Committee Secretary
Senate Legal and Constitutional Committees
PO Box 6100
Parliament House
Canberra ACT 2600
Australia

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Submission to Committee inquiry regarding the Patent Amendment (Human Genes and Biological Materials) Bill 2010

Submission from:

Dr Jennifer Leary PhD FHGSA
Laboratory Director
Familial Cancer Service
Westmead Hospital

The purpose of the private Senators' bill, to amend the Patents Act 1990 to prevent the patenting of human genes and biological materials existing in nature, is a commendable one and I welcome the opportunity to make a submission to the Committee Inquiry.

I have previously outlined my perspectives on the negative impacts of gene patents with respect to: the provision and costs of healthcare; training and accreditation of healthcare professionals; medical research; innovation in the development of new and more cost effective testing approaches; the provision of diagnostic genetic testing; and the health and well being of the Australian people, in a submission to the Senate Community Affairs Committee Inquiry into Gene Patents (2009) which I have attached as Attachment 1, for your information. Those arguments will not be restated in this current submission. My over-arching perspective is that any changes to the Patent Act which assist in the prevention of the patenting of Human genes and biological materials, such as they occur in nature and that are discovered rather than invented, should be made.

Comment on suggested Amendments 1-2
My understanding is that a discovery such as that of a biological material or human gene should not be patentable under the current Patent Act, if correctly applied, but that the amendments 1-2, as suggested, further re-iterate and strengthen that position. If that is indeed correct, I am in support of the amendments. The outcome of the amendments must be a clearly defined distinction between, and requirement for, invention over discovery in the granting of patents and a Bill that prevents the patenting of human genes and biological material.

Comment on suggested Amendment 3
Subsection 18(2) is strengthened by the suggested addition of (2) b and I am in support of this amendment.

Comment on suggested Amendment 4
I believe that the definition of biological materials may be too restrictive and that at the very least should be worded as "*including but not limited to* DNA, RNA, proteins, cells and fluids".

A goal of any society must be to strive for equitable access to the healthcare benefits that arise from the unhindered access to genetic and biological information as it is discovered. A patent that restricts access to this information potentially prevents this equity. Use of the discovery in an invented procedure, product, process etc might then be rewarded by patent protection. Any changes to the Patent Act must be in keeping with the advancement of healthcare and medical research for the benefit of all Australians.

Dr Jennifer Leary
25/2/2011

Attachment 1

Senate Community Affairs Committee Inquiry into Gene Patents
19 March 2009

Submission from:

Dr Jennifer Leary PhD FHGSA
Laboratory Director
Familial Cancer Service
Westmead Hospital
Westmead 2145 NSW
Telephone: 02 9845 6123

Submission Summary

- Human and microbial genes and non-coding sequences, proteins, and their derivatives exist as entities of the natural world and do not in any way represent an invention by an investigator, as is a requirement of a patent.
- The association between a disease and a genetic sequence is a discovery and not an invention.
- Awarding a monopoly patent to the last group involved in the research chain does not recognise the contributions of the prior investigators.
- Patent monopolies over human and microbial genes and non-coding sequences, proteins, and their derivatives will result in:
    - Increased costs of diagnostic testing;
    - Reduced access to testing and the potential for 2 classes of patients;
    - A sole provider model of laboratory services resulting in opportunity losses to the public health sector through:
        - market driven access to tests, reducing the spectrum of tests available;
        - reduced access to value adding testing for the investigation of difficult to interpret genetic variants;
        - the elimination of collegiate interpretation of scientific evidence;
        - the loss of any benefits of the academic endeavours in public laboratories with respect to discoveries of future cancer susceptibility gene;
        - reduced capacity for method innovation;
        - reduced capacity for and engagement in research;
    - Lack of access to critical information required for diagnosis where knowledge of the genetic variants is held confidentially/commercially;
    - Loss of training opportunities and expertise in molecular genetics;
    - A negative impact on medical research and the development of better genetic testing through the lack of access to sequence information and DNA resources held by monopoly testing laboratories.
    - Decreases in health and wellbeing due to (i) the loosening of the nexus between testing, counselling and decision making and (ii) lost opportunities to find other causative genes in DNA from patients without mutations in the currently known susceptibility genes.

Attachment 1

Current practice for molecular genetic testing of cancer susceptibility genes

For the majority of patients with a family history of cancer, consultation with a specialist Cancer Genetics unit (consisting of genetic counsellors and specialist physicians) is the entry point to the health system. This specialist unit, in consultation with the patient, advises on whether genetic testing is appropriate, as there are some families for whom testing is not appropriate. This process is critical in ensuring that patients receive the best advice regarding what may ultimately be a life altering test result, and also to ensure the appropriate selection of families and individuals for testing.

