FEDERAL COURT OF AUSTRALIA

Cancer Voices Australia v Myriad Genetics Inc [2013] FCA 65

Citation:	Cancer Voices Australia v Myriad Genetics Inc [2013] FCA 65
Parties:	**CANCER VOICES AUSTRALIA and YVONNE D'ARCY v MYRIAD GENETICS INC and GENETIC TECHNOLOGIES LIMITED (ABN 17 009 212 328)**
File number:	NSD 643 of 2010
Judge:	**NICHOLAS J**
Date of judgment:	15 February 2013
Catchwords:	**PATENTS** – Patent including claims for isolated DNA and RNA (nucleic acid) – whether claims to composition comprising naturally occurring DNA and RNA that has been isolated are for a manner of manufacture for purposes of s 18(1)(a) of *Patents Act 1990* (Cth) – where isolated DNA and RNA has been extracted from cells removed from human body and purged of other biological material with which it is associated in the cell – whether isolation of naturally occurring DNA and RNA results in an artificial state of affairs with a discernible effect – whether claims to isolated DNA and RNA are to a "mere discovery" and therefore not patentable – whether claims to isolated DNA and RNA are to a "product of nature" and therefore not patentable – whether order revoking challenged claims should be made **Held:** each of challenged claims is to a manner of manufacture – requirements of s 18(1)(a) of *Patents Act 1990* (Cth) satisfied – where non-compliance with requirements of s 18(1)(a) sole ground relied upon in support of application for orders revoking challenged claims – application dismissed with costs.
Legislation:	*Patents Act 1990* (Cth) s 18 Statute of Monopolies s 6 *Patents Act 1949* (UK) *Patents Bill 1990* (Cth) *Patent Amendment (Human Genes and Biological Materials) Bill 2010* (Cth) *Intellectual Property Laws Amendment (Raising the*

Bar) Act 2012 (Cth)

Cases cited:

Advanced Building Systems Pty Limited v Ramset Fasteners (Aust) Pty Limited (1998) 194 CLR 171
American Cyanamid Company v Upjohn Company [1971] RPC 425
CCOM Pty Ltd v Jiejing Pty Ltd (1994) 51 FCR 260
Diamond v Chakrabarty 447 US 303
Festo Corp. v Shoketsu Kinzoku Kogyu Kabushiki Co. 535 US 722, 739 (2002)
Funk Bros. Seed Co. v Kalo Inoculant Co. (1948) 333 US 127
Genentech Inc's Patent [1987] RPC 553
Grain Pool of Western Australia v Commonwealth of Australia (2000) 202 CLR 479
Joos v Commissioner of Patents (1972) 126 CLR 611
Kirin-Amgen Inc v Board of Regents of University of Washington (1995) 33 IPR 557
Kirin-Amgen Inc v Hoechst Marion Roussel Ltd [2005] RPC 169
Mayo Collaborative Services v Prometheus Laboratories Inc 132 SCt 1289 (2012)
National Research Development Corporation v Commissioner of Patents (1959) 102 CLR 252
Re GEC's Application (1943) 60 RPC 1
Reynolds v Herbert Smith & Co Ltd (1903) 20 RPC 123
The Association for Molecular Pathology & Ors v United States Patent and Trademark Office and Myriad Genetics Inc 653 F3d 1329 (2011)
The Association for Molecular Pathology & Ors v United States Patent and Trademark Office and Myriad Genetics Inc 689 F3d 1303 (2012)

Andrew Stewart, Phillip Griffith and Judith Bannister, *Intellectual Property in Australia,* (4th ed, LexisNexis Butterworths Australia, 2010)
Philip W Grubb, *Patents for Chemicals, Pharmaceuticals and Biotechnology* (4th ed, Oxford University Press, 2004)
Dr Matthew Rimmer, *The New Conquistadors: Patent Law and Expressed Sequence Tags* (2005) 16 J. L. Inf. & Sci. 10.

Date of hearing: 20, 21, 22, 23 and 24 February 2012

Place: Sydney

Division: GENERAL DIVISION

Category:	Catchwords
Number of paragraphs:	138
Counsel for the Applicants:	Mr D Catterns QC with Dr P Cashman
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Solicitor for the First Respondent:	Jones Day
Solicitor for the Second Respondent:	Wrays Lawyers Pty Ltd

IN THE FEDERAL COURT OF AUSTRALIA
NEW SOUTH WALES DISTRICT REGISTRY
GENERAL DIVISION **NSD 643 of 2010**

BETWEEN:	**CANCER VOICES AUSTRALIA** **First Applicant**
	YVONNE D'ARCY **Second Applicant**
AND:	**MYRIAD GENETICS INC** **First Respondent**
	GENETIC TECHNOLOGIES LIMITED **(ABN 17 009 212 328)** **Second Respondent**
JUDGE:	**NICHOLAS J**
DATE OF ORDER:	**15 FEBRUARY 2013**
WHERE MADE:	**SYDNEY**

THE COURT ORDERS THAT:

1. The amended application be dismissed.

2. The applicants pay the respondents' costs.

3. Subject to any further order, order 2 is stayed for 21 days and, if a notice of appeal is filed within that time, until the determination of the appeal.

