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HUMAN GENE PATENTS AND GENETIC TESTING IN EUROPE: A REAPPRAISAL

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Abstract

Popular and academic objections to patents over human genes are legion. Although some concerns about the negative impact of these patents have declined recently, questions persist as to the effect of gene patents on genetic testing. This paper undertakes a timely reappraisal of the patentability of human genes in Europe, by reference to EPO and English case law, and demonstrates that isolated DNA and the associated diagnostic tests remain patentable in Europe, although recent cases indicate a sensible tightening of the patentability requirements. The paper concludes by considering the potential for gene patents to affect the provision of genetic testing services.

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Recent developments in the US have once again enlivened the academic debate about gene patents. In a decision of the United States District Court for the Southern District of New York, the first in what is likely to be a series of decisions in this case, patents held by Myriad Genetics relating to breast cancer genetic testing were found to be invalid.¹ The Secretary's Advisory Committee on Genetics, Health and Society's "Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests" made controversial recommendations to address what it considered to be the negative impact of gene patents on patient care.² Although these developments in the US have no direct application in Europe, it is timely to re-consider whether European law is congruent with the US position.

This paper considers two important questions about patents for human genes: first, whether human genes are patentable under the European Patent Convention (EPC); and second, if so, whether such patents might have an impact on patient care. This paper analyses English and European Patent Office (EPO) jurisprudence relevant to the patentability of human genes, and considers the ways in which genes (as products) or genetic tests (as processes) are patentable. The paper then considers the possible implications of the existence of such gene patents for genetic testing.

1. What is a Human Gene Patent?

Traditionally, patents have been granted for tangible, usually mechanical, devices, such as mousetraps. The patent system has expanded to keep pace with developments in technology, and patents have been granted for less tangible inventions, and increasingly for inventions related to, or incorporating fragments of, genetic code. Numerous patents have been granted in relation to biotechnological inventions which claim genetic material in some manner. According to a 2005 study, at that time more than 4000 genes, or approximately 10-20% of the human genome, were claimed in some way in US patents.³ A similarly large proportion of the human genome is the subject of patent claims at the EPO.⁴

There are various possible definitions of what comprises a "gene patent". Much academic research uses the term to refer to any patent with any claim over nucleic acid or for the purposes of diagnosing a genetic condition. The Nuffield Council on Bioethics lists what it declares to be an exhaustive definition of the forms in which DNA or genes may be claimed in patents, where the common feature is that the patent claims either a DNA or RNA sequence or a method of identifying the existence of a

¹ *Association for Molecular Pathology et al v United States Patent and Trademark Office et al* 669 F. Supp. 2d 365 (2010) (United States District Court for the Southern District of New York). The decision has been appealed.

² Secretary's Advisory Committee on Genetics, Health and Society, "Gene Patent and Licensing Practices and Their Impact on Patient Access to Genetic Tests" (2010).

³ K Jensen and F Murray, "Intellectual Property Landscape of the Human Genome" (2005) 310 *Science* 239-240.

⁴ MM Hopkins and others, *The Patenting of Human DNA: Global Trends in Public and Private Sector Activity (The PATGEN Project)* (Brighton: SPRU, Science and Technology Policy Research, University of Sussex, 2006).

DNA or RNA sequence in an individual.⁵ This paper adopts an inclusive definition of “gene patents”, and considers any patent which claims DNA or RNA sequences as products, or the processes to make or identify them, to be a gene patent.⁶ Both coding and non-coding DNA is included in this definition, as are diagnostic method patents. The patenting of proteins alone, without reference to the genes coding for them, is not included.

The gene patent claims most relevant for genetic testing can be divided into four types: product claims to isolated DNA or RNA molecules; product claims for diagnostic kit tests; process claims for methods of diagnosis through genetic testing; and product claims to gene chips and microarrays.⁷ Many gene patents have claims in more than one of these forms. Of these types of claim, it is the claims to the isolated DNA (the “gene” itself) that are the most controversial.⁸ However, claims to methods of diagnosis might in practice prove more difficult to invent around.⁹

Where a gene patent claims the nucleic acid molecule as a product *per se*, the owner of such a patent has the right to exclude all uses of the molecule. A patent claim to a diagnostic method may refer to a DNA molecule but use of the molecule for purposes other than the patented process would be permissible, subject of course to any patents that might exist for the molecule itself. Selection inventions are also permitted; for example a patent over a Single Nucleotide Polymorphism (SNP)¹⁰ within a gene might exist at the same time as a patent which claims the gene as a whole.¹¹ A single gene might therefore be the subject of multiple patents, with the entire gene, gene fragments, causative mutations within the gene, and diagnostic methods in relation to that gene all patented.

Human gene patents test the traditional assumptions and boundaries of the patent system. These patents do not intuitively seem to be for novel, non-obvious and useful inventions. Human genes, and the relationship between genes and diseases, appear to be discoveries, not inventions in the traditional sense. Nor are they new, as genes are present within the body, and their relationship with disease has always existed. Until recently, the law was relatively settled and these objections were answered, more or less convincingly, by patent office practice, guidelines and decisions and in various

⁵ Nuffield Council on Bioethics, *The Ethics of Patenting DNA: A Discussion Paper* (London: Nuffield Council on Bioethics, 2002), at 25.

⁶ This is essentially the same as the definition used by Paradise, Andrews and Holbrook in J Paradise, L Andrews and T Holbrook, “Patents on Human Genes: An Analysis of Scope and Claims” (2005) 307 *Science* 1566-1567.

⁷ Secretary’s Advisory Committee on Genetics, Health and Society (SACGHS), *Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* (2009) 22; E Kane, “Patent-mediated Standards in Genetic Testing” [2008] *Utah Law Review* 836-874, at 845.

⁸ SACGHS, see note 7 above, at 22-23.

⁹ I Huys and others, “Legal Uncertainty in the Area of Genetic Diagnostic Testing” (2009) 27 *Nature Biotechnology* 903-909.

¹⁰ A variation in the human genetic code of a single base, which may be associated with normal human variation or disease.

¹¹ UK Intellectual Property Office, *Examination Guidelines for Patent Applications relating to Biotechnological Inventions in the UK Intellectual Property Office* (Newport: UKIPO, 2009), at [18].

judicial decisions.¹² However, the recent decision of the New York District Court has gone against such settled principles to declare patents for genes as compositions of matter invalid under the US product of nature doctrine, pointing out that the question of whether genes are patentable subject matter had not been considered by the Supreme Court. In this paper I consider and critically examine gene patentability under the EPC.

2. Patentability of Human Genes

2.1. *Isolated DNA as Invention or Discovery?*

Patents are granted only for “inventions”, a term not defined in the EPC or Patents Act 1977 (PA).¹³ The requirement for an invention in the EPC is the subject of much judicial and academic consideration, but the law remains highly uncertain.¹⁴ The approaches of the EPO and the English courts to this question diverge, and the divergence is particularly apparent in relation to computer programs and business methods patents.¹⁵ However, in relation to the question of whether the subject matter of a patent constitutes a discovery or invention, there is more convergence in approach.

