Response to the Senate Community Affairs Committee Inquiry into Gene Patents

Contact for this document:

Introduction

The Royal College of Pathologists of Australasia (RCPA) is the peak professional body in pathology in Australia and New Zealand. The RCPA is responsible for the training of medical specialists in pathology and is involved in many major Government Committees and Councils addressing issues of quality, efficiency, funding, and sustainability of pathology testing. The RCPA recognises that resolution of the issue of gene patents is essential for the development of effective and efficient genetic testing in the immediate future, and welcomes the opportunity to be involved in this Inquiry.

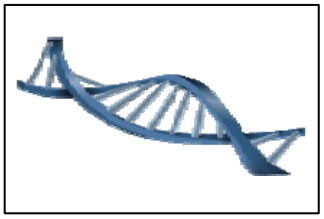
The RCPA has had a position on gene patents for almost a decade and a copy of the current Position Statement is attached as Appendix 1. The RCPA responded to the recent *ACIP Inquiry into Patentable Subject Matter* in 2008 and to the earlier Australian Law Reform Commission Discussion Paper 68 "*Gene Patenting and Human Health*"; these submissions are attached as Appendices 2 and 3.

In this submission we provide a brief summary of the basis of genetic testing in healthcare, the current and potential applications, and the place of patents in genetic testing. We then provide a more detailed analysis of issues relating to gene patents and healthcare services in Australia and conclude with summaries and recommendations linked to the Terms of Reference of the Inquiry.

What are genes?

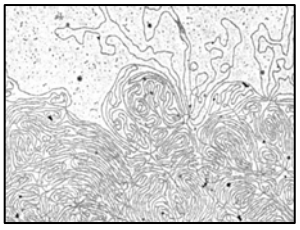
Each person starts life as a single cell, the fertilised egg in a mother's womb containing the genetic instructions that guide growth and development. These genetic instructions provide the blueprint for life, determining how the body develops and how it responds to other influences in the environment.

The genetic code is both a complex chemical and a body of information. It consists of a long chain of four different chemicals called "nucleic acids". These are arranged in the form of a long twisted ladder – the double-helix that is now the universal symbol of genetics. The sequence of these chemicals in the double helix encodes genetic information for the cell. This structure is called deoxyribonucleic acid, or DNA.



The DNA sequence is remarkably consistent in each person, accounting for the similar physical and intellectual features that we recognise as "human". But there are also sufficient differences to make distinctions between us, including variations in gender, physical form, intellect, and personality. These differences in the genetic code also cause variations in how our bodies react to the challenges of life, including responses to injury, toxins, and ageing.

A strand of DNA is only one billionth of a metre wide, but its length can be striking; the figure at right shows just a small part of the DNA from a single cell. In a fertilised egg, the DNA strand is approximately two metres long; one metre came in the sperm from the father, the other from the mother's egg. Each metre of DNA contains 25,000 different genetic instructions, or genes, which can produce a protein that is then used by the cell. Each gene can produce, on average, five different proteins. There are thousands of other genetic instructions that



regulate how the genes are switched on or off.

Why are genes important in health and disease?

This complex genetic code must be copied every time a cell makes a copy of itself so that each cell in the body has a complete set of genetic instructions. The process of repeatedly copying a genetic code of such length and complexity inside a tiny cell ($100{,}000^{th}$ of metre across) is risky, and new errors are always introduced into the genetic code when it is copied. The occurrence of such genetic errors during prenatal development is a major cause of miscarriages and birth defects. Seventy five percent of fertilised eggs miscarry because of such errors and 4,000 babies are born in Australia each year with birth defects due to genetic errors.

The adult human body has approximately one million billion (10^{15}) cells. The total length of the genetic code in an adult is long enough to wrap around the Solar System a number of times. This enormous length of complex information gradually degrades over time. The degradation of the genetic code inevitably results in the development of what we recognise as disorders of ageing, such as organ failure (heart failure, renal failure, dementia etc) and cancer. These, too, are essentially genetic disorders.

Genetic errors may also be present in the egg or sperm from which a person develops. These genetic errors inherited from one or both parents are termed familial. A familial genetic error may result in a miscarriage, or cause a birth defect / infant disorder, or place a person at increased risk of an adult-onset disorder such as cancer or dementia.

What genetic tests are used in healthcare?

Twenty five years ago, there were almost no medical tests that assessed a person's DNA. This has changed rapidly as knowledge about the genes underlying health and disease, and our ability to analyse them, has grown. It has been difficult to document the extent of genetic testing across Australia because most has occurred outside the funding and auditing processes of Medicare.

With financial support from the Federal Department of Health & Ageing, the RCPA recently completed a national survey of genetic testing in healthcare[1]. The survey found that 437 different genetic tests were provided across Australia in 2006, five funded by Medicare and the remainder by other sources, principally State Governments.

These 437 genetic tests represent the tip of the iceberg. In Australia, the variety of genetic tests increased by 7% from 2006 to 2007 and in the US, laboratories offer testing for over 1,700 different genes[2].

These genetic tests are used for different purposes. In some cases, they assist in the diagnosis of an affected person. In other settings, genetic tests are used to screen unaffected people with no family history of the disease to identify those at risk of developing disease (and thereby facilitate effective intervention strategies). If a particular familial genetic error has been identified, relatives can be offered a test to determine their risk of the disorder (and again facilitate effective interventions). Genetic tests are also increasingly used in the assessment of cancer tissue, with the result guiding the choice and dose of therapy. Each of these settings raises different ethical issues that must be addressed as part of the test process.

Patents in genetic testing

The availability of genetic testing has been driven both by improvements in genetic knowledge and by dramatic improvements in genetic methodologies. Many of these methodological advances have involved patented inventions, such as better freezers, centrifuges, analysers, and enzymes[3]. The RCPA recognises the powerful and beneficial impact of patents in the development and implementation of these methods, and applauds the operation of the IP industry in Australia in facilitating this outcome.

Unfortunately the IP regulations and processes that have facilitated these developments have also led to IP offices in many jurisdictions accepting that genes, in addition to the methods used to analyse them, can be patented. A US study in 2005[4] documented that 20% of the 23,688 genes identified at that time had been patented, with up to 20 patents and 12 patent-holders for any one gene. The RCPA does not have hard data on the proportion of the 437 tests provided in Australia[1] which are covered by Australian patents, but the high-volume tests identified in the 2005 study are also offered in Australia. One major public sector laboratory estimates that at least 50% of the genetic tests it offers could be covered by one or more Australian patents[5].

The details of gene patents vary, but essentially they give the patent holder control of the access to a gene by other parties. For example, the company holding the patent for a gene may require a laboratory to pay a licence fee each time the gene is analysed, or insist that all tests of the gene be done in the patent-holder's facility. Note that the issue at stake is not the method of testing. It does not matter **how** a laboratory might analyse the gene; it is simply a matter of **whether** the laboratory analyses the gene. Further, it is no simple matter for a pathologist to determine whether a genetic test may infringe a patent, yet responsibility for this assessment rests with the laboratory, not with the patent holder or IP Australia.

When multiple patents and patent-holders have an interest in a gene it can complicate the analysis of that gene. Moreover, genetic tests are increasingly multiplexed to provide efficient analysis of multiple genes. For example, a common form of familial cardiac arrhythmia, "long Q-T syndrome", is due to a genetic error in any one of 12 different genes. . In the US, two companies hold patent rights to different combinations of these genes. As yet, the companies do not allow analysis of these genes to be included in a single test, resulting in delays and increased cost of the analysis[6]. Within the next few years, it may become possible to rapidly sequence the entire genetic code of a person (25,000 genes) and to include such an analysis as a component of routine healthcare[7]. However, the resulting "thicket" of competing and overlapping patents would be unworkable in terms of the number of agreements required to perform each test. The cost of testing could increase dramatically, and development of tests may decline, blocking innovation and inhibiting good clinical practice. The World Health Organisation has recently explored the possibility of patent clearing houses as a way of overcoming these potential problems[8].

As discussed below, there are explicit prohibitions against patenting naturally-occurring objects yet patents have been issued for thousands of naturally-occurring genes. The issuing of these patents defies explanation, and the widespread implementation of this practice could derail the effective and equitable delivery of healthcare that uses genetic knowledge. This risk is recognised by the many leading medical, genetic and bioethical organisations worldwide that have opposed the patenting of genes.

Organisation	Extract	Source
American College of Medical Genetics	"Genes and their mutations are naturally occurring substances that should not be patented."	www.acmg.net
American Medical Association	"Patents on processes - for example, processes used to isolate and purify gene sequences, genes and proteins, or vehicles of gene therapy--do not raise the same ethical problems as patents on the substances themselves and are thus preferable."	www.ama-assn.org
Australian Medical Association	"…the human genome should be regarded as the common heritage of humanity."	www.ama.com.au
British Society of Human Genetics	"A natural gene sequence is not an invention, but is a discovered product of nature."	www.bshg.org.uk
Human Genetics Society of Australasia	"The HGSA views the patenting of genes and gene sequences with great concern."	www.hgsa.com.au
Nuffield Council on Bioethics	"We think it likely that, if left unchanged, the patent system as it is currently applied to DNA sequences in the case of diagnostic tests will have a deleterious effect on the development and use of such tests."	www.nuffieldbioethics.org
European Society of Human Genetics	"The patenting on genes and genomic sequences is intrinsically different from the patenting of methods, tools and technologies, because there is no possibility to 'invent around' a DNA or RNA sequence."	www.eshg.org
College of American Pathologists	"In summary, we are facing the unprecedented situation in which a single patent owner can prevent physicians throughout the country from performing diagnostic procedures that use certain gene-based tests. This sets an extraordinary and dangerous precedent for patients and all of medicine, and strays from the constitutional and social purpose of the patent system to promote progress."	www.cap.org
UNESCO International Bioethics Committee	"The IBC, after considering this issue, is of the view that there are strong ethical grounds for excluding the human genome from patentability."	www.unesco.org/ibc

The RCPA recognises that the European Community has legislated that human genes are patentable subject matter[9]. The legislation obliged all member states of the European Union to modify their national patent laws along these lines. This remains a vexed issue across Europe with a number of member countries, including The Netherlands, Norway, and Italy, opposing the EC Directive.

In Australia and the US, the patenting of genes appears to have been based on precedent rather than principles. In 1912, an American court held that purified adrenaline (a naturally-occurring hormone in the body) was patentable, even though the natural hormone was not[10].

This was not a patent covering the process by which adrenaline was extracted and purified; it was adrenaline itself that was patented. The RCPA is not persuaded that this precedent represents an appropriate view of patentable subject matter. Precedent *per se* does not alter the fact that purified adrenaline has the same properties as adrenaline in the body, and that the patent applicant had not synthesised the adrenaline that he purified.

The Senate Inquiry is timely, and its impact will be determined by the extent to which the Inquiry addresses the issues that lie ahead. There are approximately 25,000 human genes that produce approximately 100,000 different proteins. Approval of more patents on these naturally-occurring substances will stifle the innovation and utilisation that is necessary for us to capitalise on this rich resource of medical information.

Genes should not be patentable

Australian patent requirements

To be patentable under the *Patent Act 1990,* a subject must be

- "an invention
- a manner of manufacture
- novel
- inventive, and
- useful, in that it meets its promise"[11].

When assessed against these criteria, human genes are clearly not patentable.

- A human gene is not an invention. DNA is a chemical and information source that has been widespread across the planet for thousands of years.
- A human gene is not manufactured. The isolation of a gene sequence into a test tube does not confer any altered chemical properties or change the information content of the gene. Indeed, a pathology test would be rendered useless if the information in the test tube differed from that in the natural gene in the person. This point was confirmed by the Deputy Director of the World Intellectual Property Organisation (WIPO) when he argued that "isolated, purified and synthesized human genes are not statutory patentable subject matter because, when isolated from the human body, they maintain identical or very similar characteristics to those found in nature … [and] because they realise exactly the same function that genes inserted in their natural environment perform." [12]
- A human gene is not novel. The concept of a gene goes back 150 years to the work of Gregor Mendel. The recognition that genes are a string of information goes back 100 years to Thomas Hunt Morgan. Our understanding of the double-helix structure of DNA goes back 50 years to Watson & Crick. And the practicality of isolating the gene responsible for a particular characteristic has been repeatedly demonstrated since the 1970s. The isolation of a gene reflects the cumulative work of thousands of people over many generations and nations.
- A human gene is not inventive. The sequence existed before the patent applicant was born.
- A human gene is not useful in the sense that testing of the gene does not have industrial applicability but is applied and interpreted in a specific context involving the health care of an individual person.

During the 1990s, the requirement to specify the utility of a gene patent was not stringent, and many gene patents were granted with little or no utility specified; some applications were in fact formulated as discoveries without any industrial application, rather than as inventions. More recently, there has been a greater emphasis on applicants specifying the specific utility of their gene patents.

The RCPA strongly supports the notion of patenting a novel treatment based on genetic knowledge, or patenting a new technique for genetic analysis. It may also be appropriate to patent genetic material that does not conform to a naturally-occurring gene, such as the oil-eating Pseudomonas bacterium quoted in the case of 'Diamond vs Chakrabarty in 1980[13], which had properties unlike any other bacterium found in nature. But human genes are discovered, not made, and consequently the RCPA believes they should not have been deemed patentable subject matter, just as one could not patent, for example, a kidney.

A further tenet of patent law is access to the new knowledge embodied in the patent in order to allow further invention around it. In other words the inventor gains a limited monopoly in exchange for the dissemination of knowledge. In contrast, the patent of a discovery such as a gene serves to deter innovation because access to the gene can be denied, making it impossible for another party to generate invention based on the discovery[14]. From the perspective of the societal and economic goals of patent law, the public would be better off if such patents were withheld.

Obligations under the TRIPS Agreement

The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) makes provision for Australia to block the patenting of diagnostic tests. Under Article 27.3(a) of the TRIPS Agreement, members may exclude from patentability "diagnostic, therapeutic and surgical methods for the treatment of humans or animals" [15]. It appears this has generally been interpreted by IP officers to refer to diagnostic tests performed on a person's body, but not to diagnostic procedures where a sample is removed from the body and tested in a laboratory. As a general principle, this seems illogical; the location in which a sample is tested may relate to convenience, cost or safety but it does not relate to the inventiveness associated with the method of analysis.

The RCPA considers that the interpretation of what constitutes a diagnostic test should be revisited.

Relevance of the patentability of genes to the Inquiry

We recognise that the Senate Inquiry has not been established primarily to assess the patentability of human genes, however this lies at the heart of questions about the impact of gene patents on the delivery of healthcare in Australia. If human genes had been correctly recognised as discoveries, not inventions, we would not need to consider the downstream consequences.

The issues being examined by the Inquiry are secondary consequences of a primary failure to apply patenting principles.

Licensing strategies used by gene patent holders.

Once a patent has been granted, the subsequent regulation of licensing is managed by the Australian Competition & Consumer Commission (ACCC). The impact on the provision and costs of healthcare will depend to a large extent on the type of model employed by the patent-holder or license holder to provide access to the patented gene sequence for testing.

Three models of licensing currently used in Australia are:

- open access model
- restricted access model
- closed access model.

Open access model

In this model the patent is likely to be owned by a public hospital or institution that allows free access for laboratories to test patients using their own in-house tests. In other words, there is no fee for testing the gene. Royalties may, on the other hand, be charged to manufacturers wishing to utilise the gene sequence in a commercial version of the test and this cost may be passed on to laboratories purchasing the commercial test kits.

A good example of this is genetic testing for cystic fibrosis, a common genetic disorder. This patent is owned by the Hospital for Sick Children in Toronto and there were approximately 11,000 tests performed in Australia in 2007[1], using in-house laboratory methods or commercial test kits.

There are a number of attractive features of this model.

- The free license to public sector providers and researchers recognises the role of affected families and researchers in many disciplines in the decades leading up to the isolation of the gene.
- The patent holder secures a revenue stream from commercial entities that capitalise on the isolation the gene by making test kits to market to laboratories. Pathology laboratories will usually purchase a reasonably-priced test kit rather than make an in-house test because the company then provides the test validation and quality assurance, a significant overhead in delivering any test.
- Families and funders benefit from the reasonable cost of the test.
- A laboratory is free to develop an in-house test if required to meet the requirements of its local population, as variations in the frequency of genetic errors mean that a genetic test may not be accurate in all ethnic groups. For example, a test panel developed for people of Northern European ancestry will typically detect 90% or more of the genetic errors that cause cystic fibrosis, but this panel will detect a much smaller proportion of the relevant genetic errors in people from Spain, and even fewer in those from South East Asia[16].
- Laboratories can implement training and quality assurance processes unfettered by considerations of the patent (discussed in more detail below).