Note: Entry of orders is dealt with in Rule 39.32 of the Federal Court Rules 2011

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	YVONNE D'ARCY **Second Applicant**
AND:	**MYRIAD GENETICS INC** **First Respondent**
	GENETIC TECHNOLOGIES LIMITED **(ABN 17 009 212 328)** **Second Respondent**
JUDGE:	**NICHOLAS J**
DATE:	**15 FEBRUARY 2013**
PLACE:	**SYDNEY**

REASONS FOR JUDGMENT

GENERAL BACKGROUND

1 The issue that arises in this case is of considerable importance. It relates to the patentability of genes, or gene sequences, and the practice of "gene patenting". Briefly stated, the issue to be decided is whether under the *Patents Act 1990* (Cth) (**the Act**), a valid patent may be granted for a claim that covers naturally occurring nucleic acid – either deoxyribonucleic acid (**DNA**) or ribonucleic acid (**RNA**) – that has been "isolated". In this context, the word "isolated" implies that naturally occurring nucleic acid found in the cells of the human body, whether it be DNA or RNA, has been removed from the cellular environment in which it naturally exists and separated from other cellular components also found there.

2 The genes found in the human body are made of nucleic acid. The particular gene with which the patent in suit is concerned (**BRCA1**) is a human breast and ovarian cancer

disposing gene. Various mutations that may be present in this gene have been linked to various forms of cancer including breast cancer and ovarian cancer.

3 Whether or not a valid patent may be granted for a claim to naturally occurring "isolated" nucleic acid depends on whether such a substance is "a manner of manufacture" within the meaning of s 6 of the Statute of Monopolies: see s 18(1)(a) of the Act. This question must in turn be answered in accordance with the principles enunciated by the High Court in *National Research Development Corporation v Commissioner of Patents* (1959) 102 CLR 252 (***NRDC***) and other relevant authorities.

4 The patent in suit is Australian standard patent number 686004 (**the Patent**). The priority date of the Patent is 12 August 1994. The first respondent is the current owner of the Patent. The Patent includes 30 different claims but it is only the validity of claims 1-3 that is in issue.

5 The applicants contend that claims 1-3 of the Patent are invalid on the basis that none claim a manner of manufacture and, therefore, do not satisfy the requirements of s 18(1)(a) of the Act. The applicants claim declarations to that effect, and orders revoking claims 1-3 of the Patent. The standing of the applicants to seek such relief is not in issue.

6 The applicants contend that claims 1-3 (**the disputed claims**) cannot satisfy the requirements of s 18(1)(a) of the Act because each claim comprises "isolated" nucleic acid that is not materially different to nucleic acid that occurs in nature. In particular, they rely on evidence said to show that there is no significant or material difference between nucleic acid in their natural and isolated states. According to the applicants, naturally occurring DNA and RNA, even in isolated form, are products of nature that cannot form the basis of a valid patent.

7 The respondents contend that each of the disputed claims is valid because it claims a product that consists of an artificial state of affairs, providing a new and useful effect that is of economic significance. This is all that is required, according to the respondents, to establish the existence of subject matter that satisfies the requirements of s 18(1)(a) of the Act as interpreted in light of the *NRDC* case. The respondents rely on evidence said to show that

nucleic acid found in a human cell differs chemically, structurally and functionally from the isolated nucleic acid of the disputed claims.

8 There are a number of preliminary observations to make concerning the issues in this proceeding:

- It is common ground that the disputed claims are invalid if they encompass any isolated nucleic acid that does not constitute patentable subject matter. This is because the validity of the disputed claims must be assessed across their full breadth. Thus, the fact that the disputed claims extend to forms of nucleic acid that have been synthesized in the laboratory (cDNA) will not save them if, as the applicants contend, they also extend to forms of nucleic acid that are not patentable.
- The case was for the most part conducted on the basis that all of the disputed claims will stand or fall together, and that if claim 1 is invalid because it includes non-patentable subject matter, claims 2 and 3 will also be invalid for the same reason. However, while claim 1 is directed to "isolated nucleic acid" encompassing both DNA and RNA, claims 2 and 3, which are dependent on claim 1, are limited to "isolated nucleic acid ... which is a DNA".
- The applicants challenge the disputed claims solely on the basis that they include non-patentable subject matter. No other ground of invalidity (including lack of novelty, lack of inventive step, lack of utility or lack of fair basis) is relied upon by the applicants. In particular, it may be assumed that the inventors were the first to isolate the nucleic acids referred to in the disputed claims.
- The applicants accepted that the subject matter of each of the disputed claims satisfied the second of the essential qualities of an invention referred to by the High Court in *NRDC*. In this regard, the applicants accepted that the subject matter of the disputed claims was of "economic significance".
- Although the applicants initially sought to rely upon s 18(2) of the Act, they ultimately abandoned any argument based upon it. Even so, s 18(2) of the Act is still relevant to the issues in the case and it will be necessary to say more about it later in these reasons.

SCIENTIFIC BACKGROUND

Expert Witnesses

9 There was expert evidence given by three eminent experts. Dr Suthers (called by the applicants) and Professor Brown (called by the respondents) were both cross-examined. Professor Rasko (also called by the respondents) was not cross-examined. I found Dr Suthers and Professor Brown to be impressive witnesses. Although I did not have the opportunity to see Professor Rasko in the witness box (because he was not required for cross-examination), I found his affidavit extremely helpful. All three witnesses gave evidence that provided important background to the field of the invention. Unless otherwise indicated, the statements appearing in this section of these reasons comprise findings based upon expert evidence that was not in dispute.

