SENATE COMMUNITY AFFAIRS COMMITTEE
INQUIRY INTO GENE PATENTS

SUBMISSION
THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH

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Submission: Walter and Eliza Hall Institute of Medical Research[1]

1. Executive Summary

WEHI submits that the broad benefits of gene patents and the strengths of Australia's patent system should not be threatened on the basis of a rare but high-profile example, the Myriad BRCA test. There is no strong body of evidence that human gene patents are having major negative impacts on research, innovation, healthcare access or cost that cannot be addressed through other means. Our submission generally supports the findings of the ALRC. Our key recommendations are that:

- Active consideration of the recommendations made by the ALRC in their report should be the first recommendation of the Senate Community Affairs Committee.
- Human gene patents should continue to be allowed in Australia. Australia's patent system must be harmonised with global agreements and retain its technology neutrality.
- The patent law in place is largely effective and capable of handling the claims in human gene applications, but greater emphasis should be placed on increasing the burden of proof with respect to utility in general and not specifically limited to gene patent claims.
- The Australian Health Ministers' Advisory Council should establish processes for a) economic evaluation of medical genetic testing and other new genetic medical technologies; and b) examination of the financial impact of patents on the delivery of healthcare services in Australia.
- The assumption of research exemption should be confirmed in Australia. WEHI supports the ALRC recommendation for research exemption.

2. Introduction

We welcome the opportunity to make a submission to the Senate Community Affairs Committee with respect to Human Gene Patents.

The Walter and Eliza Hall Institute of Medical Research (WEHI) has a strong track record of research, capture and management of intellectual property (IP), and translation of research into medical outcomes. We have extensive experience of the Australian and international patent systems, particularly as they relate to human gene and sequence patents. Therefore, from our practical experience we consider ourselves qualified to present evidence to the Senate Community Affairs Committee.

Our submission specifically addresses the following issues in the terms of reference:

- The impact which the granting of patent monopolies over such materials has had, is having, and may have had on:
    - the provision of training and accreditation for healthcare professionals,
    - the progress in medical research, and
    - the health and wellbeing of the Australian people;
- Identifying measures that would ameliorate any adverse impacts arising

[1] Prepared by Carmela Monger, Intellectual Property and Contracts Manager and Julian Clark, Head Business Development

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

- Whether the *Patents Act 1990* should be amended so as to expressly prohibit the grant of patent monopolies over such materials.

As part of this submission we emphasise the direct and dominating relevance of the previously commissioned report into gene patenting delivered five years ago by the Australian Law Reform Commission (ALRC)[2]. Recognition and response to this report is essential as part of the Senate Community Affairs Committee review particularly since the ALRC had terms of reference and recommendations that embraced the broader, intimately linked issues, associated with an effective and responsible patent system. The passage of time since the ALRC report has not changed the essence of their conclusions.

It must also be recognised that a United States National Institutes of Health task force has recently released a draft report, including policy options, on its findings with respect to gene patenting, research, patient access and business[3]. Importantly this report finds that licensing practices do not appear to be impeding patient or clinical access to gene-based tests, and that when patient access to such tests may have been impeded most cases have been resolved. The report did not find a major distortion of interests due to the impact of patenting incentives on research.

[2] ALRC Report 99 (2004) Genes and Ingenuity
[3] Public consultation draft report on gene patents and licensing practices and their impact on patient access to genetic tests (Secretary's Advisory Committee on Genetics, Health and Society (2009)

3. WEHI experience in IP matters

As one of Australia's major players in medical research IP, we believe that our experience provides an important insight to the Senate Community Affairs Committee. WEHI is Australia's largest and oldest medical research institute. Founded in 1915 we currently invest approximately $70 m per year in medical research. Most of these funds are provided by public funding agencies such as NHMRC[4] and NIH[5]. Our research efforts are underpinned by more than 600 full-time equivalent employees and post-graduate students. Approximately 50 laboratories focus on major medical challenges associated with cancer, immunity, autoimmunity and malaria. We have extensive research collaborations with the public sector, and with private sector partners such as Genentech, Abbott Laboratories and Merck in the US, and CSL and Bionomics in Australia.

As a research institute, our core business is the conduct and dissemination of world-class medical research, with the goal of improving human health. As a consequence we place great emphasis on publications, having the highest citation impact of any organization in Australia[6], and are committed to translation of our discoveries, both clinically and commercially. While WEHI benefits from commercialisation of its IP, this comes as a consequence of our primary focus on uncompromising world-class medical research and accountability to tax payers who provide most of our funds. The critical issue is effective translation of knowledge into community outcomes, whether in Australia or globally.

