THE PULSE WEBINAR
PATENT LAW IN THE LIFE SCIENCES SECTOR – US AND AUSTRALIAN PERSPECTIVES

Dr. Lisa Haile & Nicholas Tyacke
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BIOPHARMA PATENT STRATEGIES: IMPACT OF MAYO/ MYRIAD/ ALICE/ SEQUENOM
• Are diagnostic tests patentable?
• What is the current state of the law surrounding personalized medicine?
• Significant Cases in the U.S. 2012-2015:
  – *Mayo Collaborative Services et al. v. Prometheus Laboratories Inc.* (Supreme Court, 2012)
  – *ACLU et al. v. USPTO and Myriad Genetics* (Supreme Court, 2013)
  – *Alice Corp. Pty. Ltd. v. CLS Bank International* (Supreme Court, June 2014)
“To transform an unpatentable law of nature into a patent eligible application of such a law, a patent must do more than simply state the law of nature while adding the words ‘apply it’...we conclude that the patent claims at issue here effectively claim the underlying laws of nature themselves. The claims are consequently invalid.”

Patent claims for methods of diagnosing diseases that merely provide “routine” steps and observations of “natural phenomena” (e.g., look at levels of a metabolite before and after administration of a drug) are no longer valid or enforceable.

Is the method of measuring the level of the marker novel or are the reagents used in the diagnostic method novel?
"A naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated”

However, the Court also held that manipulation of a gene to create something not found in nature—such as a strand of synthetically-produced complementary DNA (cDNA)—could still be eligible for patent protection.

What is the effect on patents after Myriad? How far reaching is the case?

Following Myriad, the USPTO applied the case beyond DNA sequences to include naturally occurring proteins, stem cells, etc. however, claims to fragments of DNA or proteins were still being issued at that time.
Non-naturally occurring, e.g., add labels, fusion proteins, vectors, heterologous sequences

• An isolated nucleic acid sequence as in SEQ ID NO:1 and encoding a protein having amylase activity, **operably linked to a heterologous promoter.**

• A purified protein comprising SEQ ID NO:2, **covalently bound to a solid support.**

• An isolated nucleic acid sequence of SEQ ID NO:1 **in a viral vector.**

• Gene profiles or panels, e.g., combinations.
1. A method of producing a recombinant polypeptide comprising an amino acid sequence having at least 75%, 80%, 85%, 90%, 95%, 97%, 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:16; or an amino acid sequence encoded by a nucleic acid having at least 75%, 80%, 85%, 90%, 95%, 97%, 99%, or 100% sequence identity to the polynucleotide sequence of SEQ ID NO:2, comprising:

   a) providing a nucleic acid sequence operatively linked to a heterologous regulatory sequence; and

   b) expressing the nucleic acid of (a) under conditions that allow expression of the polypeptide, thereby producing a recombinant polypeptide.

2. A vector comprising a polynucleotide encoding the polypeptide produced by the method of claim 1 operably linked to a heterologous promoter.
• What is the effect of US not allowing gene patents?
• Will research go overseas since Europe and Asia still allow gene patents?
• Will companies leave the US and go to other markets?
• More difficult for a genomics/Dx company to get funded in the absence of patents.
• How far reaching is the case? Does it extend to naturally occurring proteins, e.g., antibodies, proteins, stem cells?
• Take another look at FTO opinions and assess validity of your own patent claims before asserting them.
Alice v. CLS Bank 2014

*Alice* is a Supreme Court Case (June 2014) that sets forth the eligibility test under Section 101 for patent claims that involve abstract ideas.

*Alice* confirms that the two-part test from *Mayo v. Prometheus Labs* (Supreme Court 2012) is applicable to abstract ideas:

1. Are claims at issue directed to one of the patent-ineligible concepts (e.g. law of nature, natural phenomenon or abstract idea)?
2. If yes, is there an “inventive concept”? Do the claims include an element or combination of elements such that the claim amounts to **significantly more** than a claim to the ineligible concept (abstract idea) itself.
Alice was recently applied in a life sciences patent case:

Here, the claims merely set forth “well-understood, routine and conventional activity” engaged in by scientists at the time of the Myriad applications (e.g., ELISA, PCR)

Comparison of a sequence in the genome to a reference sequence is considered “abstract mental steps necessary to compare two nucleotide sequences”

The scope of patent eligible subject matter for method claims may be significantly narrowed following this decision.

Composition claims to primers and probes were now held to be invalid, leading to an inference that protein fragments such as epitopes will likely be patent-ineligible

Is there enough in the claims to provide sufficient inventive concept to render the claims patent eligible?
1. A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises comparing germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject.

7. The method of claim 1 wherein a germline nucleic acid sequence is compared by hybridizing a BRCA1 gene probe which specifically hybridizes to a BRCA1 allele to genomic DNA isolated from said sample and detecting the presence of a hybridization product wherein a presence of said product indicates the presence of said allele in the subject.