The eukaryotic cell

10 The human body is a multi-cellular eukaryotic organism which consists of a large number of different types of eukaryotic cells. Eukaryotic cells are cells which contain a membrane-bound nucleus. These cells communicate and co-operate with each other for the common good of the organism. The process by which cells reproduce is known as "cell division". This process is binary in the sense that each cell is able to separate into two daughter cells.

11 The human body can sense when high rates of cell division are necessary. For example, if a particular area of the body receives a severe cut with blood loss, the body can respond by producing a number of new blood cells to replace the cells that were lost. When the cut is healing, the body is able to decrease the production of blood cells to prevent over-supply. However, cells may sometimes divide in an abnormal or uncontrolled manner. The abnormal or uncontrolled division of cells is referred to as cancer.

The components of a human cell

12 Cells found in the human body consist of three main parts: the nucleus, the cytoplasm and the cell membrane. The cell membrane defines the outer boundary of the cell and separates its contents from the environment in which it exists. The nucleus of the cell appears as a cell within a cell. The boundary of the nucleus is defined by a nuclear envelope or membrane.

13 The cytoplasm comprises everything between the cell membrane and the nucleus. The majority of the cytoplasm is a liquid called cytosol which consists of water, salts and organic molecules. However, the cytoplasm also contains a number of components (including ribosomes) that have specific functions involving, amongst other things, protein and energy production.

14 The nuclear envelope separating the nucleus from the cytoplasm incorporates pores through which molecules may move between the nucleus and the cytoplasm.

15 DNA and RNA are molecules found within the nucleus of cells within the human body. DNA contains the genetic information that directs the growth, development, maintenance and reproduction of the human body. As I will explain, this information is made available for these purposes via RNA.

The chemical structure of DNA

16 Native DNA (genomic DNA) is an extremely long three-dimensional molecule consisting of a number of repeating monomeric units called nucleotides. These are linked end to end to form a strand (chain) of nucleotides (a polynucleotide chain). Each nucleotide is comprised of three separate chemical groups: a nitrogen-containing (nitrogenous) base, a phosphate group and a five-carbon sugar group comprising deoxyribose.

17 In DNA, nucleotides are linked to one another by covalent bonds running from the 5th carbon (5') of the sugar group of one nucleotide to the third carbon (3') of the phosphate group of the adjacent nucleotide. These bonds are referred to as phosphodiester bonds. They form the "sugar-phosphate backbone" of the DNA from which the bases protrude.

18 DNA chains have two distinctive ends. One end of the chain has a free 5' on the sugar group, and the other end has a free 3' on the phosphate group. By convention, DNA chains are usually depicted from left to right commencing at the free 5' of the sugar group and ending at the free 3' of the phosphate group.

19 There are four types of nitrogenous bases found in DNA. These nitrogenous bases (usually referred to by their initial letter) are adenine (A), guanine (G), cytosine (C) and thymine (T).

20 DNA chains contain repeating sugar-phosphate groups that are always linked together by phosphodiester bonds. However, the four bases of DNA (A, G, C, T) can be attached in any order along the sugar-phosphate backbone. The bases are covalently bonded to the sugar group.

21 In the cell nucleus, DNA almost always exists as a double helix formed by the intertwining of two polynucleotide chains. The two strands wind around each other to form the double helix. The sugar-phosphate backbone forms the outside of the double helix. The bases lie on the inside, in pairs, perpendicular to the axis of the double helix. They are paired along the length of the double helix and joined together by hydrogen bonds.

22 In DNA, G bonds with C, and A bonds with T. The pairing of G to C and A to T is referred to as base pairing. Base pairs can only form if two DNA strands are orientated in the opposite direction (anti-parallel) so that one strand runs in the 5' to 3' direction and the other in the 3' to 5' direction. The strand running in the 5' to 3' direction is often referred to as the "sense" or "coding" strand as opposed to the "anti-sense" or "non-coding" strand which runs in the 3' to 5' direction.

23 In DNA, if the sequence of one polynucleotide chain is known (eg ATCGG on the 5' to 3' strand), then that of the other polynucleotide chain (ie TAGCC on the 3' to 5' strand) may be inferred. These matching sequences are referred to as complementary sequences or complementary strands.

Nucleosomes, chromatin fibres and chromosomes

24 DNA is compacted in the nucleus in two main ways. First, the DNA double helix wraps around spooling proteins known as histones by way of hydrogen bonding to form complexes know as nucleosomes. Each nucleosome consists of a protein core around which double stranded DNA is wound. Second, nucleosomes are stacked on top of each other to form chromatin fibres which are organised into chromosomes.

25 In humans, the DNA in the nucleus is divided between two sets of chromosomes. There are 24 different chromosomes comprising 22 homologous chromosomes and two sex chromosomes. By convention, the homologous chromosomes are numbered from the largest (1) to the smallest (22), while the sex chromosomes are designated X and Y.

The chemical structure of RNA

26 RNA has a slightly different chemical composition to DNA. Unlike DNA, RNA consists of the sugar group ribose instead of deoxyribose, and the nitrogenous base uracil (U) instead of thymine (T).

27 RNA is much shorter in length than DNA. RNA is also single-stranded. Because of this, the nitrogenous bases of RNA are exposed which allows short stretches of these bases to form base pairs with other bases on the same strand resulting in folding of the molecule. RNA often takes the shape of a highly folded molecule.

28 There are a number of different species of RNA which perform a variety of biological functions. Those that are most relevant for present purposes are known as messenger RNA (mRNA) and pre-messenger RNA (pre-mRNA). Also relevant is RNA polymerase (RNApol), an enzyme that (in association with promoters and terminators in DNA), determine where transcription of a gene should start and finish.