Section 1(2)(a) of the PA and art 52(2) of the EPC provide that discoveries are not inventions, and therefore cannot be patented. However, case law has interpreted this to mean that the useful artefact or process that results from a discovery may be patentable. In *Re Gale’s Application* Nicholls LJ held that “it is the practical application of an idea or discovery which leads to patentability”.¹⁶ The discovery may be an integral and all-important part of the invention, but provided there is some useful object or process that arises from the discovery, that useful object or process may be patentable.¹⁷ The discovery together with its technical application can form part of the assessment for novelty and inventive step.¹⁸ This means that an obvious application of a previously unknown discovery can be considered new and inventive, notwithstanding the fact that the discovery on its own is not patentable and the

¹² *Ibid*; *Genentech Inc’s Patent* [1989] RPC 147 (CA); *Howard Florey/Relaxin* [1995] EPOR 541 (EPO (Opposition Division)); *Chiron Corporation v Murex Diagnostics* [1996] RPC 535 (CA); *Icos Corporation/Seven Transmembrane Receptor* [2002] OJEPO 293 (EPO (Opposition Division)); *Multimeric Receptors/Salk Institute (T 0338/00)* (EPO (Technical Board of Appeal)); *Method of Diagnosis/University of Utah (T80/05)* (EPO (Technical Board of Appeal)).

¹³ US law does not draw the same distinction between invention and discovery. However, US case law prohibits the patenting of products of nature: JM Conley and R Makowski, “Back to the Future: Fethinking the Product of Nature Doctrine as a Barrier to Biotechnology Patents (Part II)” (2003) 85 *Journal of the Patent and Trademark Office Society* 371.

¹⁴ J Pila, “On the European Requirement for the Invention” (2010) 41 *IIC: International Review of Intellectual Property and Competition Law* (forthcoming).

¹⁵ See for example *Aerotel Ltd v Telco Holdings Ltd* [2006] EWCA Civ 1371, [2007] RPC 7 per Jacob LJ.

¹⁶ *Gale’s Patent Application* [1991] RPC 305 (CA) 323.

¹⁷ *CFPH LLC’s Application* [2005] EWHC 1589 Pat, [2006] RPC 5 [34]; *Genentech Inc’s Patent*, see note 12 above, at 208.

¹⁸ UK Intellectual Property Office, see note 11 above, at [99]; *Genentech Inc’s Patent*, see note 12 above, at 208.

technical application decoupled from the discovery would be too obvious for a patent. Applying this in the field of genetic technology, it has consistently been held by Patent Offices that the technical or useful application of a discovery, such as the expression of a genetic sequence in a vector, or the application of a genetic sequence in a diagnostic test, is not excluded from patentability by reason of being a discovery as such.¹⁹

In relation to biotechnological inventions, the limits of the prohibition on the patenting of discoveries are further elaborated by the terms of the Biotechnology Directive,²⁰ which provides in art 5(1) that “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”. Art 5(2) provides, however, that “[a]n 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”.

The European approach to patentability is somewhat different in this respect to the approach of the court in the recent decision invalidating the breast cancer genetic testing patents held by Myriad Genetics.²¹ There is no specific prohibition of the patenting of discoveries in the US, but the court relied on the US “product of nature” doctrine, which denies patentability to substances isolated from their naturally occurring form in the absence of the isolated substance having “markedly different characteristics” to the naturally occurring substance. DNA has a dual nature; it has a chemical form, but its value lies primarily in the information which it encodes. His Honour held that, as the value of the DNA was primarily informational, and as the information was the same in isolated and natural form, then the substance in question did not have markedly different characteristics and as a result was not patentable.²² Such a reading of the nature of DNA in Europe is largely precluded by art 5(2) the Biotechnology Directive.²³ DNA has consistently been characterised as a chemical substance, without reference to the information it encodes.²⁴ However, this approach is far from uncontroversial. Commentators raise doubts as to whether the act of

¹⁹ *Method of Diagnosis/University of Utah*, see note 12 above, at [59]; *Breast and Ovarian Cancer/University of Utah* (T1213/05) (EPO (Technical Board of Appeal)) [45]; *Icos Corporation/Seven Transmembrane Receptor*, see note 12 above; *Chiron Corporation v Murex Diagnostics*, see note 12 above, at 575; *Howard Florey/Relaxin*, see note 12 above; *Genentech Inc’s Patent*, see note 12 above.

²⁰ 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 L213/13.

²¹ *Association for Molecular Pathology et al v United States Patent and Trademark Office et al* 669 F. Supp. 2d 365 (2010) (United States District Court for the Southern District of New York).

²² It must be recognised that this decision is the subject of appeal, and even if the non-patentability of DNA is upheld on appeal, different reasoning could support that decision. The Brief for the United States as Amicus Curiae in support of Neither Party in the USCAFC appeal provides an alternative, more limited view of the exclusion of DNA patents under the product of nature doctrine, where engineered DNA would remain patentable, but naturally occurring DNA would not.

²³ In the absence of a successful challenge to the Biotechnology Directive, which seems unlikely, *Netherlands v European Parliament* Case C-377/98 [2001] ECR I-7079.

²⁴ See, e.g. *Method of Diagnosis/University of Utah*, see note 12 above, at [59]; *Howard Florey/Relaxin*, see note 12 above.

isolation and characterisation of a naturally occurring substance is sufficiently different from the discovery of the substance.²⁵ The concept of allowing patents for isolated natural products is something of a legal fiction. What qualifies as isolation is a matter of degree, and the process of isolating a product from its natural surroundings may be difficult or straightforward depending on the circumstances. A process patent for the isolation of the product may be reasonable, but the technical character of the process of isolation is only an argument in support of the patent on the process, not the patent on the product *per se*.²⁶

As discussed in *Association for Molecular Pathologists*²⁷, the dual nature of DNA makes patents in this field problematic. Patent offices award patents for DNA sequences by treating them in the same way as other chemical entities. However, whilst DNA has a chemical structure, much of its value lies not in that structure, but in the information it contains.²⁸ Gene patents are in this respect somewhat different from patents on chemical compounds. The physical manifestation (physical DNA strand) of the information in the patent (sequence of bases) one could argue does not cause the desired effect in itself. In a product patent for a DNA sequence *per se*, it is that information which is the most important element, and in this sense, the isolated DNA is serving the same purpose as the natural sequence.²⁹ As the useful properties of DNA are not characteristics invented by the scientist or patent holder, but rather are inherent in the nature of DNA itself, a genetic sequence is, arguably, of its nature a discovery.³⁰ However, to treat a DNA sequence as primarily information, and as having a chemical structure which is only of secondary relevance is arguably scientifically flawed. DNA, although perhaps “relatively inert chemically”,³¹ does act via its chemical structure in the body, and moreover, most diagnostic tests rely on chemical reactions in order to act. The chemical structure is the key to the informational value of the DNA, and cannot be separated from the informational value, nor ignored. Moreover, to characterise DNA as informational in nature and therefore not patentable on the basis of this characterisation may limit the patentability of DNA which *does* have primarily chemical value, such as DNA based

²⁵ S Sterckx, “Some Ethically Problematic Aspects of the Proposal for a Directive on the Legal Protection of Biotechnological Inventions” (1998) 20 *European Intellectual Property Review* 123-128, at 124-25.

²⁶ *Ibid.*, 124-125.

²⁷ *Association for Molecular Pathology et al v United States Patent and Trademark Office et al* 669 F. Supp. 2d 365 (2010) (United States District Court for the Southern District of New York) 131-135.