WEHI has filed thirty patent applications in Australia that claim gene sequences and twenty-one of these applications have been commercialised through licensing. This outcome is underpinned by a strong organisational understanding and engagement with the global IP system. WEHI's discovery and innovation pipeline is fed by a portfolio of more than 250 research projects that result in:

- More than 250 Material Transfer Agreements per year with both academic and commercial partners
- More than 250 peer reviewed publications per year, mainly in high impact journals
- Approximately one new patent application every three weeks
- A total patent estate of around 300 patents and applications
- Approximately 35 – 40 collaboration and license agreements per year
- WEHI IP being the subject of more than 40 clinical trials currently being conducted worldwide.

WEHI has three successful spin out companies – Genera Biosystems, Nexpep and MuriGen:-

- Genera Biosystems Limited was recently listed on the ASX and focuses on high-throughput diagnostic tests for women's health. The original IP was developed by WEHI and the Australian Genome Research Facility. The first test that has been commercialised in Australia is a screen for multiple Human Papilloma Virus strains based on multiplexed DNA sequences. Genera has had clear freedom-to-operate advice from US attorneys and until now has experienced no unexpected adverse consequences of other gene patents. The company has had the benefits of Professor Ian Frazer being on the Scientific Advisory Committee and the test is already partnered with Australia's No 1 and No 3 pathology providers[6].

- Nexpep's future relies on the integrity of patents related to peptide sequences that relate to gluten. The company's focus is on diagnosis and treatment of coeliac disease. While not yet directly dependent on human gene patents, Nexpep illustrates a successful company about to enter Phase I clinical trials that is totally dependent on the strength of its

[4] National Health and Medical Research Council
[5] National Institutes of Health (US)
[6] Sonic and Healthscope

sequence-based patents. Together with partner, US-based Inova, Nexpep is developing a human diagnostic test for coeliac disease.

- MuriGen has a focus on the discovery of new drug targets through mutation of gene sequences. MuriGen completed the highest value biotechnology deal in Australia in 2008 by teaming up with CSL with IP related to antagonism of a cytokine involved in inflammatory conditions. MuriGen's discovery program is dependent on establishing an IP position based on identification, description and patenting of the human gene and gene product.

Clinical trials currently pending include an antibody therapeutic for asthma treatment partnered with Merck, an antibody for inflammatory conditions partnered with AstraZeneca and an intranasal diabetes vaccine partnered with the Diabetes Vaccine Development Centre.

The institute's many current formal collaborations based on or arising from human gene sequence IP include:

- Abbott Pharmaceutical – cancer drug discovery
- Australian Genome Research Facility – high throughput genotyping and sequencing
- BioGrid – medical informatics and patient genotypes/phenotype response
- Bionomics – multiple sclerosis/anxiety target drug development
- Cancer Therapeutics Cooperative Research Centre – developing small molecule drugs based on novel targets
- Cancer Trials Australia – not-for-profit clinical trials organisation providing early access to leading cancer therapies
- CSL – target discovery and inflammation
- Diabetes Vaccine Development Centre – intranasal vaccine clinical trial
- Genentech – cancer drug discovery
- Merck – IL13 as an asthma target
- Victorian Breast Cancer Research Consortium – collaborative cancer research
- Victorian Cancer BioBank – tissue banking for discovery of new diagnostic and therapeutic targets

Specific examples of inventions made at WEHI provide an insight into the importance of gene patents.

The cytokines G-CSF and GM-CSF were discovered at WEHI and the Ludwig Institute of Cancer Research in Melbourne during the early days of exploiting gene technology. Both human proteins, developed and marketed by Amgen and Immunex/Berlex[7] respectively, have been used to treat more than 10 million people world wide as they battle the consequences of chemotherapy for treatment of cancer. Without patent protection and specifically the gene and protein sequence claims therein, these valuable therapeutics would never have come to market.

Human Leukaemia Inhibitory Factor (LIF) discovered at WEHI in the 1990s was developed by Serono through to Phase II clinical trials for fertility management. While this application proved insufficiently efficacious, a new use for LIF was discovered and exploited. LIF is now widely used as a critical laboratory research reagent[8] for controlling the differentiation of mouse stem cells.

Asthma is a debilitating and dangerous condition that affects millions of people world wide. In the 1990s scientists at WEHI discovered a receptor called IL-13R and observed that antibodies to this receptor could modulate inflammatory responses. This innovation was commercialised by Zenyth (previously Amrad) through an exclusive license to Merck. The therapeutic antibodies are nearing the stage of Phase I clinical trials.

[7] An exclusive license whereby royalties are shared between WEHI and the Ludwig Institute
[8] Marketed by Millipore (previously Chemicon) under an exclusive license

WEHI's patent estate of 16 patent families relating to cell death was instrumental in the current major collaborative cancer drug discovery and development program together with Genentech and Abbott Laboratories. Several patent claims in this estate relate to human gene sequences.

We submit that in the absence of gene sequence claims none of these inventions would have been progressed to their current stage within the pipeline leading to clinical adoption.