The human genome

29 A gene is a functional unit of contiguous DNA which encodes a particular protein. It provides the chemical blueprint used by other parts of the cell to produce protein. When a gene is "expressed" it will often result in the synthesis of a protein by other parts of cell.

30 Human genes generally comprise sequences of DNA that specifically code for a particular protein, interspersed with sequences of DNA that do not code for a particular protein. Sequences of DNA coding for a particular protein are thought to account for approximately 1% of the human genome.

31 The sequences of DNA that comprise a gene are referred to as exons or exonic sequences. Most exonic sequences will code for a particular protein, but they also include other regulatory or non-coding regions that, although not coding for a particular protein, are important to the translation of mRNA. These non-coding sequences are referred to as untranslated regions (UTR) and occur at the 5' end (5' UTR) and 3' end (3' UTR) of the gene. Other sequences that do not code for protein, and which do not form part of the UTR of the gene, are referred to as introns or intronic sequences. Introns are found in DNA and pre-mRNA, but not in mRNA, which includes only the exonic sequences found in the DNA

from which it is copied. Introns account for about 25% of the human genome. The remainder is made up of repetitive and other intergenic DNA.

32 The term "genome" refers to the entirety of the DNA sequence within an organism which, in a human, comprises approximately 3.2 billion individual nucleotides. The human genome comprises approximately 25,000 genes arranged onto chromosomes. In the absence of mutation, all nucleated cells in the human body contain the same genomic DNA sequences.

Proteins, polypeptides and amino acids

33 A protein is a polypeptide or a number of polypeptides consisting of a sequence of amino acids linked together by peptide bonds on a phosphate backbone. Amino acids act as the building blocks of proteins and each type of protein has its own unique amino acid sequence. There are 20 different amino acids known in nature and they are as follows:

The 20 Amino Acids in Proteins

Amino Acid	Three-Letter Abbreviation
Glycine	Gly
Alanine	Ala
Valine	Val
Isoleucine	Ile
Leucine	Leu
Serine	Ser
Threonine	Thr
Proline	Pro
Aspartic acid	Asp
Glutamic acid	Glu
Lysine	Lys
Arginine	Arg
Asparagine	Asn
Glutamine	Gln
Cysteine	Cys
Methionine	Met
Tryptophan	Trp
Phenylalanine	Phe
Tyrosine	Tyr
Histidine	His

[Reproduced from the table "The 20 Amino Acids in Proteins (James D Watson et al, *Recombinant DNA* (W.H. Freeman, 2nd ed, 1992)]

34 Proteins come in an immense variety of different shapes and sizes, and perform many different and complex functions. For example, some proteins act as enzymes, others generate movement, and others act to form structures (histones) used to pack DNA or complexes (ribosomes) that synthesise more proteins. There are also proteins that regulate cell division. When the DNA that encodes these regulatory proteins is mutated or damaged, abnormal or uncontrolled cell division may result.

The genetic code

35 The genetic code consists of groups of three nucleotides, each of which represents one amino acid. These nucleotide groups are referred to as codons or triplets. The grouping of four possible nucleotides in DNA (A,G,C,T) and RNA (A,G,C,U) into different codons permits 64 possible combinations of nucleotides.

36 There are a number of codons that code for the same amino acid (eg. phenylalanine (Phe) - TTT, TTC, glutamine (Gln) - CAA, CAG). Indeed, most amino acids have multiple codons, which means that there are a number of different DNA or RNA sequences that can code for the same protein.

37 The codon ATG in DNA (AUG in RNA) codes for methionine (Met), but will frequently act as a "start" signal. A fixed point in a nucleotide sequence designated by a start codon establishes the groups (the reading frame) in which codons are translated. There are also a number of codons (in DNA, TAA, TAG and TGA, in RNA, UAA, UAG and UGA) that do not code for amino acids, but instead act as "stop" signals that terminate the process of translation.

38 The genetic code is usually presented in the form of a table of nucleotides. If the first, second and third bases in a codon are known, then the table can be used to predict the specific amino acid encoded by that codon. The table below is such an example:

The Genetic Code (Codons to Amino Acids)

FIRST POSITION (5' END)	SECOND POSITION U	SECOND POSITION C	SECOND POSITION A	SECOND POSITION G	THIRD POSITION (3' END)
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	Stop	Stop	A
	Leu	Ser	Stop	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu (Met)*	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met (Start)	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val (Met)*	Ala	Glu	Gly	G

* AUG is the most common initiator codon; GUG usually codes for valine and CUG for leucine, but, rarely, these codons can also code for methionine to initiate a protein chain.

[Reproduced from Harvey Lordish et al, *Molecular Cell Biology* (W.H. Freeman, 6th ed, 2008) 128]

I shall illustrate how this table works with just a few examples. If one wants to know what sequences of bases codes for Glutamine (Glu) one can see from the table that there are two codons that do so: GAA and GAG. In the case of Serine (Ser) one can see that there are 6 different codons that code for this amino-acid: UCU, UCC, UCA, UCG, AGU and AGC. As in the above table, the generic code is typically depicted as a table of RNA nucleotides. This table may be used to interpret DNA sequences by substituting T where U appears in the table.

39 Genetic information in DNA in the form of sequences of codons that represent specific amino acid sequences ultimately determines what particular protein will be synthesised in the cell.