²⁸ The informational value of DNA was influential in the decision of Justice Sweet of the United States District Court for the Southern District of New York to invalidate the patents on the BRCA genes held by Myriad Genetics. See also SJR Bostyn, *Patenting DNA Sequences (Polynucleotides) and Scope of Protection in the European Union, an Evaluation: Background Study for the European Commission Within the Framework of the Expert Group on Biotechnological Inventions* (Office for Official Publication of the European Communities, Luxembourg 2004) 59; AK Rai, “Intellectual Property Rights in Biotechnology: Addressing New Technology” (1999) 34 *Wake Forest Law Review* 827-847, 836.

²⁹ JM Conley and R Makowski, see note 13 above, at 395.

³⁰ LB Andrews and J Paradise, “Gene Patents: The Need for Bioethics Scrutiny and Legal Change” (2005) 5 *Yale Journal of Health Policy Law and Ethics* 403-412, at 405.

³¹ *Association for Molecular Pathology et al v United States Patent and Trademark Office et al* 669 F. Supp. 2d 365 (2010) (United States District Court for the Southern District of New York) 132.

therapeutics. Arguments will turn on questions of whether the primary value of the substance in question is informational or chemical. Moreover, other compounds exist which also have informational value, but are patented as chemicals, such as receptor proteins.

While debate as to the appropriateness of patents on isolated natural products may continue, at least in academia, it remains the case that product patents on DNA sequences *per se* have been granted by patent offices in Europe. The Biotechnology Directive is operating on a clear policy goal of encouraging researchers to obtain and isolate elements valuable in medical biotechnology, an attitude consistent with the established patent practice of allowing patents on natural substances isolated from their surroundings.³²

2.2. Genetic Tests as Invention or Discovery?

As noted above, although gene patents as products or compositions of matter have proved more controversial, patents for methods of diagnosis of genetic disease also raise concerns.³³ In *Association for Molecular Pathology*, the court concluded that the methods of diagnosis in the patents in question were invalid as abstract mental processes.³⁴ Although the EPC similarly specifies that methods of performing mental acts are not inventions, patents for genetic tests have not been invalidated on this basis in Europe, presumably because the patents as drafted include sufficient technical features to take them outside this exclusion.³⁵ Alternatively, they may instead be considered under the specific exclusion of diagnostic methods from patentability. The scope of this exclusion is narrow however, and genetic tests do not fall within it.³⁶

2.3. Novelty

In the case of inventions based on natural materials, such as gene patents, it is often contended that the invention lacks novelty because the substance in question exists in nature.³⁷ However, a gene sequence in isolated form is considered to be different from

³² *Howard Florey/Relaxin*, see note 12 above, at [4.3.1]. Pharmaceutical compounds based on natural substances have been patented in the past. See, for example paclitaxel, a cancer chemotherapy drug derived from the yew tree. M Colin and others, *US4814470: Taxol Derivatives, Their Preparation and Pharmaceutical Compositions Containing Them* (Rhone-Poulenc Sante, USA 1989).

³³ And may in fact prove more difficult to invent around in the diagnostic context: I Huys and others, see note 9 above, at 903.

³⁴ The court based much of its reasoning on the test set out by the Federal Court in *In re Bilski* 545 F.3d 943 (C.A.Fed.2008). This test has been reconsidered by the Supreme Court (*Bilski v Kappos* 130 S.Ct. 3218 (2010) and therefore it remains to be seen how this aspect of the decision will be treated on appeal. The United States Court of Appeals for the Federal Circuit decision in *Prometheus v Mayo* (remanded by the Supreme Court: *Mayo Collaborative Services v Prometheus Laboratories, Inc.* 130 S.Ct. 3543 (Mem) (2010)) should provide some guidance.

³⁵ *Aerotel Ltd v Telco Holdings Ltd* [2006] EWCA Civ 1371, [2007] RPC 7; *Symbian Ltd v Comptroller General of Patents, Designs and Trademarks* [2008] EWCA Civ 1066, [2009] RPC 1; *Duns Licensing Associates/Estimating Sales Activity (T154/04)* [2007] EPOR 38 (EPO (Technical Board of Appeal)).

³⁶ The diagnostic methods exclusion from patentability is discussed further at 3.2.

³⁷ *Howard Florey/Relaxin*, see note 12 above, at [4.1].

that which exists naturally, in accordance with established patent practice recognising novelty for a natural substance which has been isolated for the first time and which had no previously recognised existence.³⁸

The UKIPO considers that the context in which a polynucleotide sequence is published can have a bearing on whether or not an earlier publication will invalidate for lack of novelty a later claim to that sequence. A prior publication of the sequence as it occurs in the human genome would not impugn the novelty of a sequence in its isolated state. Similarly, a cDNA which corresponds to a naturally occurring polynucleotide would not be rendered non-novel by the disclosure of a naturally occurring polynucleotide, as the cDNA does not occur in nature.³⁹ A claim to a specific fragment of a larger sequence which was previously disclosed might be allowable as a selection invention if it can be shown that the fragment has some useful quality not previously recognised; for example, as a specific polymorphism.⁴⁰

2.4. Inventive Step

The question of whether an invention is obvious is a difficult question generally in patent law, and particularly so in the field of biotechnology. In an area such as biotechnology where the rate of innovation is very rapid, the state of the art at the relevant priority date will be highly determinative of the result of the case.⁴¹ In the early days of biotechnology and genetic engineering, a great deal of invention was required to reach results which are now extremely easy to produce or can be produced by machine.⁴² As more is “known about the various genomes and the function of the constituent genes, the more difficult it will be to establish an inventive step for any isolated gene”.⁴³ Data mining to identify a new polynucleotide homologous to a polynucleotide with a known function will not normally involve an inventive step. Similarly, the identification of a human homologue (the corresponding human version of a gene in a different species) of a previously characterised gene from another species is not inventive, regardless of the methods used to identify the homologue.⁴⁴ The UKIPO also considers that there is unlikely to be an inventive step in identifying from within a sequenced genome any new gene, even those without known homologues, as it is obvious to trawl the genome for previously unidentified genes, and any skilled worker would have some expectation of success.⁴⁵

However, there are areas of gene patents where there is scope for inventive step. The identification of the function of a novel gene that has not been identified by any form

³⁸ *Ibid*, at [4.3.1]; D Schertenleib, “The Patentability and Protection of DNA Based Inventions in the EPO and the European Union” (2003) 25 *European Intellectual Property Review* 125-138, at 126.

³⁹ UK Intellectual Property Office, see note 11 above, at [17].

⁴⁰ *Ibid*, [18].

⁴¹ *Biogen Inc v Medeva plc* [1997] RPC 1 (HL) 45.

⁴² PW Grubb, *Patents for Chemicals, Pharmaceuticals and Biotechnology: Fundamentals of Global Law, Practice and Strategy*, 4th ed (Oxford: OUP 2004), at 256.

⁴³ UK Intellectual Property Office, see note 11 above, at [32].

⁴⁴ *Ibid*, [34]; *Aeomica Inc BL O/286/05* (UKIPO, unreported, 25 October 2005) [62].

⁴⁵ UK Intellectual Property Office, see note 11 above, at [33].

of homology searching may be inventive, depending on the methods used to determine function and what is known in the prior art.⁴⁶ Additionally, the identification of a new SNP within a known gene may be inventive if a novel and non-obvious function can be assigned to it, such as the relationship between that SNP and predisposition to a disease. However, prior art disclosures of SNPs which are associated with the same disease are likely to render the identification of further SNPs in that same gene obvious.⁴⁷ Specific combinations of probes on a microarray might be inventive by means of a selection invention.⁴⁸

2.5. Industrial Application

With more conventional technologies the usefulness⁴⁹ of the invention in question is usually immediately apparent from the nature of the invention. However, a genetic sequence is different, because it is possible to identify the chemical structure of a genetic sequence without knowing or understanding its function. Particularly in the early stages of the Human Genome Project, gene sequences were identified, and patents applied for, without any real understanding of the function of the gene sequences in question. These patents raise serious questions as to what is necessary to satisfy the requirement of industrial application for genetic sequences.

