoring patents of questionable validity and challenging the validity of these patents in the courts.

There are also legal mechanisms for dealing with restrictions on access to patented technology post-grant. Most jurisdictions have provisions in their patent legislation that allow for use without the authorisation of the patent holder in certain limited circumstances.[161] For example, the *Patents Act 1990* (Cth) ss 133 and 135 provide that compulsory licences can be issued when 'the reasonable requirements of the public' have not been met. There is also protection from infringement for use by the Crown in s 163, where there is use of the patented invention 'for the services of the Commonwealth or State' when 'necessary for the proper provision of those services'.[162] Most jurisdictions also recognise that certain types of research should be exempt from infringement. However, it should be noted that in practically all jurisdictions the ambit of such an exemption is presently unclear and the subject of debate.[163]

The industry itself is also exploring a number of initiatives aimed at encouraging innovation, and the theoretical literature in this area is expanding. One aspect of this is a push to keep basic scientific results in the public domain. For example, participants in the Human Genome Project agreed to keep primary sequences in the public domain and to rapidly release them.[164] Other initiatives

Property Institute on behalf of the Department of Trade and Industry, UK, *Patents for Genetic Sequences: The Competitiveness of Current UK Law and Practice* (2004) 65 <http://www.dti.gov.uk/5397_DTi_Patent_Study.pdf>.

161 Article 31 of *TRIPS* prescribes stringent limitations on the extent to which member states can provide for such rights in their patent legislation.

162 Recommendations for reform of both the Crown use and the compulsory licensing provisions were made in ALRC, above n 5, chs 26, 27. See especially Recommendations 26-2, 26-3 and 27-1. However, there was no suggestion in the Report that there should be a major overhaul of these provisions.

163 In Australia, there is no express exemption in the legislation, and no relevant case law. In the ALRC Report a recommendation was made for an express experimental use exemption: ibid Recommendation 13-1. The Advisory Council on Intellectual Property has also conducted a separate inquiry and made similar recommendations in its final report: Advisory Council on Intellectual Property, *Patents and Experimental Use* (2005). See also Matthew Rimmer, 'The Freedom to Tinker: Patent Law and Experimental Use' (2005) 15 *Expert Opinion on Therapeutic Patents* 167.

164 The Wellcome Trust, *Summary of Principles Agreed at the International Strategy Meeting on Human Genome Sequencing* (1996) <http://www.gene.ucl.ac.uk/hugo/bermuda.htm>.

include patent pooling and cross-licensing,[165] clearing house mechanisms[166] and even the incorporation of open source principles from copyright law.[167]

In combination, provided that the best available mechanisms are used for granting gene patents and that these are combined with the best available post-grant practices, the biotechnology industry will survive and should flourish. There will, no doubt, be future skirmishes in the gene patent wars, future attempts to claim too much reward for too little input, and these actions could have a negative impact on innovation within the industry as a whole. However, there are many weapons in the innovator's armory, both legal and non-legal, both pre- and post-grant. Ultimately, the blunt tool of competition law is always available to be unleashed against the most egregious abuses of patent rights. In an ideal world the law relating to gene patents would be proper and certain, and only good patents would be issued. Having said this, when considering the need for reform of the law relating to gene patents, as with any other area of law reform, idealism has to be matched with pragmatism.

165 See, eg, USPTO, *Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?* (2000) 8–11 <http://www.uspto.gov/web/offices/pac/dapp/opla/patentpool.pdf>.

166 See, eg, Gregory Graff and David Zilberman, 'Towards an Intellectual Property Clearinghouse for Agricultural Biotechnology' (2001) 3 *Intellectual Property Strategy Today* 1; Gregory Graff et al, 'Intellectual Property Clearinghouse Mechanisms for Agriculture: Summary of an Industry, Academia, and International Development Round Table' (2001) 3 *Intellectual Property Strategy Today* 15; Richard C Atkinson et al, 'Public Sector Collaboration for Agricultural IP Management' (2003) 301 *Science* 174, 175.

167 See, eg, Janet Hope, *Open Source Biotechnology* (PhD Thesis, The Australian National University, 2005) <http://opensource.mit.edu/papers/hope.pdf>; Yochai Benkler, 'Commons-Based Strategies and the Problems of Patents' (2004) 305 *Science* 1110, 1111; Sara Boettiger and Dan L Burk, 'Open Source Patenting' (2004) 1 *Journal of International Biotechnology Law* 221.