Restricted access model

In this model, the patent-holder will typically offer one of two options:

either **The laboratory is licensed to perform its own in-house test**. This will normally consist of an up-front license fee and ongoing royalties for each test performed. The

royalty payments will usually be on a sliding scale with the royalty fee higher where fewer tests are performed. With this option, the laboratory can develop or fine tune a test to meet the requirements of its local population.

or **The laboratory must use a kit supplied (and method specified) by the patent-holder** (or sole licensee). This allows the patent holder to limit the number of tests that can be performed with each kit and the cost of the commercial kit may be significantly greater than an in-house test developed by the laboratory. Using a commercial kit generally prevents the laboratory from making modifications or extensions to the test to provide additional information in the local population. For this reason, the accuracy and usefulness of the genetic test may vary in different populations.

Australian examples of this model include the following: follows:

InVivoScribe Technologies

IgH and TCR gene rearrangements are commonly performed on cancer tissue from patients with lymphoproliferative disorders or acute myeloid leukaemia (AML). The results of these tests are used to guide therapy and subsequent monitoring of patients. In Australia there were a total of approximately 4,000 IgH and TCR testing performed in 2006 [1]. These analyses have been done with either an in-house method developed by a laboratory, or a commercial kit sold by the patent-holder, *InVivoScribe Technologies* of California.

The company has approached all Australian laboratories currently performing such tests and insisted that they

(i) confirm that they are testing exclusively with the company's kit and according to the company's method; *or*
(ii) confirm that they have switched to exclusive use of the company's kit and method, *or*
(iii) obtain a sub-license from the company to use their own in-house tests.

The cost of performing this test in-house is approximately $28 per patient (excluding labour, on-costs, and validation costs apportioned over each test). The cost of performing the test using the company's kit is approximately $292 per patient (excluding labour). Tests are not rebated by Medicare, and it is likely that the cost will be borne by either the public hospital or the patient. The sub-license cost is not known, but laboratories are reportedly switching to purchase the kit in preference. Some laboratories are ceasing to perform testing, choosing to refer to other laboratories; others are triaging their patient referrals for testing more actively[17].

LGC

LGC is a UK-based company which was the exclusive licensee for genetic tests of the cytochrome P450 gene; genetic errors in this gene can have a significant impact on the metabolism of some common medications. Prior to 2005 there was only modest interest in using genetic tests to guide therapy with common medications, and the test was provided by some Australian laboratories for approximately $250 [5].

In 2005, the company sought to enforce its rights by licensing laboratories offering the test. There was to be an initial fee of UK£20,000 plus 5% of any fees for tests performed. If these costs were amortised over a five year period, the test cost would have risen by 500%. The

situation was untenable and some laboratories ceased offering the test. In 2006 after these letters of demand received, there were only 140 assays of this gene performed nationwide[1].

Bio-Rad Australia

Haemochromatosis is one of the most common genetic disorders in the Australian population. In Australia there were approximately 28,000 HFE tests performed in 2007[1]. The condition causes excess iron to accumulate in the body, and this in turn leads to failure of many organs but there is a simple, cheap, and effective treatment available. Diagnosis of this condition was often difficult until the gene was identified in 1996 and genetic testing then became feasible. The HFE gene was patented and has had a complex history of ownership. Between 1999 and 2001, an American firm, Bio-Rad, acquired the patent rights covering HFE and its known mutations from other companies. The company developed its own kits for two common HFE mutations and then marketed these kits as an alternative to licence fees.

As the company began to assert its rights regarding testing of the gene, a significant number of US laboratories decided not to offer testing for this condition, either ceasing the service or declining to initiate one.[18] In Australia Bio-Rad has been less assertive in enforcing its patent rights, possibly because the market is so much smaller and testing would be likely to decline sharply. As a consequence the impact of the HFE patent in Australia to date has been minimal[19].

Genetic Technologies (GTG)

An Australian company, GTG, holds patents in many countries, which it claims cover the use and analysis of non-coding DNA in the human genetic code[20]. GTG has a policy of providing licenses at low cost to non-commercial laboratories however in 2004 the company demanded substantial license fees from public health providers in New Zealand for many standard DNA tests. This included analysis of genes such as those relating to cystic fibrosis, which are patented by other organizations (as noted above) but which require some use of the non-coding DNA adjacent to the gene. Initially, GTG demanded an upfront payment of $10 million dollars along with an annual licence of $2 million a year. The Auckland District Health Board challenged GTG's claims and the matter was eventually settled out of court[21].

Closed access model

Under this model, there is no sublicensing and the patent-holder insists that all testing be sent to a nominated laboratory.

Myriad Genetics

In the US, Myriad Genetics owns the patents for the two genes most commonly responsible for familial breast & ovarian cancer, BRCA1 and BRCA2. This has involved lodging or purchasing 17 or more patents held by seven different assignee groups[22]. There were initially four laboratories providing testing of these genes in the US, but Myriad Genetics has now become the sole US provider of BRCA testing, with all such tests performed at the company's laboratory in Utah..

Myriad Genetics sought to enforce its patent rights in Canada in 2001 when the company issued letters to public sector laboratories across the country demanding that all samples be sent to Utah for testing. The fee was to be three times greater than the cost for the hospitals to provide the test themselves[23]. Although some Provinces initially ceased testing, ultimately the Provinces continued to test and are ignoring the demands from Myriad Genetics. Myriad Genetics has also sought to impose this model in the UK where it met with strong opposition,

particularly because a British cancer research charity held a competing patent to the BRCA2 gene and was making no demands relating to testing of that gene. Myriad Genetics eventually gave up in the UK and provided free access for British laboratories to perform their own testing[24].

Genetic Technologies (GTG)

In Australia and New Zealand, testing of the BRCA1 and BRCA2 genes was introduced by public sector laboratories in most States in the 1990s and in 2007 there were approximately 2,357 BRCA1 and BRCA2 tests performed in Australia[1].

In 2002, Myriad Genetics provided an exclusive licence for testing of these genes to GTG[25]. GTG initially sought to enforce its rights against the public laboratories, a move which prompted vocal opposition, and in May 2003 the company announced to the Australian Stock Exchange that it would not be enforcing its IP rights for breast cancer susceptibility testing in Australia and New Zealand, and that these rights *"were a gift from GTG to the people of Australia and New Zealand."*[26]. In July 2008, GTG wrote to public sector laboratories performing these tests, stating that it would now seek to enforce its licence rights[27]; however the company has subsequently decided to reinstate its gift and not seek to enforce these rights[28].

This experience with breast cancer susceptibility testing highlights serious problems with the closed access model.

- Having a single service provider limits the opportunities for peer-to-peer comparisons in laboratory quality assurance, a long-standing element of laboratory QA (discussed below).
- Having a single service provider gives absolute control of price for the service, as evident in the price issues that faced Canadian healthcare providers. For two years, women in some Canadian Provinces did not have access to genetic testing for breast cancer susceptibility.
- Having a single service provider allows the patent holder to develop an exclusive and private database of the genetic variation for that gene in the population. This information is essential for determining the accuracy and utility of a test, but may not be available to independent researchers who would make such an analysis. This is the case with testing in the US for a common cause of familial cardiac arrhythmias in which the variant data is held in a private database that is not accessible[29].
- Having a single service provider exposes the delivery of health services to the risk of instability. The fact that one company could have such a significant destabilising influence on the delivery of breast cancer susceptibility testing in Australia is of great concern for laboratories performing these tests, for breast cancer health care programs and, most importantly, for patients[30].

The consequences of genetic testing monopolies

The licensing models presented above have different implications for the cost and delivery of genetic testing. These models also have collateral impact on issues of quality and sustainability in genetic testing. Quality and sustainability are "invisible" issues for most patients and requesting clinicians. It is assumed that the tests provided are accurate, and that there are people with appropriate skills to perform and interpret them.

The RCPA is the principal provider of training for medical specialists in pathology, partners with the National Association of Testing Authorities (NATA) in accrediting laboratories, provides continuing education for laboratory personnel, and is involved in identifying and managing workforce issues. Quality and sustainability are not invisible issues for us.

In particular, monopolies on providing a genetic test represent a significant threat to quality and sustainability of genetic testing. It is essential that this Senate Inquiry explore both current and future implications of gene patents and licensing practices in this regard. Our concerns in this domain are as follows:

Monopolies limit the training of genetic pathologists and scientists

By restricting testing to one laboratory, the training of the next generation of pathologists and laboratory scientists in the area covered by the patent will be impaired. Further it will limit the number of knowledgeable and trained individuals who can assist in the diagnosis and management of at-risk patients.

For example, the BRCA1 and BRCA2 genes are long and complex. An assay for a familial genetic error in these genes involves detailed analysis of 20,000 different nucleic acids (the "rungs" along the DNA double helix). The combination of complexity and size of these genes, together with the demand for testing, has made them the "flagship" of genetic testing in major public sector laboratories nationally.

In 2006, there were nine public sector laboratories providing these analyses[1]. Once the genes from a patient have been analysed, the scientist or pathologist has a major task in interpreting the 20,000 different results, and determining whether a particular genetic variation is causing disease or is simply a benign variation. The professionals performing this work gain skills that are immediately applicable in other areas of genetic testing. Involvement in this type of testing provides essential training for the next generation.

If genetic testing of the BRCA1 and BRCA2 genes were done by a single laboratory, the loss of volume, complexity, and training opportunities would significantly compromise the operation and sustainability of the public sector laboratories.

The RCPA recognises that not every genetic test will, or should, be offered by multiple laboratories across Australia. It is appropriate for many genetic tests to be offered by only one or two laboratories nationally because the demand is low. It is, however, the genetic tests that are in high demand that have commercial appeal for a patent holder – and these are the tests that should be tested in multiple laboratories.

Monopolies preclude review of test performance

One of the best ways of assessing performance of a diagnostic test is by benchmarking performance against peers and having independent assessment of external quality assurance. Establishing an open and effective regime of external quality assurance is problematic if only one laboratory is providing testing.

This is very evident in the Australian experience of testing of the breast cancer susceptibility genes. Laboratories share their experience through informal channels and a more formal consultative process brokered by a major national research study of familial breast cancer[31]. Inconsistencies between laboratories are identified, improvements in methods shared, and links between families with the same rare mutation clarified. This exchange involving

multiple professionals in different settings and with different experience is impossible if there is a monopoly on providing a genetic test.

As well as eliminating opportunities for collaboration, a monopoly removes a key mechanism for identifying errors. This is evident from the European experience of peer-to-peer assessment of laboratories providing testing of the BRCA1 and BRCA2 genes[32].

Monopolies block the development and implementation of better tests

A patent holder can block further developments of a genetic test, either by restricting analysis to one laboratory or by requiring laboratories to use a commercial kit. As noted above, this is inappropriate when providing testing to different ethnic groups because the frequency of certain genetic errors can vary widely.

A related issue arose in relation to breast cancer susceptibility testing. Myriad Genetics provided a test that sequenced every nucleotide in the two genes but this method failed to detect certain types of errors (called deletions) in these genes. A supplementary method was described by research scientists that would detect gene deletions, but for a number of years Myriad Genetics did not include this additional assessment in its testing. Other laboratories could not offer the supplementary test because they were not licensed to analyse the genes. Effectively the patent blocked the delivery of supplementary testing that would increase the accuracy and usefulness of the investigation. As a result, women were being incorrectly advised that there was no identifiable mutation in their genes, and that genetic testing in the family was impossible. Approximately 12% of women reported by Myriad Genetics to have normal BRCA1 and BRCA2 genes in fact had a deletion[33]. Myriad Genetics eventually included the supplementary assay in its test [34].

Monopolies create exclusive databases of genetic variants

Some of the genetic differences between individuals will be crucial in understanding health and disease, others may be inconsequential, and many are of unknown significance. If genetic testing is provided by multiple laboratories, they will often pool their records of genetic variants in public databases. As more data accumulate about the frequency of variants and their association with disease, this information will help laboratories to interpret variants and provide useful information to requesting clinicians and patients. These databases are in the public domain and are a resource for other laboratories, researchers, companies, and policy makers.

If testing of a gene is provided by a single laboratory, there is no incentive to create a public database of variants. In effect, the information about genetic variants becomes the property of the patent-holder, with no opportunity for this information to be reviewed by independent researchers, or made available for public analysis.

This information has commercial value. For example, the pharmaceutical industry is keenly interested in the association between genetic variants and disease. An American firm, 23andMe, offers people testing of 500,000 different genetic variants purported to define their risk of disease[35]. The company is backed by Google, which will manage the database with 500,000 data points per customer. If these data are linked with clinical information about the customers, this exclusive data resource could be sold to pharmaceutical companies[36]. The same potential exists for an exclusive database of genetic variants generated as a result of a monopoly on providing a genetic test[37].

Monopolies dictate inappropriate standards of care

This issue is discussed at some length in the draft report from the US Secretary's Advisory Committee on Genetics, Health, & Society[38]. The data are American, but the message is universal. As one clinician has stated:

> "I am outraged that anyone can control the use of medical information to the point that I cannot include the diagnosis of a disease in my medical practice. I can no longer perform testing for Canavan disease, Alzheimer's disease and Charcot-Marie-Tooth Type 1A disease because of patent enforcement. Other physicians are prevented from testing for breast cancer genetic risk."[39]

Whilst the RCPA recognises that healthcare necessarily involves costs, that healthcare providers must be financially viable, and that research and development must be funded, it is of the greatest concern that medical care could be compromised by decisions arising directly from the patenting of discoveries.

Patent holders can block access to appropriate testing, as mentioned above, and they may also promote testing that is inappropriate. Myriad Genetics, for example, has promoted genetic testing for breast cancer susceptibility to non-expert clinicians, and to the general public by placing advertisements in magazines, on television, and in the program for patrons attending a Broadway show about ovarian cancer[40,41].

Monopolies and medical research

The impact of gene patents on medical research was a key element of the ALRC report on gene patenting[42]. As a medical specialist College, the RCPA has a keen interest in research and the application of research findings in healthcare services, but recognises that other organisations are better placed to comment on the issues relating to gene patents and the future of genetic research. For this reason, we will not address this issue further in our submission.

Potential future remedies

The future of appropriate diagnostic and prognostic genetic testing for patients in Australia, provided in the appropriate clinical setting, and provided by appropriately trained and experienced genetic pathologists and scientists, will rely on finding solutions to the problems outlined above.

The RCPA considers that there is a need to:

- improve the quality of granted patents, and
- ensure broad, affordable access to the gene sequences that are subject to existing patents

Improving the quality of granted patents

Whilst the RCPA strongly holds to the view that gene sequences should not be patentable, this is clearly not a position that is shared by major patent offices worldwide including IP Australia. Furthermore many applications that have been granted have been broad to the point of speculative in regard to both their inventiveness and claimed utility. As pointed out in the

WHO consultants' report "… gene sequences without a proven utility should not be granted patents."[43]

Patent examination should be more stringent and, given the complexity in this area, IP Australia would benefit from having a scientific advisory committee to help guide the quality of their decisions. This may also reduce the time between lodgement and decision; such delays can be problematic because a new test may have been developed well before a patent is issued, and the patent can then impact upon the cost of and/or access to what has become a well established test.

The ethical aspects of gene patenting currently receive scant consideration by patent lawyers, patent applicants and IP staff during the patent process. The appointment of, or access to advice from, an ethics committee to provide comments and insight into ethical aspects of patenting within the biomedical arena should be seriously considered.

Ensuring broad access to gene sequences encumbered with existing patents

The OECD has provided firm guidelines for the licensing of gene patents and genetic inventions[44]. These guidelines, developed following a workshop held in Berlin in 2002, and published after adoption by the Council of the OECD in 2006, are designed to promote a balanced intellectual property system. The guidelines provide principles and best practices for licensing arrangements within the healthcare system so that patients may have appropriate access to new services and the healthcare system retains control of the implementation of new services. The principles and best practice guidelines in relation to healthcare are as follows:

Principles

2. A Licensing practices should seek to strike a balance between the delivery of new products and services, healthcare needs, and economic returns.
2. B Licensing practices should ensure that patients benefit from the highest applicable standards with respect to privacy, safety and good laboratory methods available pursuant to the laws of their jurisdiction or those of the jurisdiction of the service provider using the genetic invention.
2. C Licensing practices should not be used to restrict the choice of other products or services by patients and their healthcare providers.
2. D Licensing practices should encourage appropriate access to and use of genetic inventions to address unmet and urgent health needs in OECD member countries and non-member economies.