Although industry is construed broadly as being any kind of trade or industry in its widest sense, whether or not for profit,⁵⁰ industry does not exist in that sense to make or use that which is useless for any known purpose.⁵¹ A product which is definitely described and plausibly shown to be usable, for example to cure a rare or orphan disease, might be considered to be industrially applicable even though it might not be intended for any profitable use or trade.⁵² If what is described is merely an interesting research result that might, in the future, following further research, yield a practical application, this will not satisfy the requirement of industrial application. Speculative indications of possible functions are not sufficient.⁵³

The disclosure of the function of a newly discovered protein is of the utmost importance when examining the issue of industrial applicability, as the function is the gateway to understanding the concrete benefits which may derive from exploiting the invention industrially.⁵⁴ The mere characterisation of a protein, without disclosure of a potentially profitable use for that protein, will not be enough to comply with the

⁴⁶ *Ibid*, [35].

⁴⁷ *Ibid*, [36].

⁴⁸ *Ibid*, [38].

⁴⁹ EPC art 52(1); PA s 1(1)(c); EPC art 57; PA s 4; Art 5(3) of the Biotechnology Directive (Implemented via EPC rules 27(1)(f) and 23e(3); PA Sch A2) further provides that the industrial application of a sequence or partial sequence of a gene must be disclosed in a patent application.

⁵⁰ *Chiron Corporation v Murex Diagnostics*, see note 12 above, at 607.

⁵¹ *Ibid*.

⁵² *Hematopoietic Receptor/Zymogenetics* (T898/05) (EPO (Technical Board of Appeal)) [8].

⁵³ *Eli Lilly and Co v Human Genome Sciences Inc* [2008] EWHC 1903 (Pat), [2008] RPC 29 [226].

⁵⁴ *Hematopoietic Receptor/Zymogenetics*, see note 53 above, at [20].

industrial application requirement.⁵⁵ This is not to say, however, that actual experimental data is necessary to comply with art 57; if a profitable use can be identified on the basis of the description, taking into account common general knowledge, then the requirement may be satisfied.⁵⁶

Three levels of function are relevant to the question of industrial applicability; molecular, cellular and biological, and each compound may encompass multiple different functions.⁵⁷ Elucidation of one level of function might result in a straightforward industrial application, even though the other levels of activity are unknown or are only partly characterised. For example, the CCR5 receptor, which has an important role in HIV infection, was the subject of a patent application by Human Genome Sciences, who had uncovered a different function for the receptor. They applied for a patent on the receptor without knowing, or disclosing in the patent application, that it had a function in relation to HIV.⁵⁸

In *BDP1 Phosphatase/Max-Planck*, although the application described a product, the means and methods for making it and its prospective use for basic scientific activities, the application identified no practical way of exploiting the product in at least one field of industrial activity.⁵⁹ The patent was for a compound (brain-derived phosphatase 1) that was similar to other protein phosphatases. These compounds share a common activity (phosphorylation/dephosphorylation) and general function (cellular signal transduction). But the application showed that every product had unique properties that might reflect specific functions, and also that it was unlikely that there was a single function, given the complexity of cellular signal transduction pathways.⁶⁰ The application stopped short of suggestion or identifying an anti-cancer activity for BDP1 or a therapeutic use of BDP1 as a tumour-suppressor agent, and the burden was left to the reader to guess or find a practical application for it. Given the complexity of the cellular systems within which the protein was projected to act, and the fact that every phosphatase has unique specific properties, this level of non-specificity of the claims was unacceptable. As the only practicable use was to find out more about the natural functions of what was claimed, this was research for its own sake, or with the mere hope that some useful application might be identified. The application therefore fell short of industrial applicability. However, where the compound in question is identified as a member of a class of compounds which have clearly been identified as of interest to the pharmaceutical industry because of their known role in inflammatory processes, irrespective of whether that role had been clearly defined, then industrial applicability can be shown.⁶¹

⁵⁵ *Ibid.*

⁵⁶ *Ibid.*, [31].

⁵⁷ *Ibid.*, [29].

⁵⁸ E Marshall, "Gene Patents: Patent on HIV receptor provokes an outcry" (2000) 287 *Science* 1375. The patent was granted by the US Patent and Trademark Office (USPTO), but the application was withdrawn in Europe.

⁵⁹ *BDP1 Phosphatase/Max-Planck* (T0870/04) (EPO (Technical Board of Appeal)).

⁶⁰ *Ibid.*, [9].

⁶¹ *PF4A Receptors/Genentech* (T 0604/04) (EPO (Technical Board of Appeal)).

Speculative functions are not sufficient to satisfy the requirement of industrial applicability. Identification of a protein may be sufficient if it will immediately suggest a practical application (for example, human insulin), but if the function is not known or is incompletely understood, then the industrial applicability would need to be established on some other grounds.⁶² Industrial applicability is not always a disputed question in patent cases involving genetic sequences.⁶³ For example, in *Decision T 1074/03*, a claim directed to a population of vectors comprising oligonucleotides which encoded peptides which might exhibit useful properties for drug design was held by the Board to be apparently industrially applicable.⁶⁴

These cases illustrate that each case turns on its own particular facts, and therefore each case must be decided on its own merits according to its particular technical circumstances. Simply identifying a gene, sequencing it, and identifying the protein that will be transcribed from the sequence is not enough; there must be some knowledge of the function of the genetic sequence. Where a disease gene or individual disease-causing SNPs are isolated and patented, then industrial applicability is unlikely to be in issue because it is clearly useful to test patients for the disease gene.⁶⁵ Questions may however arise about the industrial applicability of SNPs associated with disease, but not shown to be causative. Similarly, if a gene is identified, but the disease with which it is associated is not known at the time of application, but is later identified, industrial applicability will not be shown.

In the US, patents must demonstrate utility which is specific, substantial and credible,⁶⁶ and this test has garnered some support in the UK as a convenient way of approaching the question of industrial application.⁶⁷ However, it has not been used as a test to the exclusion of the factors set out above.

2.6. Sufficiency of Disclosure

Gene sequence patents, which claim a sequence by reference to its chemical structure, are likely to be sufficient. However, a genetic sequence patent which claims antibodies where there is no clear idea of the function of the sequence is likely to be insufficient. For example, in *Eli Lilly*,⁶⁸ the patent claimed specific antibodies to the antigen in question. It was clear in that case that a very significant research

⁶² *Eli Lilly v Human Genome Sciences Inc* [2010] EWCA Civ 33 *ibid*; *Icos Corporation/Seven Transmembrane Receptor*, see note 12 above; *Hematopoietic Receptor/Zymogenetics* (T898/05) (EPO (Technical Board of Appeal)) [6].

⁶³ RJ Aerts, "Biotechnological Patents in Europe - Function of Recombinant DNA and Expressed Protein and Satisfaction of the Industrial Applicability Requirement" (2008) 39 *International Review of Intellectual Property and Competition Law* 282-306, at 287.