Once there is a decision to proceed with genetic testing, this can occur in either public or private laboratories. Once testing is complete, the laboratory provides the clinical service with a test report, which can be positive, negative, inconclusive or lastly not easily interpreted.
(i) Where a result is clearly positive for a deleterious change in a cancer susceptibility gene the management options are reasonably clear, albeit significant in scale, and may include surgery or increased surveillance.
(ii) Where a result is clearly negative the patient may have their risk assessment of cancer return to that of the general population, depending on individual circumstance. Savings to the health system can be calculated for both these scenarios- preventative measures can be employed and unnecessary management can be avoided.
(iii) A result can be inconclusive when, using the known genetic sequence information and the available technology, no causative mutation can be found in a cancer susceptibility gene however there still remains a possibility that other genes, other disease mechanisms and other untested regions of the genes may one day be investigated.
(iv) However for a large number of test reports the testing result is not easily interpreted. Clinicians are largely dependent on the scientific expertise of the laboratory to interpret difficult test results and often this cannot be done without initiating further, more complex testing, extensive literature review and *in silico* modelling and extensive consultation with other scientists. This extra activity is not generally provided by the private sector.

The consequences of genetic testing results, if there are errors in interpretation, or equivocal interpretations, can be disastrous for a patient who may need to make decisions on surgery and their future clinical management for life. This impact also extends to the relatives of the patient.

In summary, the importance of accurate genetic testing results cannot be underestimated for the wellbeing of patients with a family history of cancer.

Terms of Reference addressed:

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:

(a) the impact which the granting of patent monopolies over such materials has had, is having, and may have had on:

(i) the provision and costs of healthcare,

The granting of patents over genetic sequences will have a negative impact on the provision and costs of healthcare in Australia.

Costs of healthcare

Ownership of a patent inevitably leads to a demand for profit. Thus the granting of patents would most likely lead to an **increase in diagnostic testing** costs due to the imposition of **licensing fees** for the use of genetic sequence information or through the simple market forces of **lack of competition**. The provision of diagnostic laboratory services within the public sector would most likely be reduced or eliminated as a result of the increased costs due to licensing fees or the imposition of monopoly conditions on service provision by the patent holder. There is international experience of the increased costs associated with monopoly testing private laboratories compared with public sector laboratories.

There are potential impacts on the access to testing through a sole provider model of laboratory services if a gene patent were to lead to a monopoly of service provision: a lack of price competition may result in cost escalations that ultimately govern the number of requests that can be ordered by the publicly funded clinical services and the risk of creating two categories of patient – those that can pay privately and those that cannot. Some patents will always be covered by Government subsidised testing but others will miss out. This judgment is in part informed by the Canadian experience of a monopoly surrounding the breast cancer susceptibility genes, BRCA1 and BRCA2. Furthermore, those patients/individuals that cannot be tested may ultimately add to the national health burden through the development of disease that may have remained undetected without access to testing or through undergoing unnecessary surveillance and treatment procedures.

Provision of healthcare: the complexity of interpretation of gene testing results

Recent experience in the breast cancer gene-testing field has highlighted the complexities surrounding the potential granting of monopoly status to a laboratory as a result of a gene patent. Interpretation of a test result in the context of cancer related genes and its significance for the patient is not a routine activity. Consequently, experience in the field of breast cancer genetics gained over a substantial period of time has provided the basis for accurate mutation assessment. **The complexity of the interpretation of the tests is beyond a single laboratory**, and requires a broader community of scientists working in a national and even international context, to unravel the complexity of any observed mutation. We have very real examples of disparity in assessments that are being worked through regularly between Australian diagnostics laboratories. Vastly different clinical decisions that can have immeasurable impacts on patients (eg surgery versus no surgery) can be made based on the scientific interpretation of a mutation/variant in a gene and it is only with scientists working in concert that such scenarios can be minimised. **A monopoly situation created by the granting of a gene patent would reduce the numbers of scientists involved with the**

patented gene and thus the expertise necessary to make sound scientific judgements may not be available.