4. WEHI management and exploitation of IP

Researchers in the public sector are accepting more and more that patenting is an essential component of commercialisation, and that commercialising patents is necessary for attracting investment for research and development and for ensuring that products that benefit the public are developed. Public institutes do not have the skills or capital to transform research results into marketable products in the form of pharmaceuticals, therapeutic proteins and diagnostics and require private sector involvement to make possible public access to these developments. Consequently, WEHI works with other organisations to achieve these outcomes through effective licensing practices and effective collaborations.

Importantly, WEHI has two in-house patent counsels with direct experience from the global biotechnology industry. We have also invested in access to various patent data bases for freedom to operate evaluations. Furthermore, WEHI has a vibrant business development intern program to ensure engagement and training of post-doctoral scientists in IP management and translation.

As discoveries are made and intellectual property is identified, resulting innovations are partnered with development collaborators to progress into the clinic and market place. WEHI's invention disclosure system enables capture of IP and patenting without any significant delays in publication.

The use of exclusive licensing with the option to sublicense has proved effective for getting products into the market. WEHI usually licenses research reagents, such as antibodies, non-exclusively[9]. WEHI is involved in many collaborations, particularly between research institutes and "upstream" development companies. In addition, WEHI has contributed significantly to malaria research, and entered into public/private partnerships to develop a vaccine. A condition of these partnerships is to promote global access and, in particular, access to IP for the developing world.

It is particularly important to observe that:

a) WEHI has not experienced any restrictive licence requirements that have not enabled WEHI to conduct further research
b) WEHI has not experienced any infringement or enforcement challenges to date
c) Patenting of the Institute's IP has not impeded rapid publication in the public domain[10]

5. Inventions and patentability

We strongly believe that under the international patent laws human gene, peptide and protein sequences should continue to be patentable. Such sequences have been patented for many years and many form the basis of life-saving therapeutics and diagnostic tests. Under Australian Patent Law, an invention is a patentable invention if it is "a manner of manufacture"

[9] Although LIF is an exception, in which case the license is exclusive since the invention is covered by granted patent claims

[10] The only exceptions are the well-understood examples of small molecule compound structures that constitute composition of matter patent claims that often remain confidential until patent details become public.

within the meaning of Section 6 of the Statute of Monopolies, is novel and inventive, and is useful.

The term "manner of manufacture" was given a broad interpretation by the High Court of Australia in *National Research Development Corporation v Commissioner of Patents* in 1959, and subsequent decisions have followed similar arguments. Essentially, anything in the useful arts as opposed to the fine arts, of economic significance, is suitable subject matter for the grant of a patent.

In Australia, the Deputy Commissioner of Patents considered the patentability of claims defining gene sequences in his decision in *Kirin-Amgen Incorporated v Board of Regents of the University of Washington*. The distinction between discovery and invention was discussed, and the Commissioner of Patents indicated that because the natural DNA sequences were claimed as "purified and isolated" sequences, they claimed "an artificially created state of affairs" and were therefore patentable. It was held that the claims did not extend to the naturally occurring entity.

An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene may constitute a patentable invention even if the structure of that element is identical to that of a natural element. This is established law in Australia and other jurisdictions such as Europe and the US. The exclusion of gene sequences on the basis that they are discoveries rather than inventions would not follow established judicial interpretation of the distinction between discovery and invention to date. Essentially, the isolation and characterisation of a gene outside of its natural environment will be novel if its existence was not known or formed part of the prior art knowledge that was publicly available prior to its patenting. Within the Australian legal framework, claims including DNA sequences and protein sequences that have utility (unlike Expression Sequence Tags) can satisfy the invention threshold.

While in the past there may have been difficulties in distinguishing between discoveries and inventions as a consequence of gene technologies[11], these differences are increasingly clear as the possibilities and limitations of gene technology are better understood and patent examiners place emphasis on utility.

6. Objective evidence is lacking

We believe that the debate about gene patents suffers from lack of objective evidence. It is critical to distinguish between theoretical and real problems[12] particularly as the issues that arise are largely dealt with through a variety of mechanisms outside the need to tamper with the patent system. There have been occasional objections to gene patenting in Australia and elsewhere in the belief that there is something immoral or unethical about human gene patenting per se, that gene patents hamper innovation or that gene patents impact negatively on access to diagnostics and healthcare.