The process of gene expression

40 The process by which a cell produces protein is referred to as "gene expression". The production of pre-mRNA is the first step in the process of gene expression. This is followed

by the production of mRNA. RNA plays a central role in gene expression through its involvement in the processes of "transcription" and "translation".

Transcription

41 Transcription is a process that takes place within the nucleus of the cell whereby a portion of the DNA nucleotide sequence of a gene is copied into an RNA nucleotide sequence. Through this process, a single strand of the DNA double helix is used as a template (or, as it is sometimes called, the "sense" or "non-coding" strand) to synthesise a complementary strand of nascent mRNA known as pre-mRNA. Pre-mRNA includes both the exonic and intronic sequences of the gene transcribed from the DNA. The sequence of the nucleotide chain of the pre-mRNA strand is determined by base pairing with the DNA template (the "anti-sense" or "non-coding") strand. Consequently, the nucleotide sequence of the strand of pre-mRNA transcribed from the DNA template stand will correspond to the non-template (the "sense" or "coding") DNA strand.

42 During transcription, a chemical modification is made at the 5' end of the transcribed sequence which results in the addition of a "cap". The cap protects the molecule from enzymatic degradation and assists in the transport of the mature mRNA molecule to the cytoplasm. A further modification is made to the 3' end of the sequence by the addition of a string of adenosine bases referred to as a poly-A tail.

43 Once the cap and poly-A tail have been added to the ends of the pre-RNA sequence the introns are removed and the exons joined together by a process known as RNA splicing. Splicing is a process performed by an enzyme complex referred to as the spliceosome. The pre-RNA transcript of exons and introns can be spliced to produce different polynucleotide sequences by a process referred to as alternative splicing.

44 Once splicing has occurred, the resulting mRNA molecule will consist of a complementary sequence of exons found in the DNA strand from which they were transcribed with a cap at the 5' end and a poly-A tail at the 3' end.

Translation

45 Once the process of transcription is complete, the mRNA molecule is transported through nuclear pores within the nuclear envelope into the cytoplasm where it is available for translation. Translation is a complex process by which the nucleotide sequence of an mRNA molecule is used as a template for the manufacture of the polypeptide chains which takes place in ribosomes located in the cytoplasm. For present purposes, it is sufficient to note that the ribosome manufactures the polypeptide chains in accordance with the mRNA template.

ISOLATION OF DNA AND RNA

46 As previously explained, an isolated DNA sequence is a sequence of DNA that has been removed from its normal cellular environment. Professor Rasko gave a detailed explanation of how DNA may be removed from its normal cellular environment. The following summary is drawn from his evidence.

47 Typically, DNA is obtained from cells removed from a sample of tissue or blood extracted from an individual. The tissue sample is broken down into clumps of cells or individual cells using enzymes or chemicals suitable for that purpose. In the case of a blood sample, the cells are already separated.

48 The bursting of the cell membrane or the nucleus membrane is referred to as cell lysis and can be achieved through techniques known as sonication (which involves the application of ultrasonic pressure waves) or grinding (which involves the application of physical disruptive forces). In this way the contents of the nucleus, including the DNA and RNA, can be released into a free-floating liquid suspension. Cell lysis results in the entire genomic DNA being released from the nucleus of the cell.

49 Proteins associated with DNA (including histones) are then degraded by the addition of enzymes known as proteases. This results in the destruction of the nucleosomes but does not eliminate all of the protein associated with the DNA.

50 A high salt solution is then added to precipitate the degraded proteins including those which are still closely associated with the DNA. The degraded proteins are then separated from the DNA using a well known chemical procedure that takes advantage of the fact that

proteins are soluble in phenol, and DNA and RNA are not soluble in phenol (but are soluble in chloroform).

51 After centrifugation, the DNA and RNA are located in the interface between the phenol and the chloroform. Enzymes may then be applied in order to break down the RNA, leaving only purified DNA. The DNA can be precipitated from its soluble state into a solid state by the addition of ethanol or isopropanol. Further centrifugation results in a pellet of DNA.

52 Professor Rasko identified a number of techniques that may be used to create synthetic human DNA. For present purposes, that which is most relevant is a technique for template-based DNA synthesis that involves the use of mRNA as a template to create complementary DNA (cDNA). This technique is called “reverse transcription” because it involves the use of a particular enzyme (not naturally found in humans) known as reverse transcriptase.

53 The reverse transcription technique takes advantage of the existence of the poly-A tail on mRNA, allowing the mRNA to be isolated for use as a template for DNA synthesis. The result of the reverse transcription technique is to create an RNA-cDNA hybrid molecule that can then be converted to a double stranded DNA molecule using several different approaches. These hybrid molecules are better suited than mRNA molecules for use in molecular biology applications because mRNA is less stable than DNA. Nevertheless, it is clear that, like DNA, mRNA can also be isolated from the natural environment of the cell.

54 Dr Suthers explained that once a DNA sample has been isolated, the DNA sequence can be mapped using a variety of methods. Genetic testing is then completed by comparing the relevant DNA sequence of the sample to a normal reference sequence. The latter may be one of many reference sequences developed under the auspices of professional bodies or government agencies in the US or Europe. Of course, the goal of genetic testing is to determine what variations, if any, are present in a specific region of DNA and what their clinical significance is.

THE PATENT

The field of the invention

55 The title of the Patent is "In vivo mutations and polymorphisms in the 17q-linked breast and ovarian cancer susceptibility gene". The reference to "17q" in the title indicates that BRCA1, the relevant gene, is found on the long arm of chromosome 17. This part of chromosome 17 is estimated to consist of about 8 million base pairs.