Best Practices

2.1 Rights holders should broadly license genetic inventions for research and investigation purposes.
2.2 Rights holders should license genetic inventions for health applications, including diagnostic testing, on terms and conditions that seek to ensure the widest public access to, and variety of, products and services based on the inventions.
2.3 Licensing practices should permit national or local providers to use genetic inventions in order to provide healthcare services, even if the rights holder is based in another jurisdiction.
2.4 Licensing agreements relating to products and services incorporating personal health information should facilitate compliance by the licensor and the licensee with the highest applicable privacy and other relevant laws.
2.5 License agreements should not restrict access by the licensee's researchers to databases generated from licensed genetic inventions in their efforts to develop new therapies, products or services**.**
2.6 License agreements should permit licensees, for example healthcare providers, to offer patients flexibility and choice with respect to the selection of the type and nature of healthcare products and services.

As a member country of the OECD Australia has a duty to promote these principles and best practice guidelines, and should look to ensure their application in healthcare for the benefit of Australian citizens.

There are various remedies available under the Australian patent system where patent holders do not conform to the OECD guidelines and, as a consequence, may adversely impact upon the health care of Australian citizens. These are:

- Crown use
- Compulsory licenses

Crown Use

According to s.163 of the Australian Patents Act 1990:

> "*Where at any time after a patent application has been made, the invention concerned is exploited by the Commonwealth or a State (or a representative), the exploitation is not an infringement :*
>
> *(a) if the application is pending – of the nominated person's rights in the invention; or*
>
> (b) *if a patent has been granted for the invention – of the patent*"

Further, according to s.171 of the Act:

> "*The Governor General may direct that a patent, or an invention that is the subject of a patent application, be acquired by the Commonwealth. When a direction is given, all rights in respect of the patent or the invention are, by force of this subsection, transferred to and vested in the commonwealth*.[…]"

Compulsory licenses

The use of compulsory licensing under the TRIPS Agreement is normally only applied where a patentee does not exploit the invention at all nor allow others to do so under license. This is unlikely to occur in relation to gene patents. However the Nuffield Council on Bioethics suggests that compulsory licenses should be used as a remedy in cases where the owner of a gene patent will either only issue licenses at unreasonable costs or will not offer them at all and maintains exclusive rights over any test utilising the gene sequence[45]. The Australian Government should also consider adopting such an approach.

Trade Practices Act

There may also be remedies available under the Trade Practices Act where an exclusive license of a medical genetic test may have the effect of lessening competition and thus constitute a breach of Part IV of the Act, and may also constitute an anti-competitive agreement under s 45 of the Act.

Remedies that are used in other countries

Other remedies that are available in some European countries to overcome restrictive or overly expensive license fees have been outlined in a recent publication on behalf of the European Society of Human Genetics[46]. These are:

- *Ex officio* licensing
- Licenses of right
- Clinical use exemption (proposed)
- Genetic sequence right (*Sui Generis)*

Ex officio licensing

This is a statutory institution where a government minister e.g. the Health Minister may grant a license to use a patented invention for important public health reasons where agreement could not be reached between the patent holder and the laboratory. Such legislation is currently in force in France and the Netherlands, and there is a similar model in Belgium.

Licenses of right

A patent holder in the UK, France or Germany may request the patent office to endorse his patent with license of right (LOR). This then entitles any potential licensee to negotiate with the patent holder to obtain a license. If no license agreement terms can be reached then they will be settled by the appropriate patent office or court. The terms of the license, in particular the royalties to be paid, are normally on the basis of a willing licensee/willing licensor informed by actual licensing practice and, where they exist, licenses entered into voluntarily by the patent holder. All licenses issued must be non-exclusive. Where the patent holder has requested a license of right endorsement on his/her patent then the annual renewal fees for the patent are reduced by 50%.

This system has been proposed as the model for the single European patent proposed for all EC member countries. Agreement has not yet been reached on this.

Clinical use exemption

In a major survey of biotech companies conducted in Switzerland, a clinical use exemption was strongly supported by many as a way of overcoming genetic testing patents and allowing testing at affordable costs.

Genetic sequence right (Sui Generis)

This model has been proposed by Dr Luigi Palombi from the ANU Centre for Governance of Knowledge and Development, and will presumably be part of Dr Palombi's submission to the Senate Inquiry.

RCPA response to Inquiry's Terms of Reference

The RCPA notes the emphasis in the Terms of Reference on identifying the impact of granting patent monopolies, and considers that the assessment of these secondary consequences must not distract those involved in the Inquiry from the primary event i.e. the inappropriate patenting of discoveries.

Terms of Reference	**RCPA response**
The impact of the granting of patents in Australia over human and microbial genes and non-coding sequences, proteins, and their derivatives, including those materials in an isolated form, with particular reference to:	The consequences of gene patents are readily predicted and the actual impacts of these patents are increasingly becoming evident. With 20% of known genes patented, there is already clear evidence of the adverse consequences of gene patents, and as more genes (and then proteins) are patented, the problems will continue to grow.
(a) the impact which the granting of patent monopolies over such materials has had, is having, and may have had on:	There is clear evidence outlined above that patent monopolies are leading to restrictions in the provision of healthcare, and increased healthcare costs, through (for example).:
(i) the provision and costs of healthcare,	- not permitting testing outside a particular laboratory - not permitting modification of a test to address ethnic differences - requiring that a commercial test kit be used that is more expensive than the in-house equivalent.
(ii) the provision of training and accreditation for healthcare professionals,	The RCPA considers that there are significant implications for the delivery of training genetic pathologists and scientists, as patent monopolies limit the opportunities to learn and share experiences between laboratories. Accreditation of laboratories is potentially affected also, as there will be fewer people with the expertise to evaluate the standard of testing being performed.
(iii) the progress in medical research, and	Patent monopolies preclude other investigators from fundamental research into the discovered gene, and from accessing databases of gene variants that could inform research. This in turn restricts innovation in genetic testing and thus the potential for improvements in health care over time.
(iv) the health and wellbeing of the Australian people;	By restricting access to testing and/or imposing prohibitive costs for patients, patent monopolies impair the health and wellbeing of a population.

	This has been demonstrated above in regard to BRCA testing in Canada and HFE testing in the US, and this risk for Australians is a growing concern.
(b) identifying measures that would ameliorate any adverse impacts arising from the granting of patents over such materials, including whether the Patents Act 1990 should be amended, in light of the any matters identified by the inquiry; and	The RCPA considers that the Act does not need to be amended, rather there is a need for attention to the interpretation of the Act by patent examiners. Decisions should be based on principles underpinning the legislation rather than precedents. In the event that a gene patent is, or has been, granted, licensing arrangements must avoid the patent holder (or exclusive licensee) having a monopoly on testing. The RCPA believes that licensing should be based on the open access model. If a restricted or closed access model is used instead, there must be support processes put in place to assist laboratories in trying to define their legal obligations under those licensing models. Specific arrangements (for example, through the ACCC) may be required to cater for tests involving multiple patents and patent-holders, to avoid laboratories having to negotiate a "patient thicket" and the consequences of increased cost and inhibition of good clinical practice.
(c) whether the Patents Act 1990 should be amended so as to expressly prohibit the grant of patent monopolies over such materials.	The RCPA considers that the *Patents Act* does not need to be amended to expressly prohibit granting of patent monopolies because genes are simply one aspect of the natural world, and should not require special protection under law. If, however, it is determined that a prohibition of patent monopolies is to be included in the *Patents Act*, it will be necessary for this to relate not only to genes but also to patenting of the 100,000 proteins and other natural chemicals encoded by these genes.

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RCPA
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Position Statement

Subject: **Patenting of Human Genes**
Approval Date: 25 July 2001, Revised June 2006; Revised July 2008, August 2008
Review Date: March 2012
Review By: Genetics AC
Number: 3/2001

The Royal College of Pathologists of Australasia considers genetic sequences identified in natural populations to be naturally occurring substances. As such, they should be deemed to be non-patentable. Any intellectual property rights associated with such genetic sequences should be limited to the method or process by which the genetic information was ascertained, or to novel inventions arising from this genetic information.

The fundamental purpose of a patent is two-fold:

- To disseminate knowledge
- To restrict its utilisation for a finite time, thereby providing a commercial advantage for the patent holder.

The granting of patents on human gene sequences is problematic and may have far reaching consequences in the provision of health care. The College is of the view that such patents would limit development, improvement and eventual use of genetic tests based on that knowledge. The College notes that a gene can be viewed as both the chemical substrate of genetic information and the information itself. The College's concern regarding gene patents applies to both perspectives.

Restricting the utilisation of genetic information by means of patents is likely to result in outcomes which compromise the optimum delivery of medical testing. Such restrictions may include:

- reduced patient access to testing,
- increased costs of testing,
- dictation of standards of care for testing by patent holders,
- reduction in peer review in test performance,
- creation of conflicts of interest e.g. if patents covering both a medication and a gene determining drug response are held by the one party
- restriction of further research relating to diagnostic testing utilising the genetic sequence.

In addition, the patenting of genetic sequences may -lead to specific adverse consequences, particularly in relation to medically complex tests. These consequences are likely to include:

- disruption of the clinician-laboratory interface which is necessary for appropriate interpretation and utilisation of these complex tests.

- difficulties in establishing an open and effective regime of external quality assurance.

- reduced training opportunities for laboratory scientists, geneticists, pathologists and physicians.

- the development of testing strategies which are dictated by commercial rather than medical considerations. For example, it may be commercially preferable to provide a limited repertoire of high volume tests rather than offer more comprehensive assays

which can also detect less common mutations. The gene patent may prevent another laboratory from providing a more comprehensive analysis of the same gene. This would impair the standard of care.

- limited evaluation of the clinical significance of genetic variants. The identification of mutations and assessment of their clinical significance usually requires interpretation of clinical data and test results from large numbers of patients. The patent holder is unlikely to have access to this type and volume of data.

The genome sequences for many organisms, including human beings, are now freely available. Efforts to commercialize this information should be focused on developing products and applications rather than restricting use of the underlying genetic information.

The patenting of genetic sequences has far-reaching implications because of the large number of human and microbial genes and their myriad interactions in human health and disease. It is essential that appropriate public policy regarding gene patents be developed and implemented before restrictive genetic testing through patent enforcement becomes widespread.

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19 September 2008

Mr Brendan Bourke
Secretariat
Advisory Committee on Intellectual Property (ACIP)
PO Box 200
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Brendan.Bourke@ipaustralia.gov.au

Dear Mr Bourke,

Re: ACIP Review of Patentable Subject Matter

Thank you for the invitation to make a submission regarding the ACIP review of patentable subject matter. The Royal College of Pathologists of Australasia (the College) is a professional organisation with an interest in the consequences of patenting on the delivery of genetic testing in healthcare.

General comment
In 2004 the Australian Law Reform Commission (ALRC) review of gene patenting [ALRC 99] noted that, "Although one cannot deny the legitimacy of patenting processes for isolating and purifying naturally occurring materials, or the legitimacy of patenting of new chemical substances that are the product of human ingenuity, there are attractive arguments for the view that such materials *should not have been treated as patentable subject matter*. However, the time for taking this approach…has long since passed" [ACIP Discussion Paper, page 60; our emphasis].

This conclusion recognised that the opportunity to subject many gene patent applications to appropriate scrutiny had been lost. Consideration of longstanding principles regarding patentability should have precluded many of the gene patents that have now been accepted.

The College welcomes the opportunity that the current review provides but it will be useful only if the principles that are clarified are translated into appropriate decision-making by patent examiners. Consequently, we recommend that conclusions of this review be partnered with recommendations designed to ensure that the principles are actually applied. Although the opportunity to prevent many gene patents may have been lost, the same issues will apply to future applications for the patenting of genetic sequences and proteins because research in these areas continues apace.

We now address each of the questions raised in the ACIP Discussion document.

Economic objectives of limiting patentable subject matter.
One issue that is tangential to this question but fundamental to the societal benefits of patenting is that there are economic disincentives to resolving disputes about the patentability of subject matter. Such disputes would not be about ownership of a patent, but about the right for anyone to have the patent. For example, challenging the patentability of the BRCA1 gene before an Australian court could cost millions of dollars and the successful litigant would have no capacity to recoup their costs because success would, by definition, render the patent null. This disincentive to challenge patents was recognised by the ALRC

99 report (page 478) when it suggested that challenges to gene patents might need to be made by a consortium of State, Territory, and Federal Health Departments.

One objective of the test for patentable subject matter should therefore be an assessment of the economic feasibility of subsequently challenging the patentability of that subject matter. This would mean that a patent application that might be challenged on the grounds of patentability would require a more stringent assessment than applications that could be challenged solely on the grounds of priority or precedence.

Economic effects of inherent patentability test.
No comment.

Ethical reasons for limiting patentable subject matter.
Ethical considerations must form part of the test for patentable subject matter. Ethical arguments reflect the primary goal of patenting to benefit society as a whole, to encourage innovation and optimise public access to new technologies.

Ethical considerations should not be left until after a patent has been granted for the courts to resolve, rather there should be a clear understanding of ethical limitations for patentable subject matter from the outset.

Ethical effect of inherent patentability test.
No comment.

Other reasons for limiting patentable subject matter.
No comment.

Content and structure of current Australian law.
The College considers that the content of current Australian law does not meet the objectives of the system. Naturally occurring sequences of DNA have been patented under these laws which represents patenting of discoveries of natural objects and, as such, these patents should not have been granted.

A chromosome consists of a length of DNA. Fragments of this DNA are copied, split, joined, and re-arranged in the human body. The presentation of such fragments in another context (e.g. a test tube) is not an invention. While the method may represent patentable subject matter, the isolated DNA sequences do not. Nor should a sequence made of a compilation of pre-existing DNA sequences be patentable as the joining together of naturally occurring sequences is also an established process in nature. The same applies to proteins derived from naturally occurring genetic sequences.

Whilst we recognise that this view has not always been shared by the courts and that a key precedent was set in 1912 when an American court held that purified adrenaline was patentable[1], we are not persuaded that this decision represents an appropriate view of patentable subject matter.

Issues with current Australian law.

A Combination of flexible and proscriptive tests
The distinction between a discovery and an invention with utility lies at the heart of the test for patentable subject matter and should not be incorporated in the flexible concept of manner of manufacture. As noted by the US Supreme Court, “The laws of

[1] Andrews LB (2002). Genes and patent policy: rethinking intellectual property rights. Nature Rev Genetics. 3:803-808.

nature, physical phenomena, and abstract ideas have been held not patentable. Thus, a new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E= mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of … nature, free to all men and reserved exclusively to none' ".. Similarly, a newly identified genetic sequence should not be patentable on the basis of the manner in which it is presented.

There should be an explicit, proscriptive test for patentable subject matter that precludes discoveries from consideration, irrespective of the utility of those discoveries.

B Value of existing body of case law.

The existing body of case law has not provided sufficient guidance regarding the test for patentable subject matter. As noted in the Discussion Paper, in 2000 the Intellectual Property and Competition Review Committee (IPCRC) concluded that, "mere discoveries – that is, the identification and specification of the nature, structure and properties of existing matter and its interaction – should *continue* to be excluded from the class of patentable subject matter…" [page 52; our emphasis]. This statement confirms that the principle of the non-patentability of discoveries was clearly recognised prior to 2000 yet despite this patents for the discovery of many naturally-occurring gene sequences were granted.

C General inconvenience, mischievous to the state and hurt of trade.

No comment.

D Archaic language.

We support the use of contemporary language in all laws and regulations.

E Threshold of inventiveness.

Inventiveness should be an explicit element of the test of patentable subject matter. As suggested in the Discussion Paper, this may require "replacing the concept of manner of manufacture in the Act with a new concept that purely relates to inherently patentable subject matter".

F Threshold of utility.

We endorse the ALRC view regarding the need for a more stringent definition and assessment of utility. This matter has already been addressed by the United States Patent and Trademark Office (USPTO) in relation to gene patents.

G Scope of rights awarded.

We strongly oppose the view that patents for naturally occurring genetic materials be granted, particularly without restriction on their utility being identified by the discoverer.