As an example of the imbalance that enters the debate we cite the following:

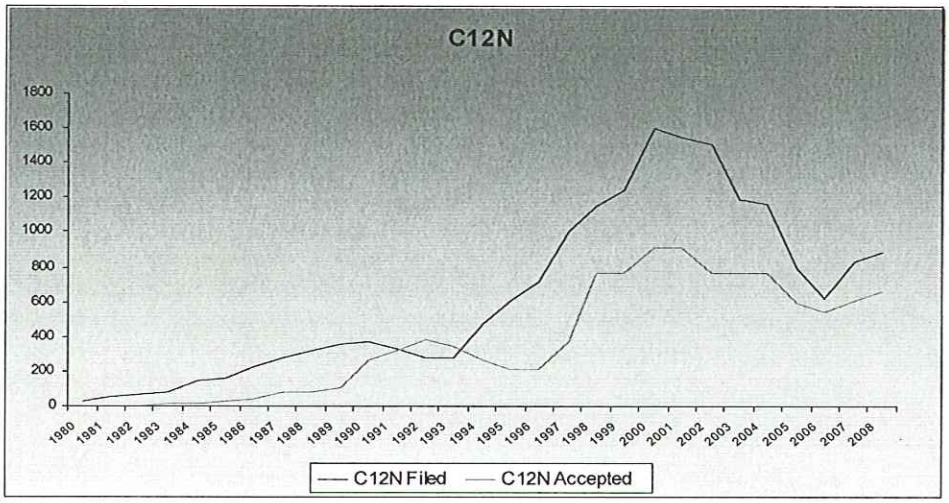
> *The fact that the Australian Patent Office has issued hundreds, if not thousands, of patents over genes, including human genes "..demonstrates a systematic failure on the part of Australia's bureaucracy to protect the public and economic interests of this country and amounts, not only to a gross abuse of the public's trust, but also a serious misuse of power"*[13]

Where is the evidence for these bold claims? What is the consequence of accepting them? There have been other inquiries in Australia and elsewhere and none of these inquiries have resulted in recommendations to exclude genes from patenting. It therefore appears that

[11] Nicol D (2006) On the legality of gene patents. Melb Uni Law Rev 29:809
[12] Nicol D (2006) On the legality of gene patents. Melb Uni Law Rev 29:809
[13] Palombi L (2008) The battle for our genes. ABC Unleashed s2440288

cases that question the public implications of gene patenting are rare (often driven by Myriad and GTG, see Section 6) and patent law reform has not been necessary to date since other avenues and actions provide corrective measures as required.

The graph below[14] clearly shows that the number of patent applications filed in Australia that claim gene sequences have dramatically decreased since the completion of the "Human Genome Project" era in 2000 – 2002. In contrast, the number of downstream applications are increasing, which indicates that contrary to the arguments of those that are opposed to gene patenting, innovation is not being hampered.



Strategies for exploitation of the GTG non-coding DNA patent (see further below) are not entirely clear, however, the situation can be likened to PCR where royalties are already part of the price for tests and products in the genetic testing and research markets.

Pressman et al[15] observed that licensing practices at the large and experienced academic institutions studied were largely in agreement with the NIH guidelines for research tools and genomic inventions. WEHI maintains that its patenting and commercialisation practises, like other Australian medical research institutes comply with NIH and NHMRC guidelines.

Klein has noted that patents on the human genes used to manufacture new drugs are central to the process of obtaining risk capital needed to introduce these important therapeutic agents into medical practice[16].

Analysis of litigation provides an important insight into the patent system, granting of patent claims and access to innovation. Few human gene patents have ever been asserted in court, so any "chilling effect" arises primarily from a perception of risk that may not comport with reality[17]. Contrary to some perceptions empirical analysis reveals that the overall number of litigated cases related to DNA sequences is declining[18].

Holman's analysis of patents and litigation in the US provides an important insight into the real dynamics of exploiting innovation and provides little empirical support for a legislative bar to the patenting of genes or DNA. The study identified 31 human gene patent litigations dating back to 1987. Considering the large number of human gene patents, the substantial amount of patent litigation that has taken place involving biotechnology patents other than human gene patents, and the high level of concern that has been expressed with respect to the negative impact of human gene patents, 31 is a relatively small number. Since 2000

[14] IP Australia – the graph presents the number of patent application that claim a gene sequence or a derivative of a gene sequence (Class C12N)
[15] Pressman L et al (2006) The licensing of DNA patents by US academic institutions: an empirical survey. Nature Biotech 24: 31
[16] Klein RD (2007) Gene patents and genetic testing in the United States Nature Biotech 25:989
[17] Holman CM(2008) Trends in human gene patent litigation. Trends in human gene patent litigation. Science 322:198
[18] Mills AE and Tereskerz P (2008) DNA-based patents: an empirical analysis. Nature Biotech 26:993

alone at least 1294 lawsuits have been filed asserting drug patents, and 278 involving molecular biology or microbiology patents. Rather than increasing, the number of human gene patent litigations pending at any given point in time has fallen off in recent years. This decline also corresponds to a similar marked decline in the filing and issuance of DNA patents in the US since 2001. In a sample of 4270 patents, none of the 7 lawsuits resulted in a decision favouring the patent holder.