56 According to the Patent, the BRCA1 gene is composed of 23 coding exons arrayed on more than 100,000 base pairs (100 kb) in genomic DNA. The field of the invention is described in the Patent in these terms:

> The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect a human breast and ovarian cancer predisposing gene (BRCA1), some mutant alleles of which cause susceptibility to cancer, in particular, breast and ovarian cancer. More specifically, the invention relates to germline mutations in the BRCA1 gene and their use in the diagnosis of predisposition to breast and ovarian cancer. The present invention further relates to somatic mutations in the BRCA1 gene in human breast and ovarian cancer and their use in the diagnosis and prognosis of human breast and ovarian cancer. Additionally, the invention relates to somatic mutations in the BRCA1 gene in other human cancers and their use in the diagnosis and prognosis of human cancers. The invention also relates to the therapy of human cancers which have a mutation in the BRCA1 gene, including gene therapy, protein replacement therapy and protein mimetics. The invention further relates to the screening of drugs for cancer therapy. Finally, the invention relates to the screening of the BRCA1 gene for mutations, which are useful for diagnosing the predisposition to breast and ovarian cancer.

Background to the invention

57 The Patent states that breast cancer is one of the most significant diseases that affects women. According to the Patent, mutation of the BRCA1 gene is thought to account for approximately 45% of familial (hereditary) breast cancer, and at least 80% of familial cancer involving both breast and ovarian cancer.

The invention

58 The Patent states that "[t]he present invention relates generally to the field of human genetics". The Patent includes a "summary of the invention" which is in identical terms to the description of the field of invention reproduced at para [56] above. The Patent also

includes a "detailed description of the invention". The detailed description includes the following statement:

> The present invention provides an isolated polynucleotide comprising all, or a portion of the BRCA1 locus or of a mutated BRCA1 locus, preferably at least eight bases and not more than about 100 kb in length. Such polynucleotides may be antisense polynucleotides. The present invention also provides a recombinant construct comprising such an isolated polynucleotide, for example, a recombinant construct suitable for expression in a transformed host cell.

59 The Patent elsewhere also explains that "[t]he "polynucleotide compositions of this invention" may include RNA, DNA and cDNA. The Patent states:

> The polynucleotide compositions of this invention include RNA, cDNA, genomic DNA, synthetic forms, and mixed polymers, both sense and antisense strands, and may be chemically or biochemically modified or may contain non-natural or derivatized nucleotide bases, as will be readily appreciated by those skilled in the art.

60 The Patent also includes additional statements indicating that the invention provides detection methods, isolated antibodies and screening methods that may be useful for identifying mutations for diagnostic and therapeutic purposes.

61 The Patent explains that it is a discovery of the invention that:

> … the BRCA1 locus which predisposes individuals to breast cancer and ovarian cancer, is a gene encoding a BRCA1 protein, which has been found to have no significant homology with known protein or DNA sequences. This gene is termed BRCA1 herein. It is a discovery of the present invention that mutations in the BRCA1 locus in the germline are indicative of a predisposition to breast cancer and ovarian cancer. Finally, it is a discovery of the present invention that somatic mutations in the BRCA1 locus are also associated with breast cancer, ovarian cancer and other cancers, which represents an indicator of these cancers or of the prognosis of these cancers. The mutational events of the BRCA1 locus can involve deletions, insertions and point mutations within the coding sequence and the non-coding sequence.
>
> Starting from a region on the long arm of human chromosome 17 of the human genome, 17q, which has a size estimated at about 8 million base pairs, a region which contains a genetic locus, BRCA1, which causes susceptibility to cancer, including breast and ovarian cancer, has been identified.
>
> The region containing the BRCA1 locus was identified using a variety of genetic techniques. Genetic mapping techniques initially defined the BRCA1 region in terms of recombination with genetic markers. Based upon studies of large extended families ("kindreds") with multiple cases of breast cancer (and ovarian cancer cases in some kindreds), a chromosomal region has been pinpointed that contains the BRCA1 gene as well as other putative susceptibility alleles in the BRCA1 locus …

Definitions

62 The various passages from the Patent to which I have referred use a number of defined terms. The following definitions are of particular relevance:

> "**Encode**". A polynucleotide is said to "encode" a polypeptide if, in its native state or when manipulated by methods well known to those skilled in the art, it can be transcribed and/or translated to produce the mRNA for and/or the polypeptide or a fragment thereof. The anti-sense strand is the complement of such a nucleic acid, and the encoding sequence can be deduced therefrom.
>
> "**Isolated**" or "**substantially pure**". An "isolated" or "substantially pure" nucleic acid (e.g., an RNA, DNA or a mixed polymer) is one which is substantially separated from other cellular components which naturally accompany a native human sequence or protein, e.g., ribosomes, polymerases, many other human genome sequences and proteins. The term embraces a nucleic acid sequence or protein which has been removed from its naturally occurring environment, and includes recombinant or cloned DNA isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems.
>
> "**BRCA1 Allele**" refers to normal alleles of the BRCA1 locus as well as alleles carrying variations that predispose individuals to develop cancer of many sites including, for example, breast, ovarian, colorectal and prostate cancer. Such predisposing alleles are also called "**BRCA1 susceptibility alleles**".
>
> "**BRCA1 Locus**," "**BRCA1 Gene**," "**BRCA1 Nucleic Acids**" or "**BRCA1 Polynucleotide**" each refer to polynucleotides, all of which are in the BRCA1 region, that are likely to be expressed in normal tissue, certain alleles of which predispose an individual to develop breast, ovarian, colorectal and prostate cancers. Mutations at the BRCA1 locus may be involved in the initiation and/or progression of other types of tumors. The locus is indicated in part by mutations that predispose individuals to develop cancer. These mutations fall within the BRCA1 region described *infra*. The BRCA1 locus is intended to include coding sequences, intervening sequences and regulatory elements controlling transcription and/or translation. The BRCA1 locus is intended to include all allelic variations of the DNA sequence.
>
> These terms, when applied to a nucleic acid, refer to a nucleic acid which encodes a BRCA1 polypeptide, fragment, homolog or variant, including, e.g., protein fusions or deletions. The nucleic acids of the present invention will possess a sequence which is either derived from, or substantially similar to a natural BRCA1-encoding gene or one having substantial homology with a natural BRCA1-encoding gene or a portion thereof. The coding sequence for a BRCA1 polypeptide is shown in SEQ ID NO:1, with the amino acid sequence shown in SEQ ID NO:2.