Provision of healthcare: Loss of clinically relevant information from the public sector

Any move to the monopolisation of testing genes could result **in information on genetic variants being locked** up as the information could be viewed as having immense commercial and scientific value and could be seen as a major asset of a company holding a gene patent. This experience has been borne out by the monopoly testing for BRCA1 and BRCA2 in the United States where knowledge of the genetic variants observed is held commercially. Sharing knowledge of mutations is essential to understanding the clinical significance of the rare variants that can be observed in genes. Access to unpublished experimental data, knowledge of the frequency of observations, knowledge of instances of co-occurrence with other variants in addition to robust exchange of ideas amongst a variety of scientists can all help to unravel the complexity faced in the interpretation of the variants. The knowledge is currently shared between the public laboratories and deposited on public databases where possible. There are currently significant initiatives in Australia and internationally to broaden this public accessibility with the development of shared databases (The Human Variome Project). If knowledge is held by any one group exclusively and not shared scientists will not gain the necessary expertise to enable the appropriate scientific interpretation and diagnosis of the clinical impact of variants. **Clinical management will be compromised where the pathogenicity of a variant cannot be determined simply through lack of access to information held by a monopoly testing-laboratory.**

Provision of healthcare: Laboratory capacity and expertise

Public laboratories generally have the capacity and expertise to extend testing beyond the routine sequence analysis that would be the primary activity of a commercial patent holder offering testing. Additional tests including RNA analysis, real-time and long range Polymerase Chain Reaction analysis, creation of cell lines and exploration of protein structure and function can be employed for the additional investigation of difficult to interpret variants. This is complemented by sharing of DNA controls, and cooperative working on standardisation of interpretation and testing in an area where rules/guidelines often do not exist, and a robust exchange of knowledge, ideas, and opinion amongst Australian and overseas laboratories. This combined experience is harnessed through regular personal, email, telephone and conference contact amongst all the public laboratories throughout Australia. This combined approach and expertise cannot exist within the limited workforce of any single laboratory and may be considered a luxury in the profit driven atmosphere of a monopoly testing laboratory.

The granting of a patent over genetic material by its very nature locks the sequence information away from others and thus stifles the opportunity to improve diagnosis and treatment of disease. **Innovation in technology and methodologies that could be introduced to improve health service delivery would be eliminated** for the patented gene. Improvements to healthcare would be at the mercy of the patent holder.

Terms of Reference addressed:

(ii) the provision of training and accreditation for healthcare professionals

Loss of training opportunity and scientific expertise

Training and subsequent accreditation of scientists in the molecular genetic discipline depends on access to the experience of others, availability of DNA and clinical resources to expand knowledge and the sharing of scientific information. The granting of patents will have a negative impact on the ability to train molecular genetic scientists and clinical trainees specialising in molecular pathology.

Public laboratories generally have the capacity and expertise to extend testing beyond the routine sequence analysis that would be the primary activity of a commercial patent holder offering testing. **An extensive test repertoire and cooperative working** on standardisation of interpretation and testing in an area where rules/guidelines often do not exist, and a robust exchange of knowledge, ideas, and opinion amongst Australian and overseas laboratories is essential. This combined approach forms the basis of a **broad capacity to train scientists** in preparation for accreditation to Memberships and Fellowships of the Human Genetics Society of Australasia and clinical trainees from the Royal College of Pathologists of Australasia. This combined approach and expertise **cannot exist within the limited workforce of any single laboratory**. Moreover, if the DNA resources for testing become concentrated in laboratories with the monopoly rights to test, **scientific skills will degrade through a lack of opportunity to undertake such training across the broad range of tests required**.

If research and testing of cancer related genes is removed from publicly funded laboratories due to the granting of gene patents that result in monopoly "ownership" it is to be expected that the **scientific expertise required for the interpretation of the variants observed in these genes will be lost** and consequently test interpretation will be solely provided by a single private laboratory. Well-trained scientists are essential for the interpretation of genetic variants as the field is complex and vast, and many variants have unknown clinical significance such that it is largely beyond the scope and time availability of referring clinicians to interpret the pathogenicity of complex variants. Clinical management of families will ultimately be affected if the communication regarding the molecular testing results is between clinicians and a monopoly testing facility rather than though a broader community of scientists. **If patent monopolies ultimately covered many genes, not just cancer genes, molecular genetic experience may be lost altogether from the public sector.**

As described above, the interpretation of a test result and its significance for the patient is not a routine activity. Experience in the field of cancer genetics gained over a substantial period of time is essential for accurate mutation assessment. **The complexity of the interpretation of the tests requires extensive training in both laboratory based and bioinformatic activity that is reliant on the use of genetic sequences.**

Terms of Reference addressed:

(iii) the progress in medical research

The granting of patents will have a negative impact on the development of better genetic testing through medical research.