WEHI emphasises that the gene patent debate is based on very few precedents and evidence and heresay, and is driven by perceptions of possible future scenarios that have largely failed to materialise. Australian concerns were based around the Myriad BRCA test and GTG non-coding DNA patent (see further below), and the ALRC inquiry did not reveal other specific major concerns. Deeper examination shows that it would be unwise to generalise and advocate major changes in patent law from these special cases alone. The ALRC report states that there are overseas precedents for intervention by government in patent processes. However, upon deeper review there were remarkably few examples, in fact the European patent action against Myriad was the only example of substance. There are no examples cited of governments (Australian or overseas) actually exercising "march in rights", Crown use and acquisition, or compulsory licensing relating to patent claims in healthcare or related areas.

7. Myriad and GTG

WEHI submits that the broad benefits of gene patents and the strengths of Australia's patent system should not be threatened and undermined on the basis of a rare but high-profile example. The case of BRCA1 and BRCA 2 genes patented by Myriad for the purposes of diagnosing breast cancer susceptibility has clearly dominated the debate about gene patents as they relate to diagnosis and therapy in humans. In Australia the rights to these genes have been licensed to GTG and GTG has rights to exercise this license in Australia. The critical issue has been how these rights have been exercised and the associated strategic confusion created by GTG's ever changing positions.

The Myriad controversy, and in Australia, the sub-licensing behaviour of GTG, coincides with the most lobbying and policy activity with respect to patenting genes. This is more likely because the controversy, more than any other, resonated so well and continues to do so with the theoretical concerns that existed in the literature[19]. There have been few similar human gene patent controversies and Caulfield et al (2006) argue that one possibility is that the Myriad story has become a cautionary tale for the holders of similar gene patents, guiding them toward more constructive patent enforcement strategies.

8. Freedom to operate and research exemption

Some people opposed to gene patents claim that such patents inhibit research and innovation, and discourage communication of research results. We submit that gene patents have had no negative impact on WEHI's research activities and ability to innovate. Furthermore, we believe that rather than hindering dissemination of research results, patents actually reduce the possibility of information being kept as trade secrets.

The effects predicted by the purported anti-commons problem are not borne out in the available data. Caulfield et al observed that despite the large number of patents and the numerous, heterogenous actors, studies that have examined the incidence of anti-commons problems find them relatively uncommon. These studies span both academics and industry,

[19] Caulfield T et al (2006) Evidence and anecdotes: an analysis of human gene patenting controversies. Nature Biotech 24:1091

and include data from the United States, Germany, Australia and Japan[20]. Importantly, Caulfied et al discovered that among biomedical researchers in the US, only 1% report having had to delay a project and none had to abandon a project as a result of other's patents. There was no empirical evidence that university researchers were becoming more secretive and less willing to share research results or materials as a consequence of patents. Lei et al also reached the same conclusion that patents in and of themselves might only rarely pose an obstacle to the research plans of academic scientists[21].

These observations suggest that neither anti-commons nor restrictions on access are seriously limiting academic research – despite the fact that these biomedical researchers operate in a patent-dense environment, without the benefit of a clear research exemption. Fears of widespread anti-commons effects blocking the use of upstream discoveries have largely not materialised.

Caulfield et al noted that in the pathology testing arena 25% of labs abandoned one or more genetic test as a result of patents, with Myriad's patents among the most frequently mentioned. This outcome only reflects an unwillingness to recognise Myriad's rights in patent law and does not necessarily equate to diminished use and access to the technology. It would appear that limitations have more to do with a lack of willingness to accept the market price and access terms.

The ALRC noted that the absence of a research exemption may result in an under-investment in basic research and hinder innovation if researchers become concerned that activities may lead to legal action. Given the explosion of patentable subject matter there should be a broad statutory defence based on experimental use. This exemption specifies that there will not be an infringement of a patent if the infringing act is done for experimental purposes relating to the subject matter of the invention.

Research institutes exist to discover and invent, and are only successful if they advance beyond existing publications and patents. WEHI believes that the research exemption can be relied upon for most of its research and if not, research directions can be modified to accommodate existing rights in patents or licenses can be obtained. There is no specific provision in the Patent Act dealing with a research and experimentation exception or defence to infringement. Yet, given the various rationales of the patent system (which include both to protect the inventor's commercial interests and to promote research and development), it is certainly strongly arguable that an experimental use exception already exists in Australia under common law. This interpretation is consistent with the Explanatory Memorandum for the Patents Bill 1990 which assumed that such an exception existed.

The Explanatory Memorandum for the Patents Bill 1990 at page 5 states that:

> *"... it is not intended that clause 13 ... modify the present law relating to certain acts which have been held not to constitute infringement - for example, use of an invention for certain experimental or trial purposes."*

The issue of the assumed research exemption should be clarified in all patent jurisdictions. US academic researchers are potentially at risk given the Madey vs Duke determination and the risk could also depend on the licensing behaviour of research institutions as they increase their focus on patenting[22]. Logically, an effective research exemption should apply to all organisations irrespective of whether they are academic or commercial. Kaye et al argue that the research exemption is particularly important for clinical translation studies that usually involve major elements of discovery, validation and reduction to practice[23].