⁶⁴ *Soluble Peptides Having Constrained, Secondary Conformation in Solution and Method of Making Same/Isys, Inc* (T1074/03) EPO (Technical Board of Appeal).

⁶⁵ This argument was unsuccessful in relation to the BRCA1 patent: *Breast and Ovarian Cancer/University of Utah*, see note 19 above.

⁶⁶ US Patent and Trademark Office, *Guidelines for Examination of Applications for Compliance with the Utility Requirement* (Federal Register, 2001).

⁶⁷ *Eli Lilly and Co v Human Genome Sciences Inc* [2008] EWHC 1903 (Pat), [2008] RPC 29 [227].

⁶⁸ *Ibid*.

programme would be required in order to generate such a specific antibody (and in fact it took many years after the priority date for such an antibody to be developed); there was therefore insufficient disclosure. Similarly, it would appear that most “reach-through” claims to pharmaceutical products developed to work on a particular claimed receptor would most probably be held insufficiently disclosed and thus invalid.⁶⁹ However, development of a genetic diagnostic test for a single gene disorder from a known genetic association or sequence would in most cases be routine. In *Chiron*, the development of a diagnostic test for Hepatitis C was described as the “straightforward application of routine molecular biology techniques”.⁷⁰ Thus, a claim to a method of diagnosis for a specified genetic sequence known to cause a particular disease will probably be sufficient without detailed elaboration of exactly how to go about the process of diagnosis.

2.7. Priority

Patents may claim the same right of priority if filed within 12 months of filing of the first patent application in another World Trade Organization (WTO) or Paris Convention party jurisdiction where the earlier patent is for “the same invention”.⁷¹ This priority will only be acknowledged if the skilled person can derive the subject-matter of the claim directly and unambiguously, using common general knowledge, from the previous application as a whole.⁷²

In relation to gene patents, difficulties arise where a patent as originally filed contains an incorrect sequence which the patent holder later seeks to correct, or where the priority document on which the patent holder wishes to rely lists an incorrect sequence, which is different from that in the patent in question. There have been successful challenges to a number of gene patents on this basis. In *Tissue Factor Protein/Genentech*, the patent claimed a polynucleotide sequence, which in the patent as filed had mistakes in five bases outside the coding region. The Board held that because the sequence in the priority document was structurally different from that in the amended claims, the corrected sequence was additional subject matter (even though the mistakes were outside the coding region) and did not enjoy the same priority.⁷³ In *Apoptosis Receptors/Genentech*, the sequence in the priority document differed from the application as filed. The application was denied the priority date of the priority document. The Board held that to allow priority based on a wrong nucleotide or amino acid sequence in the priority document would not be fair as it would allow a patentee to acquire a right over a broad area from which, only later on, the correct sequence might be selected and disclosed in a patent application. It felt

⁶⁹K Liddell and others, “Patents as Incentives for Translational and Evaluative Research: The Case of Genetic Tests and their Improved Clinical Performance” [2008] *Intellectual Property Quarterly* 286-327, at 308.

⁷⁰ *Chiron Corporation v Murex Diagnostics*, see note 12 above, at 618.

⁷¹ EPC art 87(1); PA s 5(2).

⁷² G 2/98 (EPO (Enlarged Board of Appeal)).

⁷³ *Tissue Factor Protein/Genentech* (T351/01) (EPO (Technical Board of Appeal)).

that the allowance of this approach could encourage a “mischievous use of priority rights”.⁷⁴

In *Breast and Ovarian Cancer/University of Utah* the Board of Appeal endorsed the approach of these previous cases.⁷⁵ The appellant argued that the sequence in question should be allowed to deviate within experimental error. However, as the invention in the patent was the genetic sequence in question, a difference in that sequence meant that the sequence in the application was not the “same invention” within the meaning set out in the *G2/98* case. The skilled person could not have derived the subject matter of the claim directly and unambiguously using common general knowledge from the previous application as a whole, and therefore priority would not run from the earlier document.⁷⁶ It follows that an error of even a single base in a DNA sequence in a patent application for the sequence as a product could be fatal to the priority of that application.

However, in *Method of Diagnosis/University of Utah*, a deviation between the sequence in the priority document and the patent as filed was not fatal to priority.⁷⁷ As the same results would be obtained by a skilled person performing the method of the claim when using the sequence information of either the priority document in question or the application as filed, the Board held that priority would run from the earlier document.⁷⁸

3. Exceptions to Patentability

3.1. *Ordre Public and Morality*

In Europe, patents are not granted for inventions the commercial exploitation of which would be contrary to *ordre public* or morality.⁷⁹ Most of the cases which have considered the interpretation of *ordre public* and morality are concerned with inventions such as genetically modified plants or animals or stem cells, which tend to be viewed as more morally problematic than genetic tests. However, in *Relaxin*,⁸⁰ the Green Party opposed the Howard Florey Institute’s patent for the gene coding for relaxin on three *ordre public* and morality grounds: firstly, that the use of pregnancy for profit was offensive to human dignity; secondly that the patent in question was a patent over life, and as such was immoral; and thirdly, that patenting of DNA was equivalent to slavery.⁸¹ Each of these arguments was rejected by the Opposition

⁷⁴ *Apoptosis Receptors /Genentech* (T 0070/05) (EPO (Technical Board of Appeal)) [20].

⁷⁵ *Breast and Ovarian Cancer /University of Utah*, see note 19 above.

⁷⁶ *Ibid*, [31].

⁷⁷ *Method of Diagnosis/University of Utah*, see note 12 above.

⁷⁸ *Ibid*, [33.5].

⁷⁹ EPC art 53(a); *Plant Genetic Systems/Glutamine Synthetase Inhibitors* (T356/93) [1995] EPOR 357 (EPO (Technical Board of Appeal)). The corresponding provision of the PA, s 1(3), uses the term “public policy” rather than “*ordre public*”, but the terms equate: SF Jones and others, *CIPA Guide to the Patents Acts*, 6th ed (London: Sweet & Maxwell, 2009), at [1.14]. No such exception to patentability on the basis of morality exists in US or Australian law.

⁸⁰ *Howard Florey/Relaxin*, see note 12 above.

⁸¹ *Ibid*, [6.1].

Division, which held that the prohibition on patenting was to be invoked for inventions which would universally be regarded as outrageous.⁸² The Opposition Division acknowledged that the invention would indeed fulfil the criterion of being so abhorrent to the public in general that the grant of a patent would be inconceivable if the invention did actually involve the patenting of human life, abuse of pregnant women or slavery, but held that the commercial exploitation of the Relaxin sequence was none of these things.⁸³ DNA was viewed as a chemical substance, and treated in the same manner as other chemical substances, such as pharmaceuticals.

In *Breast and Ovarian Cancer/University of Utah*,⁸⁴ one of the appellants argued that the fact that the informed consent of the donor of cells used to derive the invention did not include specific consent to commercial exploitation of the research results, nor a benefit sharing agreement, constituted a severe ethical violation which amounted to a violation of *ordre public* and morality. The Board observed in response to this argument that there was no specific requirement in the EPC for evidence of either informed consent or a benefit sharing agreement. The Biotechnology Directive provides that there must have been an opportunity to express free and informed consent in accordance with national law, but there was no procedure to verify this informed consent in the patent framework. The Board held that there was therefore no prohibition on the BRCA1 patent as a result of art 53(a) of the EPC. Another opponent argued that the socio-economic consequences of the patent should be considered as they raised ethical issues sufficient to enliven art 53(a). This opponent argued that the patent would result in increased costs for patients and would also influence the way in which diagnosis and research would be organised in Europe in a way that would be clearly to the detriment of patients and doctors.⁸⁵ The opponent claimed that the group of patients suspected to carry a predisposition to breast cancer would be faced with severe disadvantages and would become dependent on the patent proprietor and that this was contrary to human dignity. The Board rejected this argument, holding that art 53(a) applied only where the exploitation of the invention (as opposed to the exploitation of the patent) would be contrary to *ordre public*.