The utility of a discovery is not limited by context or the inventiveness of the applicant. A discovery may have unlimited potential and in such a case one must question whether the contribution of the applicant matches the benefits provided by owning the patent and the associated costs to society. When Samuel Morse sought a patent on all uses of electromagnetic waves, the US Supreme Court ruled that he could not patent every conceivable use of electromagnetic waves - he could only patent his invention, the telegraph[1]. Genetic sequences represent a discovery and the same logic should apply.

We emphasise the nexus of inventiveness and scope of utility. When there is unequivocal evidence of the subject matter being an invention, it may be appropriate not to restrict utility. But when there is hesitation about the subject matter being an invention versus a discovery, if the decision is made to grant a patent the proposed utility should be precisely described and delimited.

H Requirement for grant.
No comment.

International integration.
Whilst aiming for "best practice" could separate Australia from markets in which "adequate practice" yields significant commercial returns, Australia should not compromise on core principles such as discoveries not being patentable subject matter. There is no suggestion that compliance with the World Trade Organisation Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) would require such a compromise.

Article 27 of the TRIPS agreement mandates that patents should be available for inventions that are new, inventive, and capable of industrial application. The synthesis or method of analysis of genetic material may fulfil these criteria, and thus be patentable subject matter, but genetic material identified in nature cannot be regarded as being either new or inventive. We do not dispute the necessity for Australian patent law to comply with TRIPS. We simply reject the notion that gene sequences identified in nature are anything but discoveries, and argue that a fundamental principle of patenting has not been applied in the granting of many gene patents in recent years, both in Australia and overseas.

Our concerns are not unique to the Australian setting. There has been widespread international concern about the practice of patenting human genetic sequences. Hence Australia would not be pursuing an unusual path if human genetic sequences were deemed to be non-patentable discoveries. The same principle would apply to other biological discoveries being revealed by studies of proteomics in human health and disease.

International compliance of current Australian law.
No comment.

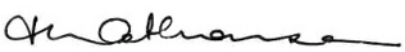
Preferred patentable subject matter.
As noted above, we do not consider it necessary or appropriate to have a special test for patentable subject matter for genetic material. The core principles of inventiveness, novelty etc should apply. But greater stringency is required if an application involves something that might be a discovery, or for which unlimited scope of utility is claimed. It may also be appropriate to have a more stringent assessment in new fields of human endeavour. For example, the introduction of computer software and genetic tests led to patent decisions by the USPTO which were subsequently questioned, with the USPTO introducing more stringent requirements for, and assessments of, utility.

We have also noted above that ethical considerations should be part of the test for patentable subject matter. Hence we do not support the position that, "all subject matters are patentable". We would support the third option noted in the discussion paper i.e. "all subject matters, except for a narrow or definable range, are patentable".

Legislative structure.
No comment.

Thank you for considering our submission and should you wish to seek clarification of any part of it please do not hesitate to contact us.

Yours sincerely,



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ALRC Inquiry – Gene Patenting & Human Health – Issues Paper No. 27
Response from
Genetics Advisory Committee
The Royal College of Pathologists of Australasia
October 2003

Chapter 4: Ethical, Social and Economic Dimensions

Q. 4-1 – *What are the principal ethical and social concerns in Australia about patents on genetic materials and technologies*?

The explosion in genetic information and technology has the potential to revolutionise health care in the coming decades. Genetic medicine will inevitably shift the focus of medical practice in developed countries more towards disease prediction and prevention. Ultimately, this should improve the quality and rationalisation of health care. It also has the potential to make billions of dollars for the companies involved.

Much of the current concern regarding the potential adverse effect of gene patents stems from the increased commercialisation of biomedical science during the past 20 years. This shift has resulted in a blurring of the distinction between not-for-profit science (previously conducted largely by universities and public hospitals) and for-profit science (previously mostly conducted by private companies). Spurred by government policy, previously wholly academic institutions, mainly in the US, have adopted business-like practices and have spun off numerous biotech companies. Underpinning these ventures are patents on genetic materials and technologies, derived largely from publicly funded basic research. A wave of new diagnostic and therapeutic inventions, based on genetic research is coming to the market. Their development has been funded in large part through private capital. These academic institutions and private companies have developed new strategies and business models for legitimate commercial exploitation of their patents, which aim to take maximum advantage of the very broad claims often included in their patents. While many of these new products will be highly beneficial, some of the new commercial practices also threaten the optimal provision of genetic healthcare and the integrated clinical services in the public sector. These largely unforseen consequences are the direct result of the imbalance between the commercialisation of science and the provision of public health care. This requires governments to devise new ways to protect public health interests from commercial excesses that arise from regulatory oversight.

A major concern regarding the commercialisation of research is that it results in disproportionate effort being placed on discoveries and inventions that would maximise short-term profits to the investor by targeting large, potentially lucrative markets, rather than on discoveries that would maximise long-term benefit to society. This exacerbates the disparities in the availability of diagnostic tests and treatments across socio-economic and ethnic groups within countries and between developed and developing countries. In addition, research into “genetic solutions” can overshaddow research into disease prevention in less glamorous, but more important, contributors to disease prevention. It is worth remembering that modifiable behavioural factors such as obseity, inactivity and smoking account for over 70% of cases of stroke, 80% of coronary artery disease and over 90% of adult-onset diabetes in developed countries and that infectious

diseases account for the majority of disease morbidity and mortality in the developing world. Overall, genetic factors account for a small proportion of human suffering. There can be little doubt, therefore, that humankind would receive much more benefit if the private funds currently invested in biotechnology were instead spent on basic public health.

The principal ethical, social and economic issue in relation to gene patenting is to ensure that the patent process facilitates a balanced and sustainable outcome over the long term for both commercial and societal interests. Balance is crucial because if patent protection is too weak, the development of technology or products may be inhibited by lack of incentives for investment. If patent protection is too strong, consumers may not gain sufficient benefit while the patent owner may gain profits that are far in excess of a reasonable reward for the research and development.

In the context of genetic health, these concerns relate primarily to equitable access to affordable genetic testing and therapies for those who require them. The challenge is to balance public access to genetic health services with appropriate commercial returns for socially beneficial research. **A major concern regarding gene patents is the <u>potential</u> for commercial patent holders to create genetic monopolies.** The potential for abuse of monopoly power will increase if a handful of large biotechnology companies emerges from existing small and medium-sized biotechnology firms. Commercial monopolies are the anti-thesis of public health because they serve the commercial interests of shareholders rather than the public.

A patent holder's absolute control of diagnostic methods is not in the public's best interest. The general public, however, is presently oblivious to the extent of genetic patenting and its potential impact (positively and negatively) on healthcare delivery. About 127,000 human genes and gene sequences are now covered by patents or applications for patents – about four times the number of human genes. To date, very few have had an impact on the delivery of clinical services but this is beginning to change. It is only in the last year that the possibility of enforcement of genetic patents in Australasia has brought the matter of gene patents to public attention. This has revealed that there is concern that patent laws may fail to provide the balance required. The public are not fools. They recognise that commercialism ultimately distils down to power and profit dictating priorities and products. They sense that big money is now calling the shots and that our public institutions are slow to respond to their needs and concerns. This feeling of disempowerment has been an important element in the rise of negative public sentiment in relation to the impact of genetic technology (eg genetically modified organisms) on human nutrition and the environment.

Holders of gene patents and licenses need to recognise that they have ethical and social responsibilities and be responsive to government, health care provider and community concerns as well as their shareholders' interests. Socially responsible patent and license holders strive to return a reasonable profit without disrupting the existing healthcare framework and by maintaining equitable and affordable access to testing. Size appears to be an important factor which seems to dictate how patent and license holders behave. Large pharmaceutical and biotechnology companies and universities are able to balance their patent portfolios to return a reasonable and sustainable profit (eg Roche PCR patent, Stanford University's Cohen-Boyer patent on recombinant DNA) without impeding research or health care provision. Smaller biotechnology companies (especially single patent holders) do not have this luxury and their economic reality and commercial aspirations sometimes force some to adopt more aggressive practices (eg exclusive testing licenses, monopoly laboratories, higher license and royalty fees, and to threaten legal proceedings for alleged patent infringement) that limit choice and affect equitable and affordable access to research tools and clinical testing.

The debate relating to gene patents is one manifestation of the collision between forces of intellectualism and commercialism. Intellectualism encourages freedom of enquiry and freedom to innovate and requires uninhibited access to information, reagents and methods. Commercialism encourages secrecy and requires protection of intellectual property. This difference is exemplified in the polarised philosophical viewpoints of the public vs private agencies involved in the Human Genome Project.

Government, business, legal, healthcare, research and community leaders need to engage the community in informed debate about how this balance can be best achieved. If we fail to do this, commercial interests will prevail and there will be a backlash from the neglected and uniformed elements of society.

Q. 4-2 – *Should ethical and social concerns about patents on genetic materials and technologies be addressed through the patent system? Are there other or better approaches for dealing with these issues?*

The patent system is an indispensable component of economic prosperity and technological advancement. It has provided enormous benefit to society. It is also a tried and tested system and works well most of the time.

The monopoly power provided by patents can act against the public interest by hindering further research and innovation and by restricting access to health care. This is exemplified by the failure of pharmaceutical companies to make affordable anti-retroviral therapies available to HIV-infected individuals in developing countries, until recent international criticism forced them to do so.

International bodies, such as UNESCO, have expressed concern about the morality of patenting human genetic material. This debate, however, has failed to influence patent policy in any meaningful way. The prime reason is that intellectual property law in many countries is not structured to handle social policy considerations. As long as patent applicants satisfy the technical requirements of their region's patent office, a patent will be issued. The European Patent Convention, however, does prohibit patentability where the commercial exploitation of an invention would be contrary to "order public" (public policy) or morality. Such provisions, however, are intended to prevent major moral transgressions, such as the development of biological weapons and to prohibit the cloning of humans, rather than to ensure equitable access to health care.

Since the patent system is essentially a social contract, it is important that it is perceived to be socially beneficial. The patent system, however, is a purely legal process and takes no account of moral, ethical or economic considerations. At present, societal concerns resulting from the misuse of patents seem to fall into "no-man's land". Society requires a system of checks and balances to ensure that the power provided by a monopoly is not misused or abused. Any attempts to address societal considerations by altering the patent system, however, could remove incentive and therefore discourage legitimate and socially responsible commercial interests. This could have unforseen and devastating consequences. Any changes to the patent system would therefore have to be made with great care and foresight.

It is probably wiser to protect society from the occasional misuse or abuse of monopoly power by imposing conditions or restrictions on the use of gene patents and by enhancement of defences, exemptions and "downstream" regulations rather than alter the patent process itself.

Q. 4-3 – *Is there any need to make special provision for individuals or groups whose genetic samples are used to make a patented invention to benefit from any profits from the patent? Are there any separate or special considerations that apply in this context in relation to indigenous people?*

Patients and patient groups are becoming more active in the promotion and facilitation of pre-clinical and clinical research. Various groups have started foundations for the funding of research, compiling disease-specific registries of patients and genealogical and medical databases, establishing tissue and DNA banks to provide resources crucial for genetics research, and developing scientific expertise that can make substantive contributions to the direction and performance of research. The motivation behind these contributions as well as the commercial interests have not been fully recognised by researchers and research organisations (Merz *et al*, Am J Hum Genet 2002;70:965-971).

There is evidence that some individuals and groups feel aggrieved at the patenting of their genes. 150 families from around the world, with children afflicted with Canavan disease, participated in an extensive research collaboration with researchers at the Miami Children's Hospital (MCH), which eventually led to the discovery of the aspartoacylase gene in 1993. These families participated in the studies, helped identify, solicit and collect blood samples from other affected families, and secured funding support from various religious groups, charities and Foundations. They also facilitated access to 6000 stored blood samples to estimate the population frequency of the mutation in the Ashkenazi Jewish population. Unbeknownst to the families, the researchers at the MCH secured in October 1997, US patent 5,679,635, which covered all diagnostic and therapeutic uses of the gene. MCH then embarked on what the families believed to be a restrictive and unduly expensive licensing programme. (Merz *et al*, Am J Hum Genet 2002;70:965-971). In October 2002, some of the families and organisations involved filed a suit against MCH in an attempt to prevent continued use of the patent in the manner they believe was immoral, unfair to those who made the research possible and likely to restrict access to the test (Greenberg v Miami Children's Hospital 2000). This dispute arose because gene patents create a conflict of ownership.

In the mid-1990's, a patient affected by psuedoxanthoma elasticum (PXE) created PXE International. The Foundation helped identify and solicit participation from affected families, established a registry and a biorepository, and raised money to support studies through the use of these resources. PXE International negotiated with researchers to whom they provided support and access to biomaterials for research and, through the use of Material Transfer Agreements, retained authorship in any papers and ownership rights in any patents to ensure broad and affordable downstream development (Merz *et al*, Am J Hum Genet 2002;70:965-971). The gene implicated in PXE was identified in 2000.

These two examples get to the heart of the paradox about "who owns your genes". All individuals have natural ownership of their genetic material, which they share with their genetic relatives and ultimately with all life. According to the principles of patent law, because genomic DNA is a naturally occurring substance, it is not patentable. Yet, tens of thousands of patents have been granted on DNA sequences that are identical to their natural form. These patents effectively confer ownership rights because they allow these sequences to be used, sold, traded, licensed and can be used to prevent others from doing so. The effect is that gene patents rob individuals of their natural ownership of their genetic material. Individuals, their families and their healthcare providers understandably become concerned when this limits access to genetic testing or genetic therapies.

The current stakeholders in genetic research include patients and families, disease-associated advocacy groups, foundations, government agencies, medical practitioners, hospitals, researchers, universities, biotechnology firms and pharmaceutical companies. All have common goals - the discovery of the genetic causes of disease and the broad availability of testing to patients and ultimately the development of treatments or cures. However, the various stakeholders have varied motives and incentives for performing, funding, participating in and promoting research. It is important to understand those interests so that strategies can be developed that best satisfy all of the parties. It is clearly unacceptable to presume that all stakeholders are pure altruists, as some policies and practices now do presume, especially when these stakeholders have contributed in some meaningful way to the research enterprise. It is unfair to these stakeholders for their "investments" to be wholly appropriated by universities and companies with no commitment to return to the community something of value that they can both access and afford (Merz *et al*, Am J Hum Genet 2002;70:965-971). Such views are in agreement with recent policy statements issued by the Human Genome Organisation (HUGO) (Science 2000;290:49).

There are ethical, moral, practical and economic concerns with a general claim that subjects should share in the financial rewards of research: subjects often stand to benefit indirectly as consumers, it may be unmanageable to provide individuals with any share in potential profits, the burden of such royalties might impede downstream research, and the contribution of individual subjects may be quite minimal given that they bear little of the risk. Furthermore, financial reward may establish a legal precedent to permit the sale of body tissues, eg kidneys for transplantation.

Entities involved in commercial aspects of research should be expected, as a matter of public policy and research ethics practice, to openly negotiate with individuals, foundations, disease associated advocacy groups to resolve issues of ownership, downstream control, limits on financial profit sharing and other acknowledgements of all contributions before the research is done. These processes should be incorporated into national guidelines (eg those of the National Health and Medical Research Council (NH&MRC)) on the ethical practice of research.

Furthermore, any use of human genetic samples from indigenous Australians must take into account their cultural values and wishes.

Chapter 5 : Funding for Research and Development

Q. 5-1 – *What are the implications of the grant of gene patents to institutions or companies whose research was publicly funded for: (a) encouraging further research into human health: or (b) maintaining cost effective health care in Australia?*

Governments rightly seek to boost commercialisation of basic biomedical research where there are health benefits. This is accomplished by various funding mechanisms and incentives.

The US Bayh-Dole Act (1980), which allows recipients of government funding to patent their inventions, is seen as being a major factor in the emergence of the biotechnology sector in the US and their dominance in the market. It is an excellent example of a social contract between government and inventors that has had highly beneficial effects. In Australia, an employing organization is still entitled to claim ownership of any intellectual property rights arising out of its

employees' research. This provides no/minimal incentives for individual researchers to develop their basic research into a commercial product.

To ensure that patent holders behave in a socially responsible manner the National Institute of Health (NIH) in the USA has promoted guidelines to discourage restrictive licensing and anti-competitive practices. **Similar guidelines should be developed in Australia, perhaps sponsored by the NH&MRC.**

Consideration should also be given to exempting non-commercial research and public genetic testing from patent infringement for inventions arising from publicly funded research.