Loss of capacity to investigate alternate cancer susceptibility genes and disease mechanisms

Using the breast cancer susceptibility genes, BRCA1 and BRCA2, as examples there would almost certainly be impacts on the further investigation of these genes and of other breast cancer susceptibility genes if there is a monopoly on testing that arose from the issue of a patent. Only a small proportion of the families currently tested for breast cancer susceptibility can be explained by mutations in BRCA1/2 and **further research is essential to identify other inherited susceptibility mechanisms**. The public laboratories and clinicians have a duty of care to such families to be involved in breast cancer research to enable this unexplained susceptibility to be investigated. DNA is held indefinitely by public laboratories to enable further research and testing. Currently as new information becomes available laboratories can return to the stored DNA to initiate further testing. If the DNA resources from these families are held by a monopoly laboratory, **the at-risk families who remain unexplained after a negative BRCA1/2 result will not be readily identifiable for independent research or testing of other candidate genes and other mechanisms of gene inactivation** in BRCA1/2 by any other laboratories. The public laboratories would have reduced capacity to initiate research proposals, as they would not have the knowledge of the families requiring the further research if family testing is directed from clinical services to monopoly testing facilities. Furthermore, the **public laboratory will not hold any DNA to perform this research**. This will be even more difficult for less common diseases. **Moreover expertise in breast cancer research will disappear from the public laboratories if these laboratories are no longer involved in testing breast cancer patients.**

If other breast cancer susceptibility genes are discovered and testing of at-risk families warranted, the clinical teams will have their **access to advances in testing directed by commercial dictates** rather than clinical need especially as the public laboratories will not have the DNA to undertake any validation studies and initiate new tests.

Gene discovery programs will also be hampered by the lack of access to the clinical cohorts and DNA that can currently be accessed through the public sector, after appropriate ethical clearances and patient consent, if DNA resources are held by monopoly testing laboratories.

Innovation in the development of new and more cost effective testing approaches

Innovation in the development of new and more cost effective testing approaches would be reduced if there was a monopoly created due to a gene patent. There is published evidence where NSW public sector laboratories have led publicly funded BRCA1/2 research using publicly held DNA and clinical information that resulted in changes to laboratory practice and then subsequent improvements in patient services. This **research would not be possible in the private sector, as more than just DNA is required for such studies,** and it most likely would not occur given the prime purpose

of a commercial enterprise is profit. Both public and private laboratories benefited from this research and the results have influenced clinical service.

If the granting of patents results in prohibitive or restrictive license fees, research would obviously be hampered by the cost of using the gene sequence.

Terms of Reference addressed:

(iv) the health and wellbeing of the Australian people

The granting of patents will have a negative impact on the health and wellbeing of the Australian people.

Patients who receive an inconclusive/negative test result need the **opportunity for re-testing of stored DNA** when new information and technology becomes available for both the currently known genes or the as yet discovered disease specific genes, in order to avoid a lifetime of uncertainty, anxiety and surveillance. **There is no guarantee that this will be possible either practically or economically if there is a monopoly**, commercial testing laboratory.

Currently, patients receive their testing results and advice through a structured and considered clinical service with a holistic view to their healthcare. However, patent monopolies, generally held within the private sector, have the potential to result in an increase in "direct to market" advertising of genetic tests. Such referrals for testing, where a practitioner or private client, who is outside of the more regulated Genetics Services setting and who would have insufficient training, qualifications and experience to manage the patient and the patient's family raises the real prospect of inappropriate testing and costs. Commercialisation of testing has the potential for longer term, wider social costs. The U.S and Canadian experience of **"direct to market" advertising has resulted in the exploitation of breast cancer anxiety and increased private testing of those for whom the clinical utility of the test is questionable**. Market driven access to testing also has the potential to reduce the spectrum of tests available.

A restriction on the use of genetic information through gene patents will impede research that may otherwise enhance health outcomes through better disease diagnosis, disease prevention or minimising impact of disease.

Terms of Reference addressed:

(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 *Patents Act 1990* should be amended, in light of any matters identified by the inquiry with respect to any genetic sequence that exists in the natural world.

Adverse impacts may be ameliorated by enforcing an exemption from licensing fees that might arise from a patent, for all testing and research using human and non-human genetic sequences in publicly funded institutions.

Attachment 1

Terms of Reference addressed:

(c) whether the* Patents Act 1990 *should be amended so as to expressly prohibit the grant of patent monopolies over such materials.

The *Patents Act 1990* should be amended to expressly prohibit the granting of patent monopolies over human and non-human genetic sequences as:

- these sequences exist as entities of the natural world and do not in any way represent an invention by an investigator, as is a requirement of a patent;
- the association between a disease and a genetic sequence is a discovery and not an invention;
- patenting part of a human undermines human dignity;
- patenting of a genetic sequence is inevitably the result of activity and information from a variety of groups/ researchers. To award a patent to the last group involved in the research chain does not recognise the contributions of the prior investigators nor acknowledge the vast amounts of money expended by such investigators in the pursuit of knowledge for the benefit of others;
- " Genes and genetic sequence have an informational content. One cannot "invent around" the sequence if it is patented." (Matthijs 2006 *Familial Cancer* 5:95-102). Building on the knowledge of others will be restricted if genetic sequences are not accessible for use by the broader research community.

Dr Jennifer Leary