Objections to gene patents on morality grounds are raised in the popular and academic press by various groups,⁸⁶ and there is a generalised and amorphous public opposition to the concept of ownership of genes.⁸⁷ There is concern that patents on human genes will result in a lack of respect for human life and a devaluation of human dignity, via commercialisation and instrumentalisation of human beings.⁸⁸ It is generally accepted

⁸² *Ibid*, [6.2.1].

⁸³ *Ibid*, [6.3].

⁸⁴ *Breast and Ovarian Cancer/University of Utah*, see note 19 above, at [47]-[57].

⁸⁵ *Ibid*, [52].

⁸⁶ Nuffield Council on Bioethics, see note 5 above; FB Charatan, "US Religious Groups Oppose Gene Patents" (1995) 310 *British Medical Journal* 1351. For a summary of moral objections to gene patents see DB Resnik, *Owning the Genome: A Moral Analysis of DNA Patenting* (Albany: State University of New York Press, 2004), at 3.

⁸⁷ See for example T Radford, "Patenting DNA 'Not in Public Interest'" *The Guardian* [London] (23 July 2002) <<http://education.guardian.co.uk/higher/medicalsceince/story/0,,761773,00.html>> (accessed 24 Sept 2009).

⁸⁸ T Caulfield and R Brownsword, "Human Dignity: A Guide to Policy Making in the Biotechnology Era?" (2006) 7 *Nature Review Genetics* 72-76, at 73; Australian Law Reform Commission, *Genes and*

that human dignity is not directly violated by gene patents, and that any effect is indirect in nature.⁸⁹ However, it seems clear that these general objections on the basis of morality are insufficient to satisfy the requirements of art 53(a); the risks of the invention are to be balanced against the potential benefits.⁹⁰

It has been argued that patent law is an inappropriate vehicle for regulation of technology on the basis of ethical or moral concerns, as a patent does not equate to a licence to use the invention.⁹¹ Refusal of patent grant is not the primary means of regulating the use of new technologies.⁹² There are national laws which restrict the uses of new technologies on public safety grounds, such as those which regulate the clinical use of new pharmaceuticals. For a patent to be revoked on the basis of *ordre public* and morality, the risk, for example, to the environment, would need to be serious and well substantiated at the time of grant. In the absence of such a threat, the regulation of use is better left to the specific regulatory agencies of the relevant jurisdictions. It is not appropriate to deny patentability on the basis of possible future risks which might or might not arise.⁹³ However, whilst patent law does not provide the only opportunity for regulation of new technologies, this does not mean that it should not include provision for refusal of patents which are contrary to morality or *ordre public*. It is inconsistent for a state to discourage or prohibit a particular activity, for example, by prohibiting or restricting use, but, at the same time, encourage innovation in that activity by offering the opportunity of reward through the patent system. It may be more appropriate that full consideration of the ethical implications of particular technologies take place in contexts other than IP law, but it does not follow that patent law should completely disregard ethical issues. A patent application is often the first point at which a new technology is considered by any organ of government and the patent examination is therefore the first time that morality can be considered by a public body. It is inappropriate for this opportunity to be ignored and patent offices should not be neutral on issues of morality. However, patents are at best a blunt tool for regulation of technology, and most regulation needs to be done by specific regulatory and public safety agencies.

3.2. *Medical and diagnostic methods*

Patents will not be granted for methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body, although this exclusion does not apply to products for use in any of these methods.⁹⁴ Prior to the EPC 2000, the prohibition on patenting of medical methods was found in

Ingenuity: Gene Patenting and Human Health Report (Canberra: Australian Law Reform Commission, 2004), at 68.

⁸⁹ DB Resnik, see note 86 above, at 95.

⁹⁰ *Harvard/Onco-Mouse (T19/90)* [1990] EPOR 501 (EPO (Technical Board of Appeal))/*Harvard/Transgenic animal (T315/03)* [2005] EPOR 31 (EPO (Technical Board of Appeal)).

⁹¹ SJR Bostyn (n28) 10.

⁹² *Plant Genetic Systems/Glutamine Synthetase Inhibitors (T356/93)* [1995] EPOR 357 (EPO (Technical Board of Appeal)), at [18.4].

⁹³ *Ibid*, [18.7].

⁹⁴ EPC art 53(c); PA s 4A.

art 52(4), which provided *inter alia* that “diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application”.⁹⁵ This fiction of lack of industrial applicability has however been abandoned in EPC 2000, and the provision has been moved to art 53(c) which excludes patentability for diagnostic methods practised on the human or animal body. The rationale for the exclusion is now clearly based on public health considerations.⁹⁶

Previous conflicting decisions at the EPO as to the scope of the diagnostic methods exception were resolved by the decision of the Enlarged Board of Appeal in *G1/04*,⁹⁷ which has subsequently been interpreted in *Australian National University/Glaucoma*.⁹⁸ The method steps to be carried out when making a diagnosis as part of the medical treatment of human beings or the veterinary treatment of animals for curative purposes include: (i) the examination phase involving the collection of data; (ii) the comparison of those data with standard values; (iii) the finding of any significant deviation, that is, a symptom, during the comparison; and (iv) the attribution of the deviation to a particular clinical picture, that is, the deductive medical or veterinary decision phase.⁹⁹ To trigger the exclusion, the test requires that each of the method steps listed above of a technical nature should satisfy the criterion of being practised on the human or animal body, that is, the performance of each and every one of the steps should imply an interaction with the human or animal body. *In vitro* diagnostic method steps, performed on samples removed from the human body, do not satisfy the criterion of “practised on the human or animal body”, and therefore are not excluded from patentability.¹⁰⁰ Genetic diagnostic tests, being carried out on tissue samples away from the human body, likewise fall outside the medical diagnostic exception.

In *Method of Diagnosis/University of Utah*, the EPO Board of Appeal held that the patent for a method of diagnosing frameshift mutations giving rise to breast cancer susceptibility was not excluded by the art 53(c) prohibition on patentability, as all steps of the diagnosis were performed on a tissue sample, not a live person.¹⁰¹

4. Genetic Testing – Infringement?

Where a gene patent is for a product, for example an isolated genetic sequence, a diagnostic laboratory isolating the patented sequence, or using the isolated sequence, will infringe the patent.¹⁰² Where a patent is for a method of diagnosis, any laboratory

⁹⁵ The corresponding provision of the PA was s 4(2).

⁹⁶ European Patent Office Administrative Council, “Basic Proposal for the Revision of the European Patent Convention” (Munich: European Patent Organisation, 2000), at 45.

⁹⁷ *Diagnostic Methods (G1/04)* [2006] EPOR 15 (EPO (Enlarged Board of Appeal)).

⁹⁸ *Australian National University/Glaucoma (T1197/02)* (EPO (Technical Board of Appeal)).