8. The method of claim 1 wherein a germline nucleic acid sequence is compared by amplifying all or part of a BRCA1 gene from said sample using a set of primers to produce amplified nucleic acids and sequencing the amplified nucleic acids.

20. A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 11 and 12 which comprises analyzing a sequence of the BRCA1 gene or BRCA1 RNA from a human sample or analyzing the sequence of BRCA1 CDNA made from mRNA from said sample.

21. The method of claim 20 wherein a germline alteration is detected by hybridizing a BRCA1 gene probe which specifically hybridizes to an allele of one of said alterations to RNA isolated from said human sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said allele in the sample.
• “First, one must determine whether the claims at issue are directed to a patent-ineligible concept, and if the answer is yes, then it must be determined whether additional claim elements transform the nature of the claim into patent-eligible subject matter.”

• On Pre-emption: “Sequenom’s attempt to limit the breadth of the claims by showing alternative uses of cffDNA outside of the scope of the claims does not change the conclusion that the claims are directed to patent ineligible subject matter.”

• The district court agreed with Ariosa’s argument that the claims of the patent were directed to the natural phenomenon of paternally inherited cffDNA and that the claims did not add enough to the natural phenomenon to make the claims patent eligible under §101.
• It is becoming abundantly clear that the courts and the US Patent and Trademark Office are consistently relaying a message that if method claims do no more than recite routine or conventional methods and steps, they will be found to be invalid or patent ineligible.

• Regardless of the significance of an invention to medicine, it may not be important enough to warrant patent protection.

• In pursuing claims today, rather than trying to pre-empt the broad scope of a natural phenomenon, law of nature or observation, it is more realistic for companies to initially focus on claiming their commercial tests and products and work outward from there.
UPDATE ON RECENT SIGNIFICANT CASES REGARDING THE PATENTABILITY OF LIFE SCIENCES INVENTIONS IN AUSTRALIA
Recent significant Australian decisions regarding the patentability of life sciences inventions:

– *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd* [2013] HCA 50 (*Apotex v Sanofi*)

Patentable inventions

- Section 18 – must be a manner of manufacture within the meaning of section 6 of the Statute of Monopolies

- National Research Development Corporation v Commissioner of Patents (1959) – upheld the validity of a patent for the use of previously unknown properties of a known chemical to effect a new purpose:

  "The effect produced by the appellant's method exhibits the two essential qualities upon which 'product' and 'vendible' seem designed to insist. It is a 'product' because it consists in an artificially created state of affairs, discernible by observing over a period the growth of weeds and crops respectively on sown land on which the method has been put into practice. And the significance of the product is economic..."  (emphasis added)
Patent claimed a method of preventing or treating psoriasis using leflunomide (not the compound itself).

In a 5:1 decision the High Court held that a "method of medical treatment" can be a patentable "manner of manufacture" and therefore patentable under Australia's patent legislation:

- "The exclusion from patentability of methods of medical treatment represents an anomaly for which no clear and consistent foundation has been enunciated. Whatever views may have held in the past, methods of medical treatment, particularly the use of pharmaceutical drugs, cannot today be conceived as "essentially non-economic". ... there is no gainsaying the economic significance of medical treatments independently of the flow-on benefits of a well-maintained work force."
Australian Patent No. 686004
Expired on 11 August 2015
30 claims. Claims 1-3 relate to an isolated nucleic acid. Claims 4-30 are for applications arising from the fact that specific mutations or polymorphisms in the BRCA1 gene are indicative of a predisposition to breast cancer and ovarian cancer.

Australian Patent No. 1995033212, p. 198
• Claims 1-3 at issue. Claim 1:
  – "An isolated nucleic acid coding for a mutant or polymorphic BRCA1 polypeptide, said nucleic acid containing in comparison to the BRCA1 polypeptide encoding sequence ... one or more mutations or polymorphisms selected from [specified] mutations..." (emphasis added)

<table>
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<th>Name</th>
<th>Exon #</th>
<th>Codon</th>
<th>Base Position¹</th>
<th>Base Change</th>
<th>Effect</th>
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<td>356</td>
<td>1186</td>
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<td>gln ⇔ arg</td>
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<tr>
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<td>11</td>
<td>1038</td>
<td>3233</td>
<td>A ⇔ G</td>
<td>glu ⇔ glu</td>
</tr>
</tbody>
</table>
Justice Nicholas held claims 1–3 to claim patentable subject matter, based on his application of his statement of the requirements of NRDC as follows:

— "a product that consists of an artificially created state of affairs which has economic significance will constitute a 'manner of manufacture'." (emphasis added)
Expanded bench of five judges of the Full Federal Court unanimously upheld first instance decision that the claimed isolated nucleic acid sequences are patentable subject matter in Australia.