There is an urgent need to clarify the attribution of priority when a patent is awarded to an inventor who was the "first to cross the line" in a research endeavour that involved multiple researchers, often in different jurisdictions, funded by a variety of public and private sources. For instance, *Myriad Genetics* obtained the BRCA1 patent but much of the break-through work was performed within, and was funded by, the public sector.

Q. 5-2 – *Should holders of gene patents that have implications for human health pay a levy on any royalties with such royalties to be used for future genetic research or for health care infrastructure? If so, should it make any difference whether or not the research leading to the patent was publicly funded?*

There is no need to invoke a levy for gene patents related to health care. Firstly, it makes much more sense to directly reduce or limit royalty and license fees. Secondly, it would be inequitable compared to other technologies.

Q. 5-3 – *In the United States, the government retains certain residual rights to intellectual property developed from publicly funded research. These include 'march-in' rights, the right to a government use license and the right to limit exclusive licenses. Is there any need in Australia for these or similar rights to be a condition of public funding of genetic research with implications for human health?*

Yes. The US government retains march-in rights to allow government to use patented inventions, funded by public funds, for the public good. This includes government-use licenses to exempt government from license and royalty payments, the right to limit exclusive (anti-competitive) licenses and to take title when the patent holder is slow to translate the invention for public benefit.

Considerations should be given for the Australian Government to retain similar march-in rights for publicly funded research (eg via the NH&MRC).

Q. 5-4 – *What are the implications of the government retaining intellectual property in any contracted genetic research with implications for human health?*

As the employing agency in contracted genetic research the government should retain IP rights. Government agencies (e.g. CSIRO) are, however, not necessarily the most suitable vehicles for product development and commercialisation.

Governmental and other agencies often use patents to block commercial interests from creating a monopoly e.g. the UK charity, *Cancer Research Campaign*, awarded the NHS free access to its BRCA2 patent and was able to block *Myriad* from enforcing its rival patent in the UK. Likewise, following the recent outbreak of SARS, the Centre for Disease Control (CDC) in the US lodged a patent application covering the sequence of the coronavirus responsible. Their motive was not commercial advantage; it was simply to ensure that the viral genome was freely available to researchers and public health laboratories everywhere. The CDC clearly recognise the potential for gene patents to limit vital research in public health.

Governments and government agencies should therefore retain all IP resulting from publicly funded research that relates to public health.

Chapter 7 : Gene Patents and the Healthcare System

Q. 7-1 *Do gene patents pose any distinct problems of cost for the Australian health care system beyond those applicable to new technologies generally?*

It is important to acknowledge that patent law does not apply uniformly to health care technologies and to recognise that gene patents may need to be treated differently. Medical skills (eg clinical examination, surgical procedures, histopathological evaluation) are a form of biotechnology that cannot be patented. Should this also apply to genetic testing?

One major difference between gene patents and those on pharmaceuticals, diagnostic tests/kits, radiological equipment etc, is that the latter can be improved and invented around. A fundamental tenet of patent law is that full disclosure permits others to try to improve the invention. DNA however, is so elemental that it cannot be improved or invented around. (Who can create a better BRCA1 gene?).

The other major difference is the relative ease of developing genetic tests compared to other technologies such as pharmaceuticals. The cost of developing, evaluating, manufacturing and marketing pharmaceuticals is so large that it requires rigorous IP protection and a secure monopoly. Genetic information and materials required to perform tests for most mutations in most genes are freely available from public domain databases or readily purchased from commercial suppliers. Genetic testing is therefore on a much smaller scale and can be established in virtually any accredited laboratory. Does this investment require the same degree of monopoly protection as for pharmaceuticals?

Q. 7-2 - *What specific problems do gene patents and future developments in genetic technologies pose for the cost and funding of genetics services?*

Gene patents *per se* do <u>not</u> pose a distinct problem to Australian health care. The potential problems arise from the way in which the monopoly power granted by patents is <u>used</u>.

Provided that genetic testing occurs in an open environment, fostering healthy competition between private sector companies and public sector organisations, then the competition will help keep costs manageable and access reasonable. Patents that preclude competition, research and innovation, whether they are patents on genes or any other item, can only harm the community.

A major problem facing clinical genetics services in Australia is the division of funding and responsibility by the State-Federal model of health care service delivery. The States are responsible for the costs of public health care, but the Federal Government is responsible for the operation of Australia's patent laws. The Federal Government is shielded from the immediate financial impact of decisions about the patentability of genes. The States will feel the impact more immediately but lack the responsibility for addressing the matter. The same issue lies at the heart of difficulties in developing a national genetics program. The Provincial Governments in Canada ran into the same problem when *Myriad Genetics* sought to enforce the BRCA patents in Canada. The Canadian Federal Government wouldn't act, and the Provinces were forced to act individually because of the financial and social costs involved.

Concern has been expressed about the potential for the enforcement of "non-coding DNA" patents held by *Genetic Technologies Limited* to adversely affect the delivery of genetic testing in New Zealand. The royalty and license fees requested from Auckland Hospital by *Genetic Technologies* (as reported by *Four Corners*) would be a significant proportion of the annual budget of many Australian diagnostic genetics laboratories. If Australian laboratories were to receive similar requests for payment, it would be difficult, in the College's view, for them to sustain a fee of that magnitude and continue to deliver their services.

A major problem likely to be experienced by diagnostic genetics laboratories in the next few years will be the difficulty of obtaining and paying for licenses to use gene patents to screen genomes for haplotypes and expression profiles. These tests will examine thousands of genes simultaneously. Thousands of individual licenses will have to be obtained from numerous separate companies. The administrative burden alone will be prohibitive.

Q. 7-3 – *What steps, if any, should be taken to facilitate the economic evaluation of the impact of gene patents on the cost of genetics services and other healthcare in Australia?*

There are no national programs in clinical genetics and hence no vehicle for national evaluation of issues such as this. All of the costing analyses in clinical genetics services are being done with very limited resources at the level of individual laboratories and States.

There is an urgent need for a national approach addressing service delivery and evaluation in clinical genetics. This program should include, but not be limited to, economic evaluation of the impact of gene patents on the delivery of clinical genetics services.

The OECD is reported to have concluded: "The few examples used to illustrate theoretical economic and legal concern [about gene patents] … appear anecdotal and are not supported by economic studies" (paragraph 10.47). It is true that there have been limited studies of the impact of gene patents on health care. However, there has been limited opportunity so far for gene patents to impact on health care. This is a new field and the advent of genomic medicine is very much in its infancy. It is inappropriate to suggest that a lack of evidence about the adverse impact of gene patents represents evidence of a lack of adverse impact of gene patents. It is essential that there be careful evaluation of the <u>potential</u> impact of gene patents on the delivery of health care. History is not necessarily a useful guide in a new discipline.

Chapter 8 : Overview of Legal Framework

Q. 8-1 *Do applications for gene patents raise special issues that are not raised by patent applications relating to other types of technology? If so, what are those issues and how should they be addressed?*

There clearly have been specific issues relating to the issuing of gene patents. This is exemplified by the US Patent and Trademark Office (USPTO) largely ignoring, in their granting patents on genes in the late 1980s and early 1990s, the requirement that a patent have substantial and specific utility. Recognizing that many of these patents, mainly those on ESTs with no known function, lacked utility the USPTO revised its utility guidelines specifically for gene patents.

There has been widespread concern that the USPTO has been too generous in its interpretation of novelty and inventiveness and too expansive in defining the scope of patents. This generosity flows to other nations who are required to follow suit because of their obligations under various international agreements that harmonize patents. These concerns need to be addressed by ensuring that patent offices apply the above criteria stringently and consistently.

Q. 8-2 - *Under Australian law, two types of patent protection are available—a 20-year term for a standard patent and an eight-year term for an innovation patent. Should the duration of gene patents be limited to a term less than 20 years? Would this conflict with Australia's obligations under the TRIPS Agreement? (See also Question 9 - 1.)*

The College has no specific comment to make.

Q. 8-3 - *Under the Patents Act 1990 (Cth) (Patents Act), in order to accept a standard patent application (or certify an innovation patent), an Australian patent examiner must be 'satisfied' that an invention is novel and inventive (or innovative) and must 'consider' that no lawful ground for objection exists. Should the threshold for acceptance of an application for a gene patent be raised? If so, what should the threshold be?*

This probably lies at the heart of many of the controversies arising from gene patents. The goal of patent officials is to apply the technical rules of patent law to permit the greatest number of patents. As such, the criteria that determine whether a patent application should be denied are generally narrowly interpreted.

The requirement that the examiner be "satisfied", "consider" and decide on "the balance of probabilities" appears to be too lenient. From an administrative perspective such lax guidelines allow the examiner discretion and flexibility. However, it also permits mistakes and misjudgements as well as omissions, and misinformed or deceptive patent applications to go uncorrected. More stringent criteria, based on objective evidence, clearly need to be developed and implemented. If a patent application is judged to be novel or inventive then the examiner must be certain, not satisfied, that this is indeed the case.

Do patent examiners have sufficient specialised knowledge and training to make informed decisions in complex areas such as biotechnology? This is especially pertinent when an application makes an excessively broad claim or does not fully disclose all prior art. Similarly, how are the various contributions to be attributed when an application overlaps with, builds on or

pieces together several pieces of prior art? Do these new applications eclipse all previous patents? These are not simple issues and require depth of knowledge and breadth of experience.

Q. 8-4 - *Are the mechanisms available under the Patents Act to challenge an accepted patent application or a granted patent (ie, opposition, re-examination and revocation) adequate in relation to gene patents and applications? What additional or alternative mechanisms might be required?*

The opposition, re-examination and revocation procedures are all effective mechanisms, however, they are not easily accessible. The process can be expensive and time consuming. Smaller organizations and companies are much more likely to make a pragmatic commercial decision to cease the alleged infringement activity or pay the requested licenses and royalties even though they may believe the patent to be invalid or illegitimate.

A very serious issue is the availability of "patent insurance". A patent holder can take out patent insurance on the grounds that a hostile challenge from a larger competitor could spell ruin. Patent insurance, however, can also be used to defend a weak patent, even one that should never have been issued in the first place. Once a patent-holder takes out patent insurance the merit of the patent becomes immaterial – it merely becomes an issue of money. The value of the patent then lies, not in its intrinsic worth, but in the cost of the legal proceedings. A patent holder protected by patent insurance is in a virtually unassailable position compared to small companies or institutions that cannot afford a costly legal battle. What little equality there may be in opposing the patent in the courts is lost. **Patent insurance therefore places much more responsibility on the patent office to ensure that patents are stringently assessed.**

The public sector has additional difficulties with these provisions. When public institutions face an infringement notice or wish to challenge a patent they believe to be invalid they have neither the resources to mount a challenge nor the support of government. Governments are understandably wary of opposing patents as it suggests that their patent laws and processes are flawed, yet they alone have the resources to mount a public challenge that may takes years and millions of dollars to resolve.

Q.8-5 - *Does IP Australia have the capacity to scrutinise applications for gene patents effectively? Is there a need for IP Australia to develop new procedures or guidelines in this area?*

The College has no specific comment to make.

Q. 8-6 - *Would the administration and enforcement of gene patents benefit from concentrating jurisdiction for patent matters in a single court? If so, how might concerns about the cost and complexity of enforcing gene patents be addressed?*

The College has no specific comment to make.

Chapter 9 : Patentability of Genetic Materials and Technologies

Q. 9-1 - *Would changes to the requirements for patentability under Australian law for inventions involving genetic materials and technologies, or to the application of those requirements to such inventions, conflict with Australia's obligations under the TRIPS Agreement?*

A key principle of the publicly funded Human Genome Project was that all human genetic sequences be freely available to all people as a resource for research, development, and wonder.

Dr Francis Collins, Director of the National Human Genome Research Institute in the US, is of the view that genes, except those that encode therapeutic substances (such as insulin), should never have been patented. He is not alone in expressing disquiet about gene patenting. Communities and legislatures in the USA, Canada, and Europe have vociferously opposed the granting of gene patents by their own patent offices.

The fact that gene patents are currently accepted in other jurisdictions does not *per se* indicate that Australia should follow suit. Under Section 27.3 of the TRIPS agreement, Australia does not forgo its right to make its own examination of patent applications and can grant exemptions. Genes could be declared as being exempt from patenting in Australia because gene patents represent a hazard to society. Such an exemption, however, would represent a major deviation from the spirit and the letter of current patent law in Australia and the TRIPS agreement.

Q. 9-2 - *How should the novelty requirement apply to applications for patents over isolated genetic materials or genetic products? Are special considerations relevant in assessing the novelty of such inventions?*

Natural materials are only novel in the sense that they had not previously been discovered by humans. Natural DNA sequences are the result of over a billion years of evolution and exist independent of inventors.

Q. 9-3 - *In light of the DNA sequencing technology now available, does the identification and isolation of genetic material involve an 'inventive step' or an 'innovative step' under current Australian law? Are the current tests for 'inventiveness' and 'innovation' appropriate for assessing the patentability of genetic materials and technologies? What alternative or additional considerations might be relevant in assessing the 'inventiveness' or 'innovation' of such inventions?*

The invention of methods for sequencing DNA was one of the most significant and revolutionary advances in biological science. The sequencing of genes in the late 1970s and 1980s was a heroic task. Today, all the reagents and equipment required for sequencing known and unknown DNA sequences are commercially available and it can be performed on an enormous scale.

Are the criteria for inventiveness still being met today? The methods for DNA sequencing are now obvious to people working in this field with good knowledge and experience of the subject. The test of inventiveness, therefore, now rests entirely on whether the sequence of a particular gene was not obvious. This test will apply in most instances because the sequence of bases of an unknown gene cannot be known before it was isolated. This, however, is a test of novelty not inventiveness, highlighting the problems and confusion that arise when biological discoveries are (wrongly) regarded as inventions. The issue is further confounded because information from homologous genes in other species, known functions and *in silico* predictions etc can all provide some clues to the sequence of a gene.

The process of identifying unknown DNA sequences is now commonplace and can be easily performed by someone skilled in the art, even if the sequence is novel and non-obvious.

Identification and isolation of unknown genetic material today is routine and it is, therefore, difficult to justify it as being innovative or inventive.

Q. 9-4 - *In applying the 'usefulness' requirement for patentability under Australian law to inventions involving genetic materials and technologies:*

- *Do patent applications claiming such inventions raise specific issues that are not raised by other technologies? If so, what are those issues?*
- *What alternative or additional considerations might be relevant in assessing the 'usefulness' of such inventions? Would it be appropriate to require that inventions demonstrate 'specific, substantial and credible' utility to be patentable?*
- *Should 'usefulness' be considered as part of the examination of a patent application? Should lack of utility also be a ground upon which a patent application might be opposed or re-examined?*

One of the major criteria for patentability is demonstration of utility. **One of the major problems relating to the utility of genes is that we do not know the varied roles of most genes and claims about their actual or potential utility are largely grounded in ignorance.**

Further complications arise because patent law has not firmly established how much knowledge the inventor must possess of the specific function of a novel genetic sequence. The requirement for patents to have substantial and specific utility was largely ignored by the USPTO in granting patents on genes until the late 1990's. Recognising that many of these patents, mainly those on ESTs with no known function, lacked credible utility, the USPTO revised its utility guidelines to require demonstration of utility that was specific, substantial, and credible. With regard to *IP Australia*'s approach, it is important that the criteria for "usefulness" of a genetic patent be the same as the criteria for other patent applications. There should not be special rules regarding the utility of genetic patents.

It seems sensible to include an assessment of usefulness in an opposition or re-examination of a patent – however, it is unlikely that anyone would seek to oppose or re-examine a patent on an invention that was not useful.

Q. 9-5 - *In applying the 'sufficiency' and 'fair basis' criteria to applications for gene patents:*

- *Do claims in applications for gene patents raise specific issues that that are not raised by other technologies? If so, what are those issues?*
- *Are any additional or alternative considerations relevant to assessing the appropriate scope of patent claims involving genetic materials or technologies?*

Claims in genetic patents do not raise specific issues that require special consideration. Genetic patents should be assessed using generally applicable criteria.

However, the patent office is not always adequately equipped to assess complex applications relating to genetic materials and technologies. This is especially problematic when an application relates to a claimed method that has broad applicability. If the basic nature of the claim is genuine then such broad claims may be appropriate. However, unreasonably broad claims may be approved as a result of lack of expertise on the part of patent examiners. In the early 1980's the USPTO granted a number of broad patents in the newly developing area of software. They subsequently reviewed and revoked some of these patents because they were recognised as being too broad.