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[20] Caulfield T et al (2006) Evidence and anecdotes: an analysis of human gene patenting controversies. Nature Biotech 24:1091

[21] Lei Z et al (2009) Patents versus patenting: implications of intellectual property protection for biologicl research. Nature Biotech 27:36

[22] Yancey A and Stewart (2007) Are university researchers at risk for patent infringement. Nature Biotech 25:1225

[23] Kaye J et al (2007) Patents and translational research in genomics. Nature Biotech 25:739

9. Gene patents and healthcare provision

The ALRC observed that there was little indication that holders of patents related to disease genes were actively enforcing their patents against Australian genetic test laboratories. While there is a high degree of concern about the potential impact of patents over isolated genetic materials on public sector laboratories, enforcement by patent holders has been limited. Public sector laboratories generally have not been approached by patent holders seeking to enforce their rights over such materials. Actual enforcement activity remains more limited in Australia than in the United States, possibly because Australia is a small market and cost of pursuit and enforcement may outweigh any potential benefits. The ALRC remained of the view that there is little evidence to date that gene patents and licensing practices with respect to genetic testing have had any significant impact on the cost of healthcare provision in Australia. We believe that this conclusion is still generally true.

The ALRC concluded that what is clear is the need for healthcare providers and healthcare policy makers to be proactive in responding to problems as they emerge rather than tamper with the patent system to address issues that can be solved through other more flexible means.

We have found no evidence that gene patenting *per se* has any significant impact on access to tests or to costs. The ALRC found that concerns about the implications of gene patents for public healthcare funding have arisen primarily in relation to medical genetic testing, potential fears over excessive costs and the likely increased role of the private sector in provision of genetic tests. Concerns about gene patents have generally been based on assumptions about the future development of the market in medical genetic testing and about the intentions of patent holders. In particular they have been based on assumptions that patent holders will use exclusive licences as their business model and that exclusive licences will charge monopoly prices. These fear-based assumptions must be challenged in view of the paucity of supporting evidence.

The lack of adequate economic evaluation is a fundamental issue in determining whether technologies and specific tests provide benefits to the healthcare system. We believe that thorough economic evaluation is critical to determining whether gene patents, or any other patents, have a negative impact on price, access and outcomes. The costs attributable directly to patents are unclear and are only one component of the overall costs of providing genetic testing and they need to be considered in the context of other influences on healthcare costs. Importantly, the determination must take into account the probability that the invention would not have been available without patent protection.

10. Possible actions and consequences

Three important observations will clearly temper the type of actions, if any, that are required specifically with respect to human gene patents.

Firstly, a large number of patents claiming human gene sequences have been granted in Australia and elsewhere according to internationally agreed patent principles with respect to patentability.

Secondly, there is no strong body of evidence that human gene patents are having major negative impacts on research, innovation, healthcare access or cost that cannot be addressed through other means.

Thirdly, most of the debate has been stimulated by the action of Myriad and GTG, and such actions can be addressed without major systemic changes to the fundamental patent system

Exploring potential actions we submit the following:

a) Disallowing human gene patents in Australia

We submit that the *Patents Act 1990* should not be amended so as to expressly prohibit the grant of patent monopolies over human gene sequences and related materials. Taken together, the observations above show that it would be folly to adopt any suggestion that human gene patents are no longer valid and should not be granted in the future in Australia. Immediate simple questions would follow:

- If human gene sequences are not considered patentable subject matter, then what will be the future of those patents that have been granted to date?
- If their validity is to be challenged, who will challenge them and undertake the associated costs?
- Who will be responsible for the cost of compensation if legislation is passed to disallow the patenting of sequences?
- How will it be possible to allow granted patents but disallow future claims to similar subject matter?
- Will the total cost of such an action result in any benefits beyond those already being achieved?
- What will be the cost to Australia of a seriously anomalous patent system?

Significantly, Australia has obligations under the international agreements relating to intellectual property to which it is a party. One of these is the TRIPS Agreement, which provides a minimum standard for the intellectual property laws of the signatories to the agreement. The TRIPS Agreement was negotiated as part of the World Trade Organisation (WTO) Agreement and for a country to be in breach of TRIPS is to place its membership of the WTO in jeopardy. Article 27 of the TRIPS Agreement directs member states to allow patents "for any inventions, whether products or processes, in all fields of technology, provided they are new, involve an inventive step and are capable of industrial application." Simply put, Australia cannot alienate itself from the rest of the world and there is no case whatsoever to consider turning Australia into an IP pariah. The effectiveness of our patent system and subsequent exploitation of inventions depends on integrity with respect to technological neutrality.