The Full Court said of NRDC:

- "The Court held that it is sufficient for a product to result in 'an artificially created state of affairs', leading to 'an economically useful result'." (emphasis added)

Applying that test, the Full Court held:

- "The isolated nucleic acid, including cDNA, has resulted in an artificially created state of affairs for economic benefit. The claimed product is properly the subject of letters patent. The claim is to an invention within the meaning of s 18(1) of the Act." (emphasis added)
In holding that the claimed invention was patentable subject matter, the Full Court characterised the invention as a chemical composition, rather than one directed to genetic information, and held:

- "What is being claimed is not the nucleic acid as it exists in the human body, but the nucleic acid as isolated from the cell. The claimed product is not the same as the naturally occurring product. **There are structural differences but, more importantly, there are functional differences because of isolation.**" (emphasis added)
• *D'Arcy v Myriad* (FCAFC) and *Apotex v Sanofi* (HC) decisions had instilled confidence in Australia as a jurisdiction that recognised and appropriately afforded intellectual property rights for innovation in the life sciences sector.

• *D'Arcy v Myriad* was appealed to the High Court, with hearings held in June 2015.
On 7 October 2015, the High Court unanimously (in three separate judgments) allowed the appeal, setting aside the unanimous Full Court decision and revoking claims 1 to 3 of Myriad's patent.

ORDER

1. Appeal allowed.

2. Set aside paragraph 1 of the order of the Full Court of the Federal Court of Australia made on 5 September 2014 and, in its place, order that:

   (a) the appeal be allowed; and

   (b) paragraph 1 of the order of Nicholas J made on 15 February 2013 be set aside and, in its place, order that claims 1, 2 and 3 of Australian Patent No 686004 be revoked.
The majority held that the lower courts had asked the wrong question:

"The question for ... determination ... was not whether a claimed invention, prima facie patentable, should be denied patentability by judicial fiat. The question was whether the claimed invention lay within the established concept of a manner of manufacture and, if not, whether it should nevertheless be included in the class of patentable inventions as defined in s 18(1)(a) of the Act."
• Myriad submitted that the Court ought to treat the impugned claims as claims for a chemical compound. It argued that there was "no jurisprudential basis or normative principle upon which claims to isolated nucleic acids should be treated differently from any other product claims."

• The majority held that to treat the claims as directed to chemical compounds, as Myriad submitted and the Full Court had done, was to elevate form over substance, and that the substance of the invention is information embodied in arrangements of nucleotides.

• The majority further held that, properly construed, the subject matter of the claims were not within the established boundaries of patentability and wider considerations than Myriad's characterisation of them as an "artificially created state of affairs of economic utility" come into play.
Wider considerations:

1. Whether claimed invention is a product made or a process producing an outcome as a result of human action.
2. Whether the claimed invention has economic utility.
3. Consistency with the purposes of the *Patents Act*:
   - Whether claimed invention could give rise to a large new field of monopoly protection with potentially negative effects on innovation.
   - Whether claimed invention could have chilling effects on activities beyond those within the formal scope of the claims.
   - Whether according patentability would require the court to assess important and conflicting public and private interests and purposes.
4. Whether according patentability would enhance or detract from coherence of the law relating to inherent patentability.
5. International legal obligations and laws in other jurisdictions.
6. Whether according patentability would involve law-making of a kind which should be done by the legislature.
The substance of the invention is not "made":

- "The information is not "made" by human action. It is discerned. That feature of the claims raises a question about how they fit within the concept of a "manner of manufacture". As appears from s 6 of the Statute of Monopolies, an invention is something which involves "making". ... Whatever it is, it must be something brought about by human action. The requirement, in each claim, that the sequence in the isolate bear specified mutations or polymorphisms raises the same problem in a particular way. Satisfaction of that integer depends upon a characteristic of the human being from whom the nucleic acid is isolated, a characteristic which is not shared by all human beings. It has nothing to do with the person who isolates the nucleic acid bearing the mutant sequence." (emphasis added)

- "[T]he fact of the existence of the requisite mutations or polymorphisms is a matter of chance. It is not something "made". It is not "artificially created".
Wider considerations militated against characterisation as a "manner of manufacture":

- "Claims 1 to 3 include the products of applying any process, known or unknown, to the cells of a human being which extracts or replicates from them nucleotides which code for mutant or polymorphic BRCA1 in the sequences specified in the Patent, whether or not the isolate contains other components and sequences. The size of the class of the products as defined is large. ... The boundaries of the class are not defined by a limiting range of chemical formulae. There is a real risk that the chilling effect of the claims, on the use of any isolation process in relation to the BRCA1 gene, would lead to the creation of an exorbitant and unwarranted de facto monopoly on all methods of isolating nucleic acids containing the sequences coding for the BRCA1 protein. The infringement of the formal monopoly would not be ascertainable until the mutations and polymorphisms were detected. Such a result would be at odds with the purposes of the patent system." (emphasis added)
The majority held that the claims would not fall within the scope of a 'manner of manufacture' unless its scope was extended, and that this was for the legislature:

- "The substance of the invention as claimed and the considerations flowing from its substance militate against that characterisation. To include it within the scope of a "manner of manufacture" involves an extension of that concept, which is not appropriate for judicial determination." (emphasis added)

- "The proposition that a broad statutory concept [manner of manufacture] applies to a new class of case on the boundaries of existing judicial development of that concept requires consideration of the limits of judicial law-making... Where an affirmative application of the concept is likely to result in the creation of important rights as against the world, to involve far-reaching questions of public policy and to affect the balance of important conflicting interests, the question must be asked whether that application is best left for legislative determination. The patentability of nucleotide sequences derived from human DNA is in that category. The inherent patentability of the invention as claimed would powerfully imply patentability of any claim for an isolated nucleic acid coding for a specified polypeptide." (emphasis added)
The majority also held that:

– unlike in the *Sanofi v Apotex* case, to include this class of claim within the concept of manner of manufacture would not contribute to coherence in the law;

– Australia's international obligations and the differently framed patent laws of other jurisdictions do not support the conclusion that this class of claim should fall within the concept of manner of manufacture.
A broad or narrow decision?

- the patentability of the other claims of the patent-in-suit, directed to probes, vectors, methods of production, and methods of diagnosis, had not been challenged in the litigation. Thus, the High Court did not make any finding with respect to those claims.

- The majority stated:
  - "This court is not concerned in this appeal with ‘gene patenting’ generally but whether the invention as claimed in claims 1 to 3 falls within the established concept of manner of manufacture."

- Context also suggests a narrow decision.

- What about cDNA? The majority stated:
  - "the information stored in the sequence of nucleotides coding for the mutated or polymorphic BRCA1 polypeptide is the same information as that contained in the DNA of the person from which the nucleic acid was isolated. It is the existence of that information which is an essential element of the invention as claimed. The product is the medium in which that information resides. That characteristic also attaches to cDNA, covered by the claims, which is synthesised but replicates a naturally occurring sequence of exons." (emphasis added)
On 16 October 2015, IP Australia issued its proposed revised examination practice.

Comment sought by 6 November 2015.

In the interim, examination of patent applications containing claims directed to technology that could be impacted by the *D'Arcy v Myriad* decision is on hold until examination practice is settled.
• IP Australia has interpreted the *D'Arcy v Myriad* decision as holding that a claim to an isolated nucleic acid that merely represents information coding for a polypeptide is not patent eligible.

• On that basis, it has indicated in the proposed revised examination practice that it considers the following are not patent eligible in Australia:
  
  – Naturally occurring human and non-human nucleic acid sequences encoding polypeptides or functional fragments thereof - either isolated or synthesised;
  
  – cDNA;
  
  – Naturally occurring human and non-human coding RNA - either isolated or synthesised.
IP Australia has further indicated that it will continue to treat claims directed to the following as patent eligible as "they do not merely represent information coding for a polypeptide":

- Naturally occurring isolated regulatory DNA (e.g. promoters, enhancers, inhibitors, intergenic DNA);
- Isolated non-coding (e.g. "Junk") DNA and RNA (e.g. miRNA);
- Naturally occurring isolated bacteria and viruses;
- Isolated polypeptides and synthesised/modified polypeptides;
- Isolated polyclonal antibodies and monoclonal antibodies;
- Chemical molecules purified from natural sources (e.g. new chemical entities, antibiotics, small molecules);
- Isolated cells including isolated stem cells;
- Probes and primers;
- Isolated interfering/inhibitory nucleic acids (e.g. antisense, ribozymes) and fusion/chimeric nucleic acids; and
- Transgenes comprising naturally occurring gene sequences and vectors, microorganisms, animals, and plants comprising a transgene.
For decades, the practice in Australia has been to recognise as patent eligible subject matter a broad range of inventions in the life sciences sector, including isolated naturally occurring material and methods of medical treatment.

In 2013, the High Court confirmed the patent eligibility of methods of medical treatment.

In 2015, the High Court held that the claims in suit to an isolated nucleic acid coding for a particular mutant or polymorphic polypeptide are not claims to patent eligible subject matter.

IP Australia has proposed a relatively narrow application of the High Court's decision, such that it will continue to treat the isolated naturally occurring material specified on the previous slide as patent eligible.

It thus appears that Australia will not head down the path adopted by US courts and the USPTO, where broad areas of technology have been deemed patent ineligible.

The Australian legal environment thus remains one conducive to research and development, and investment, in the Australian biotechnology industry.
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