The patent office therefore needs to maintain specialist expertise in emerging technologies, including genetics.

Q. 9-6 - *Should ethical considerations be relevant in assessing applications for gene patents? If so, should a specific provision to that effect be introduced into the Patents Act 1990 (Cth), or is the current 'manner of manufacture' test sufficient to accommodate such considerations?*

This is difficult. Ideally, gene patents should not be treated any differently from other types of patents. **The existing rules, however, need to be stringently and consistently applied**.

However, there has to be some recognition that the patent offices have been too lenient in issuing gene patents and have potentially created a enormous problem with ethical and social implications. The best way to address these issues is through broadening the defense and exemption criteria for infringement (ie declare that private use includes non-commercial genetic testing of individuals), rather than by incorporating ethical considerations into the patent process.

Q. 9-7 - *If ethical considerations became relevant in assessing applications for gene patents, who should be responsible for developing guidelines, providing advice, and ultimately making determinations about such issues?*

The proposed Human Genetics Commission of Australia may provide a mechanism for assessing the ethical and societal consequences of certain genetic patents and for implementing and overseeing "downstream" processes.

Q. 9-8 - *Should isolated genetic materials and genetic products be regarded as 'discoveries' rather than 'inventions' for the purposes of Australian patent law, and thus excluded from patentability?*

The distinction between a discovery and an invention is an unresolved issue in the current debate about gene patenting. The word "discovery" means finding something that is already there. The word "invention" refers to the process of using human ingenuity to put something together that could not have existed otherwise.

In Europe and most other countries, patent law excludes the protection of discoveries. In the US, although both discoveries and inventions can be protected under patent statute, in practice the law does not permit the patenting of discoveries. In Europe, the US and elsewhere, a discovery that has a useful application can be protected by a patent if it is claimed as part of an invention.

There are two polarized ideological viewpoints regarding the patentability of genetic material. Both pivot on whether it is inventive to determine the sequence of DNA that has been isolated from its natural state. One view maintains that a novel isolated substance cannot be regarded as an invention because nothing that did not exist before has been created. The BRCA1 gene, for example, could not (and still cannot) be improved, there is no prospect of another person inventing a better version in the future, and there is no conceivable way that it could be made redundant by a new invention. The other view, in essence, argues that a novel isolated substance is an invention because it has been rendered useful.

In 1988, the European Patent Office (EPO), the USPTO and the Japan Patent Office issued the following joint statement clarifying their position on this matter: ”Purified natural products are not regarded as products of nature or discoveries because they do not in fact exist in nature in an isolated form. Rather, they are regarded for patent purposes as biologically active substances or chemical compounds and eligible for patenting on the same basis as other chemical compounds” (Crespi. Bio-Science Law Review 2001; 3; 199-204). Isolated human genes and their variations are therefore deemed to be patentable, if they are of demonstrable utility despite their origin as products of nature. Furthermore, patent offices have chosen to regard each gene as a new chemical compound and to grant “composition-of-matter” patents, which cover the use of the substance for any potential use, even ones not disclosed or known to the patentee. The USPTO rejected the counter-argument that genes should not be treated as novel chemicals but as biological software comprising a programme written in the sequence of the nucleotides and hence subject to copyright rather than patent law. Patent offices have instead taken the view that without isolating a gene, it is not possible to know its sequence. Genetic material, although contentious from a biological perspective, is now well established in law as being an invention.

Overall, this approach is socially preferable because the advancement of genetic science and medicine requires knowledge of the DNA sequence. Arguments that patents on human genes in particular should remain within the public domain have also lost out to the pragmatism of the patent offices.

Q. 9-9 - *Should methods of diagnostic, therapeutic and surgical treatment of humans involving genetic materials or technologies continue to be patentable under Australian law? If not, how should the exclusion of such inventions from patentability be justified, and what should be the scope of the exclusion?*

Yes, the College agrees that genetic materials and technologies should continue to be patentable. However, holders of gene patents need to recognize that society has effectively granted them control of access to everyone’s genetic material.

The RCPA believes that there should be a social contract that guarantees freedom of access or affordable access to genetic sequences for non-commercial research and genetic testing for health care. This could be achieved within the framework of the existing patent system by imposing specific conditions or restrictions, by permitting defense under the “private use” provisions or by governments granting exemptions for performing non-commercial research and genetic testing for health care reasons.

Chapter 10 : Licensing and Enforcement of Patent Rights

Q. 10-1 - *Is sufficient information available to holders of Australian gene patents to allow them to protect their patent rights? If not, what alternative or additional information or facilities might be required?*

The College has no specific comment to make

Q. 10-2 - *To what type of gene patents are Australian companies, researchers, health care providers or other organisations seeking or granting licenses? What uses are being made of such licensed gene patents?*

Most genetic tests are currently developed and evaluated "in house" using commercially available reagents and genetic information that is freely available from public domain databases and publications. A laboratory performing a genetic test that uses patented genetic information may require a license from the patent holder to legally perform that test. However, such licenses are rarely requested by the testing laboratory or demanded by the patent holder. As such, many laboratories may be performing a number of their tests "illegally" and may be leaving themselves open to being sued.

In relation to patents covering genetic materials (ie gene sequences) used in diagnostic genetic testing in Australia, it appears that patent and license holders are not pursuing their rights. Of the 200 or so genetic tests listed on the HGSA website, over 40 are covered by patents filed with the Australian Patent Office (Nicol D. Today's Life Sciences Sept 2003). However, the RCPA is not aware of a single example of an Australian company seeking licenses from, or granting licenses to, Australian diagnostic laboratories. The College understands that *Genetic Technologies* has an exclusive license from *Myriad Genetics* to perform BRCA1 and 2 testing but has issued a statement that this will not be enforced against other laboratories in Australia.

Patents covering genetic technologies (ie methods and reagents) fall into two groups – those with and without products. Most companies sell products and incorporate royalty payments in the product price. In the US, *Bio-Rad* sell a kit for haemochromatosis testing. The company permits laboratories to perform the haemochromatosis test using in-house methods and reagents but charges royalty and license fees that, on a per test basis, are considerably more than the cost of using the test kit. A survey of US laboratories previously performing this test revealed that approximately one third of laboratories ceased performing the test because of patent considerations (Merz et al, Nature 2002; 415:577-9)

Of particular concern are the detrimental effects that could occur if a patent or license holder refused to license, issued cease and desist orders or imposed onerous or unreasonable terms in the license. Such terms may relate to test price, the quantity of tests that can be performed, which laboratories the tests can be performed in, whether further research is allowed to improve the quality or specificity of the test or its applicability to a particular ethnic group and so on. This is a very real concern to most diagnostic genetics laboratories.

Q. 10-3 - *Are requests for licenses to Australian gene patents being refused by patent holders? If so, why? If not, are the terms of such licenses fair and reasonable?*

The College is not aware of any refusals to grant licenses for Australian gene patents.

Q. 10-4 - *Are gene patents being enforced against Australian companies, researchers, healthcare providers or other organisations? If so, what types of gene patents are being enforced and by what means (for example, with cease and desist letters, offers to license, or the threat of infringement proceedings)?*

A US study (Cho M, J Molecular Diagnostics 2003;5:3-8) identified 12 genetic tests that US laboratories have stopped performing due to patent enforcement. *Myriad Genetics* has effectively

prevented all laboratories in the US, other than its own, from performing BRCA1 and 2 testing. Notably, seven of the 12 tests mentioned above are covered by equivalent Australian patents or are subject to patent applications in Australia. Therefore, Australian laboratories may be exposed to such actions in the future (Nicol D, Today's Life Science. Sept/Oct 2003;22-27)

The RCPA is not aware of any Australian company seeking to enforce gene patents against Australian diagnostic laboratories. The RCPA, however, had been concerned following the announcement by *Genetic Technologies* on October 28 2002 that it had acquired an exclusive license from *Myriad Genetics* to perform BRCA1 and 2 testing and had been quoted in the media as saying that "public clinics providing the screening service were operating illegally" (Watts K, West Australian December 7 2002 and Quinlivan B, Business Review Weekly January 16 2003). Concerns over possible litigation resulted in one Australian public laboratory temporarily ceasing BRCA testing. Subsequently, in July 2003, *Genetic Technologies* issued a statement that it "does not intend to enforce these *Myriad* patents".

Of more immediate concern are *Genetic Technologies'* "non-coding DNA" patents. Various aspects of human genetic research and a number of common genetic tests performed by diagnostic laboratories could infringe these patents. Several Australian organizations have received offers for licenses from *Genetic Technologies*. *Genetic Technologies* has negotiated a range of sums from nominal fees eg $1500 for Sydney University (Smith D, Sydney Morning Herald Aug 4, 2003) to $ $2.5 million for CY O'Connor ERADE Village Foundation (http://www.gtg.com.au/) from Australian organizations and companies. Concern has been expressed about the potential for the enforcement of "non-coding DNA" patents held by *Genetic Technologies* to adversely affect the delivery of genetic testing in New Zealand (see response to Q7.2).

Ultimately, Australia may be protected by virtue of its small market size, by the fact that most genetic testing in Australia is performed free of charge by public hospital laboratories, and because patent holders might be wary of creating adverse publicity by targeting public institutions. Nevertheless, it is hardly desirable for the cloud of patent infringement proceedings to hover over the delivery of health care services (Nicol D, Today's Life Science. Sept/Oct 2003;22-27).

Q. 10-5 - *Are the potential costs involved in litigating patent infringement actions preventing the enforcement of Australian gene patents? Are there any other factors influencing the decisions of holders of Australian gene patents about whether or how to enforce such patent rights?*

The high costs of litigation are an issue for any company contemplating pursuing patent infringements.

Chapter 11: Patents and Human Genetic Research

Q. 11-1 - *Is there any evidence about whether gene patents or licenses are encouraging or inhibiting research in biotechnology in Australia?*

Patent protection is clearly an indispensible aspect of commercial biotechnology. This is best summarised by the well known business maxims "if you can't patent it, don't invest in it", "no

patent - no product" and "technology is only as strong as its patents. " The importance of patents to biotechnology can also be assumed from the maintainance of a pro-patent liberal policy framework.

It is important to distingush between two types of invention or innovation - breakthrough discoveries and those that improve on existing technology by creating a better or alternative product. Prior to 1980 basic "upstream" discoveries, such as the H2 receptor responsible for gastric acid secretion, were considered to be in the public domain. Only specific tests or therapies ("downstream discoveries") that harnessed this basic knowledge, such as H2-receptor antagonists, were patentable. Following a 1980 landmark decision of the US Supreme Court, upstream discoveries such as genetic sequences and genetic variants became patentable. Excessively broad patents, particularly on an upstream discovery, can block or place severe constraints on the ability of others to develop new tests or therapies that build on the patented discovery or invention. There is evidence that such practices have inhibited research in biotechnology (Heller and Eisenberg, Science 1998;280:698-701, Knoppers. Nature Genetics 1999; 22; 23-26).

Many researchers, particularly in academia, assume that basic experimental "upstream" research is exempt from patent infringement. In the US, the so called "research exemption" is rooted in an 1813 case (*Whittlemore v. Cutter* [9.F Cases 1120 D.Mass, 1813]). In approving a jury instruction that defined patent infringement as "the making of a machine fit for use, and with a design to use it for profit, " Justice Story speculated that "it could never have been the intention of the legislature to punish a man, who constructed a [patented] machine merely for philosophical experiments." (Eisenberg R, Science 2003;299:1018-9). However, such gratuitous statements have no binding legal authority which has led to calls for this dicta to be given statutory status (Bruzzone, Am Intell Prop Law Assoc 1993;21:52, Parker, J Int Law 1994; 16:615). The US Federal Circuit, however, has been signalling its discomfort with the experimental use defence for almost 20 years (Eisenberg R, Science 2003;299:1018-9).

The recent ruling in the *Madey vs Duke University* case (No 01-1567, Federal Circuit Court of Appeals, 3 October 2002) is about to turn the long-standing belief in the research exemption on its head. The judgement held that academic research is not "philosophical inquiry" but rather a means to advance the 'legitimate business objectives" of a university that "increase the status of the institution and lure lucrative research grants, students and faculty". It is hardly surprising that the court should hold that such exemptions no longer apply since universities have been increasingly acting like commercial entities, profiting from their own patents and suing infringers. In the two decades since the Bayh-Dole Act, US universities have embraced the patent system as patent owners and have been in the vanguard of claimants seeking patents on "upstream" research discoveries that would have looked far too removed from the commercial marketplace to qualify for patent protection just a generation ago. As their patent portfolios have grown, universities have become more aggressive about enforcing their patents in court. The University of California's $200 million settlement with Genentech (Barinaga M, Science 1999; 286;1655) and the University of Minnesota's $300 million settlement with Glaxo-Wellcome (www1.umn.edu/urelate/newsservice/newsreleases/99_10glaxofacts.html) have emboldened others to follow with their lawsuits. However, universities have barely begun to contemplate the implications of the patent system for their interests as users of the patented technology of others. Generally, it is only when scientists have sought access to materials and data that they could not readily duplicate for themselves that universities have entered into negotiations. They have largely ignored the growing number of patents covering technology that their scientists use without license. While universities have become increasingly aggressive as patent owners, they have left themselves vulnerable to patent infringement claims as defendants. With their endowments and their habit of documenting their activities in scientific publications, universities

might make worthwhile and easy targets (Eisenberg R, Science 2003;299:1018-9). The full impact of this development is not yet known but it has the potential to significantly inhibit research if the payments requested of universities by patent holders are too high.

There is evidence that Australian patent holders have already begun requesting Australian researchers for royalty and license fees for research tools and methods once considered free for the picking. It has been reported that *Genetic Technologies* has sent letters to several Australian academic institutions requesting royalty and licence payments for use of their "non-coding DNA" patents, prompting leading international reseachers to criticise this practice (Smith D, Sydney Morning Herald, July 8, 2003).

So far there has been no documented adverse effect in Australia, however, the field is very new and there has been little time to observe such impact. It is not, however, appropriate to stand back and wait for problems to occur. Given overseas experience, it is particularly important that legal review be fostered pro-actively with a view to avoiding problems because it takes years for such processes to be completed. The failure to tackle similar issues rapidly in the late 1980s and early 1990s led to thousands of gene patents being filed and granted before the patent offices awoke to issues that have now been addressed with revised guidelines for patent examiners (e.g. new USPTO Utility Examination Guidelines were issued on 5 January 2001 [USPTO Fed Reg 66:1092, 5]). It will be difficult (if not impossible) to "wind the clock back" and have gene patents of unspecified utility or inadequate specificity revoked. The ALRC must learn from the overseas experience and evaluate not only the previous or current problems but also the potential problems. If we are to avoid retrospective legislation in an attempt to address problems after the event, then the ALRC must take a pro-active stance in looking for problems that have yet to arise. Given the ingenuity of Man and the billions of dollars at stake in genomic medicine, there is no doubt that problems can and will arise.

Q. 11-2 - *Do any of the following affect biotechnology research into human health in Australia: (a) broad patents over isolated genetic materials; (b) patents over expressed sequence tags (ESTs) of unknown utility; (c) patents over single nucleotide polymorphisms (SNPs); or (d) a multiplicity of patents (sometimes known as 'patent thickets')?*

Broad patent rights over genes and their mutations make it difficult for alternatives to be developed. This occurs because the broad patents granted on genetic material extend to all modes of diagnostic testing for that and any other disease associated with the gene, including methods that are subsequently discovered or invented by others. One US survey has suggested that research on genetic testing has been inhibited by patents on DNA sequences. Half of all research laboratories surveyed had ceased to pursue research because of existing patents (Cho, In Laboratory Medicine for the 21ST Century. 2nd ed. AACC Press, Washington DC, USA 1998;47-53). Broad claims, therefore, discourage others from undertaking research to identify new mutations and disease associations and from investing in improved testing methods. It would have been far more preferable for patent protection to have been applied not to the gene, but to specfic diagnostic methods. This would then provide an effective means of rewarding the inventor while providing an incentive for others to develop better alternatives.

A major concern is the potential for the extension of patents on ESTs to patent applications involving full length DNA sequences (containing the previously filed EST) of known biological function. This is because composition of matter patents extend to all potential uses of an invention including those subsequently developed by others. Research and development on the full length DNA sequence may, therefore, be inhibited by such "dependent patents" when they are held by different owners. The Human Genome Organisation has called on patent offices not to

issue patents on ESTs without having found a balanced solution to this problem The College is not aware of any patents on ESTs that are affecting biotechnology research into human health in Australia. It is our understanding that very few patents on ESTs have actually been granted and that none have been challenged in court (Bobrow and Thomas, Curr Opinion Molec Therapeutics 2002;4:542-7).