⁹⁹ *Diagnostic Methods (G1/04)*, see note 97 above, at 171-172.

¹⁰⁰ SF Jones and others, see note 79 above, at [4A.07]; UK Intellectual Property Office, see note 11 above, at [58].

¹⁰¹ *Method of Diagnosis/University of Utah*, see note 12 above, at [62]-[63].

¹⁰² Depending on the wording of the patent and the method of diagnosis used, questions may arise as to whether the sequence is “performing its function”: *Monsanto v Cefetra* (2010) OJ C 234/7, Biotech Directive, art 9. Such issues seem unlikely to arise in the context of diagnostic testing, in contrast for example to plants.

using that method will infringe the patent. It is clear that it is important to examine the actual granted patent claims in order to determine whether conduct infringes a patent. There may be possibilities for inventing around the patent, especially where the patent is old and new laboratory or diagnostic techniques have been developed. Some gene patents may not be infringed by methods of diagnosis that utilize new sequencing technologies, for example.¹⁰³

4.1. Relevant Defences to Infringement

If a valid human gene patent exists, and infringing conduct within the scope of the patent can be proved, there will be no liability for infringement if a defence can be relied upon. The most relevant defence for the purpose of human gene patents and diagnostic testing is the experimental use defence.

4.1.1. Experimental Use

Section 60(5)(b) of the PA provides a defence to patent infringement for acts done for experimental purposes relating to the subject matter of the invention. Despite being commonly termed the “research exception”, s 60(5)(b) in fact provides a defence to infringement of a valid patent, and does not exclude patentability itself.¹⁰⁴

The defence is recognised as having two limbs. The first of these concerns whether or not the conduct in question can be construed as being for experimental purposes. An act will fall within the defence if its purpose is to discover something unknown or to test a hypothesis.¹⁰⁵ The UK Court of Appeal has held that conduct will not be for experimental purposes if it is carried out in order to demonstrate to a third party that a product works or in order to amass information to satisfy a third party, whether a customer or a regulatory body.¹⁰⁶ More recently, it has been suggested, *obiter*, that it is insufficient that one of a number of mixed purposes is experimental, and that, in such a case, it should be shown that the preponderant purpose is experimental. In such a case, the fact that the immediate purpose of the transaction in question is to generate revenue is relevant, although the mere fact that there is a commercial aim in the venture does not render all activities outside the defence.¹⁰⁷ However, in Germany, the term “experimental purposes” has been construed more broadly and the use of results of clinical trials for the purposes of regulatory approval does not bring the trials outside the defence, provided the trials serve to gain some information.

¹⁰³ C Holman, “Survey of US Gene Patent Litigation”, Workshop on “Diagnostic DNA Patents: What Lies Ahead?” (Durham, NC: Duke University, 4 April 2009).

¹⁰⁴ Even the UKIPO refers to the patent research exception: UK Intellectual Property Office, “UK-IPO launches a Consultation on the Patent Research Exception” <<http://webdb4.patent.gov.uk/about/press/press-release/press-release-2008/press-release-20080707.htm>> (accessed 17 Aug 2009).

¹⁰⁵ *Monsanto Co v Stauffer Chemical Co* [1985] RPC 515 (CA) 542.

¹⁰⁶ *Ibid*, 542.

¹⁰⁷ *Corevalve Inc v Edwards Lifesciences AG* [2009] EWHC 6 (Pat); [2009] FSR 8 [66]-[81].

Limitations on the scope of the defence are instead imposed through the second limb.¹⁰⁸

The second limb concerns whether the conduct relates to the subject matter of the invention. A distinction is drawn between “experimenting on” or “experimenting into” a patented invention (generally within the scope of the defence) and “experimented with” or “experimenting using” the patented invention (generally outside the scope of the defence).¹⁰⁹ The subject matter of the invention is construed purposively, by reference to the patent as a whole, and not only to the claims.¹¹⁰ If experiments are directed to the invention, such as testing whether the product can be made, an article made to work, or experiments to test modifications or improvements to the product, these should fall within the defence.¹¹¹ However, use of the invention in research for the purpose for which it was designed will not fall within the defence. For example, use of a patented measuring device for research to improve its efficiency would fall within the terms of s 60(5)(b), but use of the device in order to measure something in the course of a research project would not.¹¹² The research exception is an established defence in most European jurisdictions,¹¹³ but it is not clearly defined or uniformly applied across jurisdictions.¹¹⁴ Most of the case law in Europe on the scope of the defence relates to clinical trials for the purposes of regulatory approval.¹¹⁵ Inconsistencies and difficulties in this regard may be largely resolved by the Regulatory Review Defence, introduced under art 1(8) of Directive 2004/27/EC,¹¹⁶ which provides certain exceptions to the provision of clinical trial data for generic pharmaceuticals.

In the context of gene patents it is likely that the following activities will fall within the terms of the defence:

- research to determine new functions of a patented gene sequence;

¹⁰⁸ T Cook, *A European Perspective as to the Extent to which Experimental Use, and Certain Other Defences to Patent Infringement, Apply to Differing Types of Research: A Report for the Intellectual Property Institute* (London: Intellectual Property Institute, 2006), at 28; *Clinical Trials II* [1998] RPC 423 (Federal Supreme Court of Germany (Bundesgerichtshof)); *Clinical Trials I* [1997] RPC 623 (Federal Supreme Court of Germany (Bundesgerichtshof)).

¹⁰⁹ T Cook, see note 108 above, at 31.

¹¹⁰ F Bor, “Exemptions to Patent Infringement Applied to Biotechnology Research Tools” (2006) 28 *European Intellectual Property Review* 5-14, at 6; *Auchinloss v Agricultural & Veterinary Supplies Ltd* [1999] RPC 397 (CA) 402.

¹¹¹ *Monsanto Co v Stauffer Chemical Co*, see note 105 above, at 522.

¹¹² F Bor, see note 110 above, at 5-14.

¹¹³ *Community Patent Convention* at art 27(b).

¹¹⁴ G van Overwalle and others, “Models for Facilitating Access to Patents on Genetic Inventions” (2006) 7 *Nature Reviews Genetics* 143-154, at 143; For a summary of what law does exist, see T Cook, “Responding to Concerns about the Scope of the Defence from Patent Infringement for Acts Done for Experimental Purposes Relating to the Subject Matter of the Invention” [2006] *Intellectual Property Quarterly* 193-222; T Cook, see note 108 above.

¹¹⁵ T Cook, see note 108 above, at 27.

¹¹⁶ Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community Code Relating to Medicinal Products for Human Use [2004] OJ L136/34.

- verifying the functions of a patented gene sequence;
- finding new SNPs within a patented gene sequence;
- finding new information related to a gene sequence;
- research directed at improving a known genetic diagnostic.