Disallowing gene patents would also have a direct negative impact on uptake of inventions that are patented in other jurisdictions. The correlation between wealth, health, healthcare access and strong IP protection is not a coincidence when comparing different countries.

In our opinion there is no basis for specifically narrowing claims to disallow molecular diagnostic applications based on human gene patents. Such narrowing, apart from probably being contrary to our TRIPS obligations, is likely to have a negative spill over impact since, to date, it would not be founded on evidence and patent holders would regard Australia as a less attractive territory for commercialisation.

Disallowing human gene sequences or disallowing diagnostic claims would result in many complex questions that would further restrict Australian access to leading healthcare technology. For example:

- How would products of gene sequences such as RNA, peptides and proteins be handled?
- How would antisense molecules be regarded?
- Would change of a single base or amino acid in the sequence with retained activity be allowable?
- Would high levels of homology between species coupled with sequence modification be allowable?

b) Control through government purchasing

Perhaps a national strategic approach should be adopted to maintain the costs of healthcare and in particular, the cost of diagnostic testing, rather than the current state/territory approach, but this has to be balanced against the costs of research and the cost of getting

the end product to the market.

Government purchasing power may provide mechanisms to control the availability and cost of medical genetic testing, including those costs that may be attributable to patent rights[24]. The ALRC recommended that Australian Health Ministers Advisory Council should examine options for using government funding and purchasing power to control the cost of goods and services that are subject to gene patents and used in the provision of healthcare. WEHI is of the strong belief that the analysis and subsequent exercise of purchasing power must be coordinated at the national level and that appropriate economic analysis will also inform conditions to be negotiated for purchase.

c) Crown use and acquisition

Crown use and acquisition provisions are rarely used but nevertheless constitute an important safeguard in helping ensure that patent protection does not have an adverse impact on significant public interests. Crown use provisions should not be relied upon too readily and should be invoked only in exceptional circumstances if confidence in the patent system is to be preserved. It should be noted that the *Patents Act* provides for compulsory acquisition by the Commonwealth of an invention covered by a patent or patent application but this does not authorise compulsory acquisition by a State or Territory.

The ALRC inquiry noted that where the provisions are invoked, adequate remuneration or compensation must still be paid to the patent holder. The Australia - US Free Trade Agreement appears to set a higher level for remuneration, by providing that patent holders must be entitled to "reasonable" compensation. The ALRC recommended that the *Patents Act* be amended to provide that, when a patent is exploited or acquired under the Crown use or Crown acquisition provisions, the remuneration or compensation that is to be paid by the relevant authority must be paid promptly and must be just and reasonable.

The ALRC recommended that AHMAC should develop a policy regarding the circumstances in which it may be appropriate for the Commonwealth or a State to exploit a patented invention under the Crown use provisions of the *Patents Act 1990* for the purposes of promoting human health. Similarly, the Department of Health and Ageing should develop a policy regarding the circumstances in which it may be appropriate for the Commonwealth to acquire a patent for the purposes of promoting human health.

WEHI submits that in order to retain confidence in Australia's patent system, to be competitive and to secure access to leading technologies such "march-in" provisions must be cautiously used. There is no evidence that this is required in the case of human gene patents.

d) Compulsory licensing and patent challenge

Other avenues such as compulsory licensing and effective sublicensing practices could be reviewed. However, it is noted that the compulsory licensing provisions have not been used in Australia, which may suggest that licensing practices in Australia are in fact working effectively. Under the *Patents Act*, a prescribed court may grant a compulsory licence to work a patent if it is satisfied that the "reasonable requirements of the public" with respect to the patented invention have not been satisfied. The ALRC was not aware of any compulsory licences having been granted since Federation and none in other jurisdictions (e.g. UK, Japan, NZ, Canada) at least since 1993. No examples have arisen since the ALRC report was published.

The ALRC recommended that the Commonwealth should amend the *Patents Act* to insert the Intellectual Property and Competition Review Committee's competition-based test as an additional ground for the grant of a compulsory licence. This test would address those circumstances in which there is a public interest in enhanced competition in a market, and the patent holder has not met reasonable requirements for access to the patented invention. The ALRC did not consider it necessary to recommend any reforms to the compulsory licensing

[24] This already occurs through the monopsony on pharmaceuticals for the PBS

provisions to address circumstances involving dependent patents, and also did not consider it necessary to recommend any reforms to the compulsory licensing provisions to address circumstances of emergency, or public non-commercial use of patented inventions.

The ALRC considered that where particular gene patent applications are believed to have an adverse impact on medical research or the cost-effective provision of healthcare, health departments should consider legal intervention, including challenging patents or patent applications and exercising Crown use powers. WEHI notes that such options have always been open. However, WEHI submits that the cost and ramifications of a government department challenging issued patents would need to be seriously considered particularly in the light of the need for evidence of restricted access and harm. Such actions are likely to have significant ramifications in areas beyond diagnostics and healthcare.

e) Skills and training

The current shortage of molecular pathologists in Australia is linked to lack of funds and career attraction and rapid growth in molecular diagnostics rather than because of human gene patents. We believe that disallowing human gene claims in itself will not have any positive impact on Australia's skill base. Again it should be noted that the most skilled countries in this area are those that allow practice of human gene patents.