The Patent also states that the term "BRCA1 polypeptide" refers to the protein or polypeptide encoded by the BRCA1 locus, variants or fragments thereof.

63 The terms "mutations" and "polymorphisms" as used in the Patent are not defined. However, a mutation is a variation in a gene that is not found in the same gene in its typical and most common (wild-type) form. Mutations may be disease-causing or they may be benign. A polymorphism is also a variation in a gene. According to Dr Suthers,

polymorphisms do not cause disease and are not clinically relevant. They are found in the DNA of a large proportion of the population. While nothing turns on the point, the term polymorphism seems to be used somewhat differently in the Patent.

The SEQ ID No.1: the "wild type" sequence

64 SEQ ID No.1 is a sequence listing for the BRCA1 wild-type gene. It consists of 5,914 base pairs and represents the coding sequence of a nucleic acid (cDNA) which encodes the BRCA1 polypeptide. Since SEQ ID No.1 is a cDNA sequence, it contains only the exonic sequences including the non-coding sequences that appear at the beginning and end of the sequence.

65 SEQ ID No.1, as reproduced in the Patent, shows nucleotides and codons, both of which are numbered sequentially. The particular amino acid encoded by each of the codons in the numbered sequence is also shown. The coding sequences start with ATG (the "start" signal, codon number 1) and terminate with TGA (a stop signal, codon number 1864). To more clearly illustrate how SEQ ID No.1 is presented I shall set out the first 263 nucleotides shown:

```
AGCTCGCTGA GACTTCCTGG ACCCCGCACC AGGCTGTGGG GTTTCTCAGA TAACTGGGCC      60

CCTGCGCTCA GGAGGCCTTC ACCCTCTGCT CTGGGTAAAG TTCATTGGAA CAGAAAGAA      119

ATG GAT TTA TCT GCT CTT CGC GTT GAA GAA GTA CAA AAT GTC ATT AAT        167
Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
  1               5                  10                  15

GCT ATG CAG AAA ATC TTA GAG TGT CCC ATC TGT CTG GAG TTG ATC AAG        215
Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
             20                  25                  30

GAA CCT GTC TCC ACA AAG TGT GAC CAC ATA TTT TGC AAA TTT TGC ATG        263
Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
         35                  40                  45
```

66 The first 119 nucleotides do not code for a polypeptide but nevertheless form part of the exonic sequences. Codon number 1 (ATG), the first of the separately number codons, codes for methionine (Met) which in this sequence acts as the start signal. The coding

sequence shown in SEQ ID No.1 ends at codon 1864 (TGA) which acts as a stop signal, which is then followed by about three lines of additional non-coding nucleotides.

67 Because SEQ ID No.1 is a coding sequence for cDNA, the bases making up the sequence include T (found in DNA) but not U as found in a RNA sequence. However, a person skilled in the art would know that the corresponding RNA sequence may be obtained by substituting U for T where the latter appears in SEQ ID No.1.

The Tables

68 There are tables set out in the Patent that identify mutations or polymorphisms by reference to the sequence listing in SEQ ID No.1. In particular:

- Tables 12, 12A and 14 identify "predisposing mutations" found in the BRCA1 gene of various patients. These mutations are recorded as variations in coding sequences as shown in SEQ ID No.1. Here is an example drawn from Table 12:

Patient	**Codon**	**Nucleotide Change**	**Amino Acid Change**
BT098	**1541**	**GAG→TAG**	**Glu→Stop**

  SEQ ID No.1 shows that codon numbered 1541 is normally GAG, not TAG as found in the BRCA1 gene of this patient.

- Table 18 identifies what are referred to as "Polymorphisms in BRCA1 Genomic DNA Exons". Information included in this table is presented in much the same style as in Tables 12, 12A and 14.

- Table 19 identifies what are referred to as "Polymorphisms in BRCA1 Genomic DNA Introns". However, since the polymorphisms identified in Table 19 occur in intronic sequences, it is not possible to relate them to SEQ ID No.1 which, as previously mentioned, only includes the exonic sequences of the BRCA1 gene. For this reason, the parties agreed that the reference to Table 19 in each of the disputed claims was an error and should be disregarded.

The disputed claims

69 The disputed claims are in the following terms:

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 set forth in SEQ.ID No:l one or more mutations or polymorphisms selected from the mutations set forth in Tables 12, 12A and 14 and the polymorphisms set forth in Tables 18 and 19.