The research and development of a genetic diagnostic test will most probably fall within the research exception, with the exception of the use of research tools, such as Polymerase Chain Reaction (PCR),¹¹⁷ which will require a licence. However, once the test has been validated and becomes routine, the use of the diagnostic in the clinical setting will not be an act done for experimental purposes relating to the subject matter of the invention, and will not be covered by the defence.¹¹⁸

5. Implications of Gene Patents for Genetic Testing

Many gene patents have been granted by patent offices around the world, and many of these patents claim gene sequences or methods of diagnosis that are relevant to genetic testing. Those conducting genetic testing should survey the patent landscape in order to determine their freedom to operate. If patents which appear to cover the area in which those conducting genetic testing wish to work exist, then decisions need to be made as to how to proceed. If the patent appears to be valid, and the conduct in question would clearly infringe it, then a decision may be made to license the patent. Questions as to patent validity or infringement may provide leverage in bargaining the terms of the licence. If the validity of the patent is open to question, then an active challenge to the validity of the patent may be taken, through proceedings seeking revocation, either in the national courts, or, if within nine months of grant, by opposition proceedings at the EPO. Alternatively, the potentially infringing conduct could proceed, and a counterclaim for revocation could be made should the patent proprietor issue proceedings for infringement. This course of conduct would however result in exposure to damages for the infringer should the patent be found to be valid. In these respects, gene patents operate no differently from patents in other areas of technology. There are however some issues that arise because of the nature of genetic testing, that do not arise generally in areas of patented technologies.¹¹⁹

Gene patents, unlike patents in most other technical areas, are difficult to invent around.¹²⁰ There is a substantial degree of dependency between downstream DNA patents and upstream DNA patents. This is not necessarily the case for more traditional biomedical inventions, where there might be a number of ways to cure a non-genetic condition. In this sense, it is frequently said that it is impossible to

¹¹⁷ Polymerase chain reaction (PCR) is a technique in molecular biology to amplify a single or few copies of a piece of DNA across many orders of magnitude. It is particularly useful for genetic diagnosis. National Institutes of Health National Center for Biotechnology Information, "PCR" <<http://www.ncbi.nlm.nih.gov/projects/genome/probe/doc/TechPCR.shtml>> (accessed 25 Sept 2009).

¹¹⁸ T Cook, see note 108 above, at 133-134; F Bor, see note 110 above, at 10.

¹¹⁹ J Kaye, N Hawkins and J Taylor, "Patents and Translational Research in Genomics" (2007) 25 *Nature Biotechnology* 739-741.

¹²⁰ I Huys and others, see note 9 above, at 903; MA Heller and RS Eisenberg, "Can Patents Deter Innovation? The Anticommons in Biomedical Research" (1998) 280 *Science* 698-701, at 700.

“invent around” a gene patent.¹²¹ A recent study of disease gene patents (both product and method patents) found that, for certain relatively common genetic diseases, there were a number of patent claims which it was virtually impossible to invent around.¹²² Even if it is possible to invent around a patent, it may be costly, difficult or time-consuming to do so.

Thus, there is the potential for “patent thickets” to arise in genetic testing. A patent thicket arises where a multitude of patents is held by a multitude of owners.¹²³ Patent thickets can arise on either the technology for genetic testing (such as PCR, which is useful for a broad cross-section of disease tests) or in diagnosis-specific patent protection. In the case of diagnosis-specific patent thickets, there are two forms: vertically oriented and horizontally oriented gene patent thickets.¹²⁴ Vertical patent thickets arise where there is a broad patent granted over the gene-disease link, and later additional patents on specific mutations within that gene. Horizontal thickets arise where a disorder is caused by multiple genes, either independently or cooperatively, and multiple genes need to be examined in a test. In the future, both horizontal and vertical thickets are likely to become problematic. Narrower and more specific gene patents are likely to be granted in the future giving rise to increasing vertical thickets. Horizontal thickets will increase as genetic tests for more complex genetic disorders are developed, in which many different mutations in many different genes will need to be tested.

The transaction costs of investigating the patent situation, including identifying relevant patents, determining whether the conduct in question falls within the scope of the claims, and then negotiating necessary licences, or defending infringement proceedings, are high for individual patents. When multiple patents are held by multiple owners, the cost increases accordingly.¹²⁵ A related problem which arises from patent thickets is “royalty stacking”. If many patents need to be licensed, and each requires the payment of a royalty, then the resulting test may become very expensive.¹²⁶

As genetic testing becomes part of mainstream medicine, it is reasonable to assume that companies will increasingly develop and supply kit tests for genetic testing. Where such a company is developing a test for sale within the marketplace, then arguably it is well placed to carry out such due diligence and license or challenge relevant patents. However, as it currently stands, the vast majority of genetic tests

¹²¹ T Caulfield and others, “Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies” (2006) 24 *Nature Biotechnology* 1091-1094, at 1091; SJR Bostyn (n28) 60.

¹²² I Huys and others, see note 9 above, at 903.

¹²³ G van Overwalle, *Gene Patents and Collaborative Licensing Models: Patent Pools, Clearinghouses, Open Source Models, and Liability Regimes* (Cambridge: CUP, 2009), at 386 citing C Shapiro, “Navigating the Patent Thicket: Cross Licenses, Patent Pools and Standard Setting” in AB Jaffe, J Lerner and S Stern (eds), *Innovation Policy and the Economy*, National Bureau of Economic Research, Innovation Policy and the Economy Group (Cambridge, MA: MIT Press, 2001).

¹²⁴ B Verbeure, “Patent Pooling: Conceptual Framework” in G van Overwalle (ed), *Gene Patents and Collaborative Licensing Models: Patent Pools, Clearinghouses, Open Source Models, and Liability Regimes* (Cambridge: CUP, 2009), at 21.

¹²⁵ MA Heller and RS Eisenberg, see note 120 above, at 700.

¹²⁶ B Verbeure and others, “Patent Pools and Diagnostic Testing” (2006) 24 *Trends in Biotechnology* 115-120, at 115.

which are conducted in the medical context are carried out by laboratories which are ill-equipped to investigate the patent landscape, and in such cases, gene patents could become a substantial burden.

However, to date there is little evidence of the negative impact of patents in the field of diagnostic testing. This is partly due to the fact that very few studies have been carried out. However, the studies to date indicate some divergence in the effects between the US and Europe. The US studies have uncovered some negative impact on genetic testing services in certain disease areas,¹²⁷ and the SACGHS committee recommended legislative changes to address the negative impact.¹²⁸ In Europe, two studies have found minimal or no effect.¹²⁹ However, both these studies found that the lack impact was largely due to patents being ignored, rather than being appropriately managed.

6. Conclusion

Patents on human genes could have a negative effect on the translation of basic biomedical research into clinical application. Consideration of the legal framework alone suggests that gene patents can become problematic at the point at which research begins to have potential clinical application. Gene patents could result in reduced access to tests where disputes over licences for particular patents cannot be resolved or in the case of high royalties for individual patents, or high additive royalties.

These are significant potential problems, which could have a considerable effect on the delivery of genetic tests to patients. The purpose of the patent system is to maximise innovation, not to limit patient access, and if patents do in fact have a negative impact on patient access to genetic tests, without any demonstrated benefit in encouraging innovation, then action should be taken to ameliorate this effect. The analysis above indicates cause for some concern, which necessitates an analysis of the law in practice, in order to identify the nature and extent of any problem caused by the operation of patent law in practice in this field.

¹²⁷ (2010) 12 (4) *Genetics in Medicine* S1-S211 April 2010; MK Cho and others, "Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services" (2003) 5 *Journal of Molecular Diagnostics* 3; JF Merz and others, "Diagnostic Testing Fails the Test" (2002) 415 *Nature* 577.

¹²⁸ Secretary's Advisory Committee on Genetics, see note 2 above.

¹²⁹ N Hawkins, "The Impact of Human Gene Patents on Genetic Testing in the United Kingdom" (2011) *Genetics in Medicine* (forthcoming); S Gaisser and others, "The Phantom Menace of Gene Patents" (2009) 458 *Nature* 407.