The SNP Consortium, a collaboration of several pharmaceutical firms and the UK Wellcome Trust (Masood, Nature 1999;398:545-6), is one mechanism researchers have found to overcome "patent thickets". Consortium members place commonly used SNPs in the public domain with the aim of preventing research into the human genome from being impeded. Nevertheless, it is highly likely that patent applications will be filed to protect the "association" which links SNPs to particular coding region alleles or mutations. Many such associations, however, may be already covered generally by the "non-coding DNA" patents held by *Genetic Technologies.* These patents cover the use of PCR to amplify unspecified non-coding DNA regions containing at least one polymorphism and their use in genetic linkage, haplotyping and mapping. They are of particular concern because their breadth is enormous, applying to 97% of the human genome as well as to the non-coding regions of the genomes of all other eukaryotic species.

Royalties charged for gene tests affect cost and availability of clinical diagnostic testing. These are often in addition to substantial up front payments for permission to perform the test. Mostly the royalty fees are modest (eg $US20 for haemochromatosis testing). Of particular concern is the effect of multiple royalty payments on a single gene or royalty payments on multiple genes being tested for in certain ethnic groups. Such "royalty stacking" occurs for laboratories that offer a panel of tests such as those for the Ashkenazi Jewish population, including testing for Tay-Sachs disease, Gaucher's disease, Niemann-Pick Disease and Canavan's Disease.

Q. 11-3 - *Is there any evidence that licenses granted to researchers in relation to patents over genetic materials or technologies encourage or hinder research into human health? Is there any evidence that materials transfer agreements encourage or hinder research into human health?*

Refer to response to Q. 11-1.

Q. 11-4 - *Does the recent amendment to the Patents Act 1990 (Cth), which permits a 12 month grace period before filing, encourage the publication of scientific results? Does the grace period overcome the problem of secrecy or delay in publication?*

The College has no specific comment to make.

Q. 11-5 - *Is there any need for Australian guidelines similar to those published by the United States National Institutes of Health to ensure that research is not being withheld from the public domain?*

The College has no specific comment to make.

Q. 11-6 - *Is publicly or privately funded research being impeded because of lack of access to data about human genetic material? If so, does the National Health and Medical Research Council's Celera Subscription provide an appropriate model for seeking to increase Australian researchers' access to information about the human genome?*

The College has no specific comment to make.

Chapter 12 : Gene Patents and Healthcare Provision

Q. 12-1 - *Do existing patent laws and practices favour the development of genetic testing monopolies in Australia? If so, are reforms needed and what should they be?*

Existing patent laws and practices do favour the development of genetic testing monopolies in Australia. Exclusive licensing results in the patent or license holder effectively controlling access to and use of genetic material. There is, however, little empirical data about the effects of patents on the translocation of genetic discoveries into medical advances, so it is not clear how justified these concerns might be. The following examples describe some of the observed adverse effects of genetic monopolies:

- **grant patent holders the ability to dictate standards of care for genetic testing**

Ultimately, commercial considerations will dictate priorities and products, not the public need. Patents grant companies the ability to dictate what kind of test may be done (eg sequencing instead of less sensitive but substantially less costly screening methods such as dHPLC or protein truncation tests) or limit the conditions in which testing may be done (eg refusing to perform prenatal testing for late-onset diseases).

- **restricting research on disease genes by other parties**

Freedom to undertake research on disease genes is critical to genetic health care. A lot of clinical study is needed to validate and extend the early discovery of a disease gene and much of this data emerges naturally from broad medical adoption of genetic testing. In respect of *Myriad's* patents, European researchers discovered that deletions account for approx 28 % of all BRCA1 mutations associated with breast cancer risk in Dutch families (Hogervorst *et al*. Cancer Research 2003;63:1449-53). In other nations, including Australia, such exon deletions may account for 5-10% of all the mutations identified in the BRCA genes. These mutations may have remained undiscovered had *Myriad* successfully enforced its patents in Europe because *Myriad's* testing methodology is unable to detect these deletions.

The function and diagnostic utility of a gene may not be apparent to the patent holder. There are many examples of genes whose functions have taken years to untangle. At first, *Human Genome Sciences* did not appreciate the relevance of their patent on the CCR5 gene in relation to AIDS research and treatment. Had this research not been performed by another laboratory, in defiance of the patent, this may have gone undiscovered.

- **restriction of access to research materials**

In a national survey of data withholding in genetic research in the US (Campbell *et al* JAMA 2002;287;473-80), 47% of geneticists who asked colleagues for additional information, data or materials regarding published research reported denial of at least one request in the preceding three years. In 28% of cases, the respondents were unable to replicate the published research as a direct result of this refusal to share information.

- **loss of consumer choice**

Take, for example, the situation where a particular test is licensed exclusively to a limited number of commercial genetic laboratories within specific geographic regions. An exclusive licensing practice effectively creates a diagnostic monopoly. For example, in North America, it is our

understanding that *Myriad Genetics* requires all diagnostic BRCA gene testing be done at its laboratories in Utah. Licenses to test these genes have not been provided to other laboratories.

- **loss of competitive pricing of the gene test**

In Canada, the cost of BRCA gene testing by the public sector laboratories was 2-3 times less than the cost of testing through *Myriad Genetics*. The likely effect of such pricing on publicly funded genetic services would be to significantly reduce the number of tests available.

- **loss of access to testing**

For example, when *Myriad Genetics* enforced the BRCA gene patents in Canada, the public health services in British Columbia determined that it could not bear the increase in cost and ceased to offer testing. More recently the Province has started testing of the BRCA genes again, choosing to act in defiance of the patents rather than pay the prices requested.

Another example concerns Haemochromatosis which is the most common genetic disorder in Caucasians and is readily treated by regular phlebotomy. Accordingly, there was very rapid adoption of testing by US laboratories soon after the cloning of the HFE gene was published and before the patent was issued. In October 2001, the current patent holder, *Bio-Rad* began offering a kit for haemochromatosis testing and negotiating licensing terms with laboratories that perform testing without its kit. A survey conducted during this period revealed that 30% of laboratories that had set up HFE testing stopped testing due to concerns regarding patent infringement (Merz *et al*, Nature 2002; 415:577-9).

- **disruption of testing from clinical and counselling services.**

Mandatory referral of samples to licensed laboratories disrupts the normally close relationship between clinical genetic and laboratory services. This is especially important for complex genetic disorders. Notably, the NH&MRC and HGSA both recommend that genetic testing should be performed according to best practice guidelines, which include the use of laboratories with close links to clinical genetics services.

- **inhibition of further development of tests on the gene**

License terms often exclude the development and use of complementary or alternative technology.

For example, several diagnostic laboratories in Australia are now offering tests for BRCA1 deletions. These tests are performed using affordable kits ($35 per test) that are commercially available from Europe. Not all American women are tested for these mutations because all BRCA genetic testing in the USA is provided by *Myriad Genetics*.

Another example is the two common mutations that account for 99% of the cases of haemochromatosis in Caucasians. Different mutations are more prevalent in other ethnic groups and these communities require different tests. The kit developed by *Bio-Rad* only tests for the presence of the two Caucasian mutations, but does not detect the rarer mutations.

- **lack of data about the prevalence and penetrance of genetic variants in populations.**

Interpretation of genetic test results and the prediction of the risk of developing genetic disease require detailed knowledge of the prevalence and penetrance of genetic variants. This often varies by ethnic population. If there are no readily available assays to test for a variety of mutations in the haemochromatosis gene, then research into the frequency and impact of mutations in haemochromatosis in different ethnic groups will be curtailed.

Myriad Genetics has accumulated a database on 10,000 cases with BRCA1 and 2 mutations. This data has been published in limited form (Frank *et al*. J. Clin. Oncology 2002;20;1480-90) that is not useful clinically.

- **delays in access to testing**

The paper reporting the cloning of the HFE gene was submitted more than a year after the first US patent application was filed and several months after the last of the four applications. Because laboratories can rapidly develop, validate and offer clinical tests, delay in publishing scientific findings of clinical importance can adversely affect patients by delaying access to diagnostic testing. A survey of over 2,100 biological scientists revealed that 20% reported delays in publication of 6 months or more to allow for patent applications, to protect their scientific lead, to slow dissemination of undesirable results, to allow time for patent negotiation and to resolve disputes over ownership of intellectual property (Blumenthal *et al* JAMA 1997;287;1224-8), indicating that delays are commonplace.

- **monopoly on subsequent research and testing**

If *Myriad* had succeeded in becoming the only laboratory to perform BRCA testing then its collection of DNA samples would have constituted the only sample bank in the World. This could create another monopoly concerning future research on other breast cancer predisposing genes and enable it to file more patents as a result of such discoveries.

Such monopolistic approaches to health care are contrary to the approach to public health taken in many European countries. Many prominent European research organisations, including the Institut Curie; the Belgian, Dutch, German, Danish and British genetics societies and various governments including the French, Belgian, Dutch and Austrian Ministries of Health and the European Parliament have declared their opposition to *Myriad's* monopoly (Lecrubier A, EMBO reports 2002;3;1120-2). The European Patent Office (EPO) is currently re-examining *Myriad's* BRCA patents. The French Ministers of Health and Research have both indicated their intention, if the EPO does not revoke any of *Myriad's* patents, to support an extension of the French *ex officio* system to genetic diagnosis (Lecrubier A, EMBO reports 2002;3;1120-2).

The RCPA believes that monopolistic genetic testing is fundamentally wrong because:

1) **It is the antithesis of the policy objective underlying the Australian public health care system which aims to ensure equitable access to health care for all Australians. Publicly funded hospitals and institutions provide these genetic tests through an integrated clinical framework that ensures they are offered equitably to individuals and families with strong evidence of hereditary disease. Monopolistic business practices and exclusive licensing arrangements disrupt this public system.**

2) **Patents on genetic material can act contrary to the fundamental policy objectives underlying the patent system – to foster innovation. Because genetic material is not an invention (see 8.9), it cannot be improved or invented around. Consequently, there is little or no incentive to improve diagnostic testing by the patent holder and the development of complementary or alternative testing methods, by third parties, can be retarded. Furthermore, because there is no real prospect of competition, patent holders are able to maximally exploit their monopoly position by adopting business practices that would not normally be tolerated by health care providers.**

Recognising these issues, the Royal College of Pathologists of Australasia, Human Genetics Society of Australasia and the Amercian College of Medical Genetics all recommend that diagnostic genetic tests be broadly and non-exclusively licensed.

The most effective mechanism to curb these undesirable effects is to <u>introduce legislation that prohibits the exclusive licensing of diagnostic genetic tests</u>.

Q. 12-2 - *What are the implications of current patent laws and practices for the cost and public funding of, and equitable access to, medical genetic testing and to related health care services such as genetic counselling?*

See response to 12.1

Q. 12-3 - *Is medical practice compromised by exclusive licensing arrangements that limit the types of medical genetic tests that can be performed using a genetic sequence covered by a gene patent? If so, in what ways, and with what possible consequences?*

Medical practice can be compromised by exclusive licensing arrangements. If testing were restricted to one laboratory it would limit the current model of health care delivery in a number of ways:

- the testing would be divorced from the essential related genetic counselling
- there would be loss of the current strong clinical/laboratory liaison
- the sole laboratory would not be able to participate in peer-reviewed quality assurance
- no drive to develop better/cheaper tests by others or by the patent holder
- no opportunity for clinical research on gene variants
- there is potential loss of local expertise in being able to provide this type of testing
- should the providing laboratory cease its function, there would be no backup service available to the community.

Overseas experience has confirmed fears about the use of exclusive licenses to monopolise genetic tests. In a 1999 US study (Schissel et al, Nature Genetics 1999;402;118), of 33 patents that broadly cover the diagnosis of human genetic disorders (13 for neurological, 6 for cardiovascular, 6 for metabolic and 3 for immunological disorders, and 5 for cancer), 14 (42%) were subject to exclusive licensing arrangements that were used by the license holder to monopolise genetic testing services. Two thirds of the patents were based on research funded, at least in part, by the US Government. In a subsequent study (Henry, Science 2002;297:1279), although non-profit organisations, such as universities, were found to generate more genetic discoveries and were less likely to file genetic patent applications than for-profit companies, they tended to favour exclusive licensing. Overall, an average of 68% of all licensed genetic patents from non-profit research organisations were exclusive, compared to 27% for for-profit companies. This suggested that academic institutions, which would be predicted to grant non-exclusive licenses, preferred exclusive licensing in order to minimise licensing expenses and to maximise short-term revenues.

Q. 12-4 - *What potential do patent laws and practices have to encourage the inappropriate marketing and supply of genetic testing services and products?*

At a time when patients seek out information from a variety of sources it is important to acknowledge that the health care system is not the only source of information to individuals at genetic risk of disease. Advertising is one vehicle for information delivery. The prime purpose of advertising is not education but to increase awareness and sales of a commercial product. The

recent launch of a television and magazine advertising campaign in the US by *Myriad Genetics* to market BRCA tests to consumers is an example of this (Gray S, Olopade OI. J. Clin Oncol July 21, 2003). Whilst in the US, the Food and Drug Administration (FDA) and Federal Trade Commission share responsibility for regulating and monitoring the advertisement of genetic tests, they have no clear guidelines for what must be included or excluded in advertisements for genetic testing.

Arguably, genetic testing is a much more complex "product" than prescription drugs with a variety of associated medical, legal and psychosocial risks. Pharmaceutical companies in the US have been cited for violating existing regulations, charged with the oversimplification of drug risks and indications and overstatement of drug benefits. There is, therefore, concern, that commercial pressures to increase test requests will encourage a similar oversimplification of the risks and benefits of genetic testing and the creation of an environment of fear.

Direct-to-consumer marketing of genetic testing also challenges one of the most fundamental components of genetic counselling - careful patient selection. Currently, there are no commercial genetic tests approved for general screening of the population and it is the general population who are exposed to direct-to-consumer marketing. Furthermore, there is the additional concern that non-specialist medical practitioners may feel pressured to order genetic tests that are not indicated. It is well known that some medical practitioners are susceptible to patient pressure when prescribing drugs and ordering pathology tests.

None of the currently available cancer genetic tests have adequate sensitivity and specificity for general population screening. Put simply, positive tests do not always mean that an individual will develop cancer and a negative test is not a guarantee that they will remain cancer-free. There are complexities such as missed genes, polymorphisms, low penetrance genes, and sporadic mutations that factor into the interpretation of genetic tests and cancer risk. In fact, a major limitation of genetic testing for common cancers is the number of negative or inconclusive results, leaving consumers and their healthcare providers confused and frustrated. There is no guarantee that either the consumer or the health care provider will accurately interpret a genetic test result outside of specialist centres. It is very difficult, therefore, to expect individuals to decide if they are suitable for genetic testing given the limited information they receive through advertising. It is especially difficult to expect them to make an accurate assessment of their risk when the advertisements build a strong case for testing based on fear and an ignorance of both epidemiology and risk assessment tools.

There have been no examples to date of direct-to consumer or inappropriate marketing of genetic tests in Australia.

Another concern is the inappropriate supply of genetic tests. Commercial genetic practices and laboratories are more likely to request and perform tests on patients with lower genetic risk than public services. For example, when Caulfield and Gold compared *Myriad* Genetics' indications for its BRCA test with those recommended by independent academic bodies, they found that the latter exclude women without a family history of breast or ovarian cancer, whereas *Myriad's* guidelines include these lower risk women (Caulfield and Gold, Clin Genet 2000; 57:370-5). One may argue (correctly) that individuals deemed ineligible for a particular test or treatment within the public health care system should be allowed to purchase these out-of-pocket.

Without controls on direct-to-consumer marketing and test requesting, similar to those in place for pharmaceuticals, over-consumption is likely to occur. **Guidelines, therefore, need to be developed for the advertisement, marketing and requesting of genetic tests and the laboratories that provide them.**

The above concerns arise from commercial practices and not from the patent system *per se*.

Q.12-5 - *Are gene patents necessary to encourage investment in research that leads to the development of new, clinically useful, medical genetic tests?*

The rationale for patent protection is based on the assumption that patents are necessary to encourage investment in research and development. Genetic patents were intended to be beneficial through more rapid access to innovations that improve the health and well being of society. Thus it is appropriate to ask whether the intended benefits from patenting of genetic materials are actually occurring, and whether these assumptions are actually borne out in practice.