Paradise et al observed that of 74 US gene patents, 448 claims of 1167 had problems and did not comply with existing patent law[25]. Such a study is by nature retrospective and reflects interpretation several years ago of the use of a new technology in the context of patent law. In our experience patent examiners in Australia, the US and other jurisdictions have appropriately exercised in recent years stricter scrutiny with respect to written description, enablement and utility, novelty and non-obviousness and definiteness. This change is as a consequence of both experience and a better understanding of the scope and limitations of a new technology. This increase in scrutiny and rigour has occurred without any radical changes to patent law on the assertion that gene patents are in someway different from all other patents.

11. Conclusions and recommendations

WEHI submits that the earlier difficulties, inconsistencies and ambiguities that have been observed in the case of human gene patents are the consequence of any new technology being exploited. Genes are not inherently difficult and outside patent law as it has so effectively evolved. Furthermore, any discussion about gene sequences must also be related to their variants and gene products. In conclusion we highlight the following areas:

a) ALRC Report[26] - WEHI generally supports the findings of the ALRC which remain relevant and current. There has been no response from the Federal Government(s) to this report and active consideration of its recommendations should be a first priority for development of Australia's system of intellectual property management and the first recommendation of the Senate Community Affairs Committee.

b) Gene patents and the patent system

We maintain that despite the initial high level of potential concern that often occurs with the introduction of a new technology, the issues associated with gene patenting are being managed through mechanisms already in place and that, while improvements can be made, a radical change is not required.

There is no case to amend the *Patents Acts* with specific reference to human gene patents and human gene patent claims should continue to be allowed in Australia. It is essential that Australia's patent system is harmonised with global agreements and retains its technology

[25] Paradise J et al (2005) Patents on human genes: an analysis of scope and claims. Science 307:1566

[26] Australian Law Reform Commission (2004) Genes and Ingenuity

neutrality. In addition, no new moral or ethical issues have arisen in the last nearly 30 years since the first patents were allowed.

Any changes that restrict human gene patent claims would undermine the importance of a dialogue between the public and private sector players with respect to patents, licenses and access. There were few cases, if any, beyond the Myriad/GTG case, presented as examples of threat to healthcare costs and access in Australia.

We conclude that the patent law in place in all major jurisdictions, including Australia, is largely effective and capable of handling the claims in human gene patent applications. Validated examples of real problems are rare and appear to resolve themselves through other mechanisms. Our recommendations relate to clarification, improved coordination, better surveillance and economic analysis.

c) Examination practices - As a new technology develops, stringency in examination practices increases to accommodate the novelty and inventiveness of any new developments in the light of what is already known. There is already evidence of increased stringency in examination in Patent Offices such as Australia, US and Europe with respect to novelty, inventive step and utility. We recommend that IP Australia place greater emphasis on increasing the proof of burden with respect to utility. This recommendation is general in nature and is not specifically limited to human gene patent claims.

d) Objective evidence – WEHI, emphasises the need to focus on facts more than opinions or theoretical objections and changes to policy and patent law must be based on sound evidence. We recommend a national approach to the economic evaluation of new medical technologies, including gene tests, and examination of the financial impact of granted patents. Such a program would allow principled and comprehensive policies to be developed and WEHI believes that such economic evaluation would be an essential precursor with respect to decisions to challenge patents, negotiate terms with patent holders or exercise Crown rights.

Economic evaluation will identify which medical technologies are the most beneficial or cost-effective for the community and would place Commonwealth, state and territory health departments in a better position for decisions with respect to gene patents. We recommend that the Australian Health Ministers' Advisory Council should establish processes for a) economic evaluation of medical genetic testing and other new genetic medical technologies; and b) examination of the financial impact of patents on the delivery of healthcare services in Australia.

e) Freedom to operate and research exemption – From its own considerable experience WEHI has observed no negative consequences of human gene patent claims granted in Australia. Furthermore, WEHI submits that patents are an important mechanism for encouraging disclosure rather than discoveries and inventions being kept as trade secrets. WEHI recommends that the assumption of research exemption be confirmed in Australia and supports the ALRC recommendation for research exemption.

In closing, we emphasise the importance of human gene patents in realising such valuable biotherapeutics as insulin, growth hormones, erythropoieitin, interferons and cytokines, as well as their contribution to diagnosis and targeted therapies, for example in the case of *Herceptin* for breast cancer.

We trust that the above will be of assistance to the Senate Community Affairs Committee and offer our services should further information be required.