Patents are certainly necessary to encourage investment in research and development in the private sector, however, much genetic research is performed within and is funded by the public sector. The entire sequence of the human genome is available on the internet as a result of publicly funded research. Furthermore, the majority of the disease-associated genes and their mutations were identified by publicly funded research institutions (NIH, public hospitals, universities) or charities (eg UK Cancer Research Campaign discovered BRCA2) and several of those that were discovered by private companies (BRCA1) were based on ground-breaking basic research performed by public institutions.

Some of the discoveries made by public institutions have been patented, but not for the purpose of commercial exploitation. They were patented to stop others from not making the information freely available to all for the benefit of humankind. Others were patented and licensed because the researchers and their institutions wished to cash in on the windfall profits from research supported in part by taxpayers (Cho and Merz, Nature 1997;390:221). Indeed, the NIH is one of the largest owners of US patents that claim rights over human genes (Cook-Deegan *et al*, Science 2001;293:217) from which it receives approximately US$50 million/year in royalties. The need for patent protection to foster the discovery of human disease-related genes is unclear, and it can be argued that genetic discoveries made by private companies would have been made shortly thereafter anyway by public endeavours. It is presently unclear whether a twenty year monopoly is a price worth paying to have a gene discovered by a private company six months earlier than a public enterprise.

The private sector has been much more active in filing patents on large numbers of, often anonymous, human genetic sequences. The US company, *Human Genome Science Inc*, for example, has filed 450 patent applications with claims to more than 34,000 sequences (Bobrow and Thomas, Curr Opin Molec Therapeutics 2002;4;542-7). This genetic “gold rush” has been and continues to be stimulated by international enthusiasm for the commercial applications of biotechnology. There has certainly been a speculative aspect to this, presumably grounded in the optimism of major shareholders in some biotechnology companies that the USPTO would readily grant broad patents on genes with no demonstrable function or utility. Once granted the broad scope of gene patents would give the patent holder exclusive use of the genetic sequence for all conceivable uses including medical testing and pharmaceutical products. These companies presumably hoped to stake as many claims as possible with the anticipation that some would eventually turn out to be important disease-associated genes. Although the USPTO rejected an application for human ESTs with no known biological function in 1991, large numbers of patent applications on ESTs have since been filed. Most, however, would now probably fall below the threshold of the USPTO’s new Utility Guidelines. Also notable, is the fact that exceedingly few of these discoveries have been translated into clinically useful products.

The elemental nature of DNA also has the paradoxical effect of encouraging investment during the discovery phase while discouraging downstream research and development. Since it is not possible to improve DNA sequences, it is effectively impossible to create a new “invention”. Even if it were possible to improve DNA sequences, the fact that patent protection on genetic material extends to all imaginable uses, means there is no incentive for others to undertake downstream research and development. This paradox is another example of the problems and confusion that arise when biological discoveries are (wrongly) regarded as inventions.

In contrast to gene discovery, the role of the private sector, and hence patent protection, are almost indispensible in bringing most diagnostic medical products to the market place. Very few public institutions are able to commercially develop and market new, clinically useful, diagnostic medical tests. Because many of these tests can be easily copied, patent protection allows companies to prevent unauthorised “free-riding” which is a major cause of market failure. This, however, does not necessarily apply to genetic tests. The vast majority of diagnostic genetic laboratories develop tests “in house” using genetic sequences freely available from public domain databases and publications as well as equipment and reagents obtained from commercial suppliers. The latter invariably incorporate their royalty fees and license agreements into their products. Most clinically useful genetic tests, therefore, are presently based on discoveries made by public institutions and involve payment of appropriate royalties for use of patented reagents and methods.

It is important to keep in perspective what patented genes will be used for. Some genes will be used as therapeutic agents (gene therapy), as diagnostic reagents and as targets for drug discovery. The vast majority, however, will be used as research tools in biological investigations. It is, therefore, worth asking whether pharmaceutical companies and academics really need to have “ownership” of these genes? Certainly, there are a handful of genes such as those used in gene therapy or that encode proteins that could be novel therapeutic agents (eg human growth factor, insulin, erythropoietin, granulocyte colony stimulating factor) that require patent protection analagous to that afforded by other drug development. Pharmaceutical companies, however, only need access to, not ownership, of genes as potential drug targets (eg G-protein coupled receptors, tyrosine kinases). Indeed, making successful new drugs is difficult and expensive and it is in the public interest that there is extensive competition to invent the best drugs against each target. Monopolies on gene targets are therefore not in the public interest.

When a gene sequence has diagnostic utility (eg screening for mutations that confer predisposition to breast cancer), the inventive step is the development of the assay not the discovery of the gene. The best assay should win in the market so claims on a gene sequence that covers uses in all diagnostic assays are unlikely to be in the public interest. All of these potential uses can be accommodated by “method-of-use” patents. It is therefore difficult to justify on utilitarian grounds, why genes have been afforded the status of ‘composition of matter’ patents.

The validity of the conventional wisdom, that monopoly control, which comes with the granting of a gene patent, will serve as an incentive to innovate needs to be questioned. Put simply, gene patents encourage private sector investment in biotech, add value to biotech companies, and provide windfall profits for public institutions, but they are no guarantee that this will result in medically useful genetic tests or therapies. Likewise, many disease-associated genes and mutations have been discovered by not-for profit research organisations and developed into medically useful genetic tests by public hospital laboratories without the need for patent protection. It is questionable, therefore, whether patent protection is necessary for the discovery of genes and genetic variants associated with human disease and whether composition-of-matter

patents are necessary for the development of diagnostic genetic tests and therapeutic drugs. Almost all conceivable uses of human genes can be adequately covered by "method-of-use" patents.

It is therefore difficult to justify the necessity for patent protection on human genetic material.

Q. 12-6 - *What impact might patent laws and practices have on the future provision of gene therapy, medicines based on therapeutic proteins, and medical treatment involving stem cells?*

Gene patents have the potential to both encourage and limit the development of gene-based therapies. It is unlikely that public institutions will take the risk to progress a gene-based therapy through the rigorous regulatory processes, conduct clinical trials and market their products, especially those where the therapeutic potential is less obvious. The role of the private sector and the need for patent protection cannot be overestimated here.

However, the broad scope of many patents on genetic material is likely to discourage competitors from investing in gene-therapy-based research. Potentially useful therapeutic agents may not be developed when the patent holder is too small to support the risk or negotiates terms that are regarded as unreasonable. *Myriad Genetics* for example claims the rights to use the BRCA1 and BRCA2 genes for both diagnosis and potential therapies. There is no obligation, however, on *Myriad Genetics* to develop gene-based therapies based on BRCA1 and BRCA2, while the threat of legal proceedings for infringement or the imposition of license fees could discourage others.

Q. 12-7 - *Should government funding and purchasing power be used to control the cost of medical genetic testing that is subject to gene patents? If so, how might this best be achieved?*

No, the appropriate role for government is to create the legal and regulatory framework that achieves the right balance between the patent holder's right to profit from their inventions and the public policy objective of high quality, equitable health care.

Q. 12-8 - *Should there be new regulation of medical genetic testing to address concerns about the possible adverse consequences of patent laws and practices on health care provision? If so, how might this best be achieved?*

Yes, there is a need to regulate all aspects of genetic testing. In many instances this can be achieved through existing government initiatives eg National Association of Testing Authorities / Royal College of Pathologists of Australasia (NATA/RCPA), National Pathology Accreditation Advisory Committee (NPAAC), Therapeutic Goods Administration (TGA).

However, because the adverse consequences are largely a result of commercial practice that arise as a result of a monopoly granted by a patent, regulations alone may not achieve the desired outcome. If there is to be additional regulation it should be in relation to achieving a balance between commercial and trade practices and public health policy objectives. These are probably best achieved through the Trade Practices Act etc.

Q. 12-9 - *Should patent pools or clearing houses be created to make it easier for laboratories to obtain licenses for patented genetic inventions? If so, how might this best be achieved?*

The USPTO has recently suggested the use of patent pools, which are a form of cross-licensing agreement between patent holders allowing for sharing of technologies in a common field. This is likely to be attractive to the commercial sector particularly those companies with large gene portfolios. However, this will not assist researchers and laboratories who are currently developing genetic tests that examine hundreds or thousands of genes simultaneously. An effective administrative mechanism has to be developed if these tests are to be cost effective. Patent clearing houses are one possible option.

Chapter 13: Patents and the Biotechnology Sector

Q. 13-1 - *What effects do Australia's patent laws and licensing practices have on the development of Australia's biotechnology industry as it relates to human health?*

The College has no specific comments to make.

Q. 13-2 - *Is there any evidence that broad patents, trivial patents, defensive patents, dependent patents, multiple patents or reach-through claims may adversely affect the development of Australia's biotechnology industry as it relates to human health?*

The College has no specific comments to make.

Chapter 14 : New Defences

Q. 14-1 - *Should the Patents Act 1990 (Cth) (Patents Act) be amended to include a defence for research use? If so, should the defence be limited to activities involving research on an invention claimed in a gene patent? Should the scope of the defence also encompass research use of a gene patent directed to: (a) improving upon the claimed invention; (b) finding a new use for the claimed invention; or (c) creating a new product or process using the claimed invention?*

Yes, serious consideration should be given to exempting non-commercial research from patent infringement, especially for inventions arising from publicly funded research. This view is based on the principle that public institutions should be free to conduct research of a non-commercial nature. Although not codified in law, there is a long standing scientific convention that non-commercial research is exempt from patent enforcement (see 11.1).

The European Commission recently proposed an exclusion from the effects of European Union patents for "acts done privately and for non-commercial purposes" and for "acts done for experimental purposes relating to the subject-matter of the patented invention" (Commission of the European Communities, Proposal for a Council Regulation on the Community Patent, art 9 (1 August 2000), Off Eur Communities 43 (C 337E), P278 (28 November 2000), (available at europa.eu.int/eur-lex/pri/en/aj/dat/2000/ce337/ce33720001128en02780290.pdf) The national

patent laws of many EU member states contain similar provisions, as does Japanese law (Muller J, Wash Law Rev 76,1 [2001]).

However, the distinctions between public and private institutions and commercial and non-commercial research are becoming blurred. Almost all public research institutions have active programmes to commercialise their intellectual property and conversely many private companies receive substantial public funding to support their research programmes and business development. This is, therefore, likely to make such proposals unworkable.

Q. 14-2 - *Should the Patents Act be amended to include a defence for private, non-commercial use of a patented invention? If so, what would be the relationship between a 'private use' defence and a 'research use' defence of the type identified in Question 14 - 1?*

Yes, serious consideration should be given to including non-commercial genetic testing into the definition of private use. A genetic test performed on an individual could be regarded as private use so long as the individual does not to seek to profit financially from the test result (ie share in any profit dervied from their genetic material).

Individuals ought to retain a "natural" right of access to their own genetic material for their own healthcare. It would be ethically objectionable for this to be denied by a patent or license holder.

The development of special defences and exemptions such as private-use genetic testing could, however, undermine commercial research into genetic disorders. There is a danger that such initiatives could lead to a cascade of other consequences, eg reduced investment in genetic technologies generally.

Q. 14-3 - *Should the Patents Act be amended to include a defence to allow for the use of a patented genetic material or technology by a medical practitioner for the purposes of medical treatment of humans? If so, who should qualify as a medical practitioner for the purposes of such a defence and what types of activities should be exempt? Should any activities be expressly excluded from the scope of such a defence?*

Yes, serious consideration should be given to granting laboratories exemption from patent infringement to perform non-commercial genetic testing on patients for private purposes. The exemption should apply to the approved pathology authority, approved pathology laboratory and approved pathology practitioner.

A similar scheme was proposed as an amendment to US patent law by Sen. Lynn Rivers.

Q. 14-4 - *Would amendment of the Patents Act to include new defences, such as those identified in Questions 14 - 1, 14 - 2 and 14 - 3, be consistent with Australia's obligations under the TRIPS Agreement?*

The College has no specific comment to make.

Chapter 15 : Crown Use and Compulsory Licensing

Q. 15-1 - *Are the Crown use provisions in the Patents Act 1990 (Cth) (Patents Act) capable of applying to the provision of health care services using patented genetic materials and technologies? If not, should these provisions be amended to apply to such use?*

These provisions appear to be adequate and do not require changing specifically for gene patents.

Q. 15-2- *In relation to the provisions in the Patents Act relating to the grant of compulsory licenses:*

- *Do the provisions encourage patent holders to exploit or license gene patents?*
- *Is the grant of a compulsory license an adequate and appropriate mechanism to remedy the possible adverse impacts of gene patents on access to health care or the ability to conduct research related to human health? If not, should the current provisions be amended to make specific reference to such matters?*
- *Should compulsory licenses be available only by order of a court (as the Patents Act currently provides), or should the Act be amended to allow the Commissioner of Patents, or another tribunal or agency, to grant compulsory licenses?*
- *If compulsory licenses were to be granted more frequently, should the Patents Act be amended to provide increased protections for patent holders, such as mechanisms for determining the compensation due, or certain mandatory terms to be included in such licenses?*

Yes, serious consideration should be given to loosening the criteria for granting compulsory licenses. This is probably the most appropriate and effective solution for resolving disputes between patent and license holders and genetic testing laboratories, especially public laboratories which cannot afford to pay unreasonable license fees or bear enormous legal fees.

Likewise, **serious consideration should be given to create or appoint a patent ombudsman, tribunal or commissioner** to hear such cases and to grant compulsory licenses, determine appropriate fees and compensation, and to be empowered to penalise companies that behave in a socially irresponsible manner.

Guidelines should also be established to determine reasonable fees and compensations eg limited to 5-10% of the cost of performing the test.

Serious consideration should also be given to protecting laboratories from business practices by patent and license holders armed with patent insurance.

It is noteworthy that France has recently introduced legislation that permits the country's Minister of Health to grant compulsory licenses to provide a genetic test in return for a reasonable royalty, in order to protect the public health (*Projet de loi relatif a la protection des inventions biotechnologiques*. France Senat Seeion ordinare de 2001-2002; 2001 Nov 6 No 55, Article 11 – available: www.senet.fr/lcg/pjl01-055.html). This measure, being contemplated by other countries, would not only reduce the cost of genetic tests but would ensure that patients have acess to the most appropriate tests available. It would also ensure that all laboratories that wish to perform the

test could do so, as long as they meet their country's regulatory requirements and accreditation standards for genetic testing.

Q. 15-3 - *What latitude is there for amending the Crown use or compulsory licensing provisions of the Patents Act consistently with Australia's obligations under the TRIPS Agreement?*

The College has no specific comment to make.

Chapter 16 : Copyright, Trade Secrets and Designs

Q. 16-1 - *What role should copyright law play in dealing with genetic materials and technologies in relation to human health?*

It has been argued that genes should not be treated as novel chemicals but as biological software comprising a programme written in the sequence of the nucleotides and hence subject to copyright rather than patent law. This has the advantage that copyright law provides weaker commercial protection but is of longer duration. These arguments were rejected by the USPTO.

Q. 16-2 - *Does Australian copyright law provide adequate protection of databases that hold factual compilations of genetic sequences and other genetic data? What would be the implications of introducing into Australian law a special database right—as distinct from copyright—in relation to such databases?*

The College has no specific comment to make.

Q. 16-3 - *Does trade secrets law have any significant application to the conduct of genetic research and its commercialisation? If so, does the law require reform?*

The College has no specific comment to make.

Q. 16-4 - *Do the existing or proposed design laws have any significant application to the conduct of genetic research and its commercialisation? If so, do the laws require reform?*

The College has no specific comment to make.

Chapter 17 : Patents and Competition Law

Q. 17-1 - *Following the report of the Intellectual Property and Competition Review Committee in 2000, and the Federal Government's response, are there any competition issues specifically relevant to gene patents that need to be dealt with in the course of this Inquiry?*

The College has no specific comment to make.

Q. 17-2 - *How should competition law and policy deal with 'patent pools' relating to gene patents?*

The College has no specific comment to make.

Q. 17-3 - *Is there a role for the Australian Competition and Consumer Commission (ACCC) in monitoring prices that are charged for medical genetic tests or any other products or services arising from the grant of gene patents or licenses?*

The College has no specific comment to make.

Q. 17-4 - *Is there a role for the ACCC in monitoring the impact on competition of gene patents and licenses?*

The College has no specific comment to make.