2. An isolated nucleic acid as claimed in claim 1 which is a DNA coding for a mutant BRCA1 polypeptide, said DNA containing in comparison to the BRCA1 polypeptide encoding sequence set forth in SEQ.ID No:1 one or more mutations set forth in Tables 12, 12A and 14.

3. An isolated nucleic acid as claimed in claim 1 which is a DNA coding for a polymorphic BRCA1 polypeptide, said DNA containing in comparison to the BRCA1 polypeptide encoding sequence set forth in SEQ.ID No:1 one or more polymorphisms set forth in Tables 18 and 19.

70 Claim 1 extends to isolated DNA, RNA and cDNA that has a BRCA1 polypeptide encoding sequence as shown in SEQ ID No.1 with one or more of the mutations or polymorphisms specified in the relevant tables. By contrast, dependent claims 2 and 3 extend only to DNA containing one or more such sequences. Claims 2 and 3 both refer to an isolated nucleic acid as claimed in claim 1 "which is a DNA coding for" one or more of the identified mutations (in claim 2) or polymorphisms (in claim 3). Here, the reference to "a DNA coding" is a reference to the relevant DNA sequence that encodes for a relevant mutant or polymorphic polypeptide.

71 The word "coding" (as in "coding" for a mutant or polymorphic polypeptide) is not defined in the Patent. However, the word "encode" (as in an "encoding sequence") is defined by reference to the ability of a polynucleotide (ie. a chain of nucleotides) in its natural state, or when manipulated by well known methods, to "encode" a polypeptide. A polynucleotide that "codes" for or "encodes" a polypeptide is one that exhibits the sequence of bases that can, in the natural environment of a cell, result in the expression of such a polypeptide. In this regard, I do not understand there to be any difference in meaning between the words "coding" and "encoding" in the present context. Encoding sequences are those that code for polypeptides either in the natural environment of the cell or when manipulated by well known methods.

72 Each of the disputed claims is to a chemical composition. That is to say, they claim substances that are defined by the presence of particular atoms that are arranged in particular ways. However, the disputed claims do not say anything about the length of the polynucleotide chains with which they are concerned. In this regard, there is nothing to

suggest either in the claims themselves or in the body of the specification that a complete molecule of DNA as originally found on chromosome 17 that has been isolated, and that includes one or more of the relevant mutations, would be outside the scope of the disputed claims. This is important because the respondents' submissions to me suggested that, at least in the case of DNA, covalent bonds must necessarily be broken as part of the isolation process, and that this was in itself something that differentiated naturally occurring DNA from isolated DNA in terms of their chemical composition.

73 The respondents pointed to the following evidence of Dr Suthers in support of the proposition that there will be at least some breaking of the covalent bonds in the sugar phosphate backbone as a result of the isolation process:

> … Now, if you had a gene in the chromosome, and you were going to isolate a sequence not by synthesising it but by extracting it, what you would need to achieve would be at least the following – I'm not saying all the steps?---Sure.
>
> You would need to break the hydrogen bonds between the bases?---Yes.
>
> And you would need to have at least some breaks in the covalent bonds so that you could take out an extract?---Yes.
>
> Now, when you break the covalent bonds between the sugar and the phosphate so that you can pull out your extract from the strand, in breaking that bond what you have isolated is chemically different, isn't it, to what was in the hole?---It is in terms of, I guess, the molecular weight; the length of the molecule that you're dealing with. It's part of the hole. If the part – you could have a very long strip of DNA which contains in the middle of it a coding sequence sufficient to define a particular polypeptide. If you are able by the means you describe accurately to remove that coding region from the longer stretch of DNA, then what you have removed is shorter, and in that sense, different to what it was before. But in terms of the information content, you may not have lost anything.
>
> In fact, in the mid-1990s when you had something – we will say 100,000 bases, 100 kilobases long, you would normally break it up into much small pieces, wouldn't you, and then amplify them?---Absolutely.
>
> And isolate them?---Yes.

74 I do not think Dr Suther's evidence establishes the broad proposition which it is said to support. It is not apparent to me that every isolated DNA sequence within the scope of the claims must have had at least some covalent bonds broken as a result of the isolation process. Nor would I imply any such requirement into the claims merely because, in Dr Suther's experience, this is what occurs. To interpret the disputed claims in this way would require me to impose an impermissible gloss upon the words of the claim.

75 There are two other important points to make concerning the scope of the claims.

76 First, the disputed claims are not to genetic information *per se*. They claim tangible materials. Much emphasis was placed by the applicants upon the informational character of DNA as a storehouse of genetic information. But the disputed claims are not to information as such. They could never be infringed by someone who merely reproduced a DNA sequence in written or digitised form.

77 Secondly, because each of the claims is to an *isolated* chemical composition, naturally occurring DNA and RNA as they exist in cell are not within the scope of any of the disputed claims and could never, at least not until they had been isolated, result in the infringement of any such claim.

LEGAL ANALYSIS

Relevant Statutory Provisions

78 The basic requirements of patentability are set out in s 18 of the Act. Section 18(1) relevantly provides that:

> … an invention is a patentable invention for the purposes of a standard patent if the invention, so far as claimed in any claim:
>
> (a) is a manner of manufacture within the meaning of section 6 of the Statute of Monopolies; and
>
> (b) when compared with the prior art base as it existed before the priority date of that claim:
>
> (i) is novel; and
>
> (ii) involves an inventive step; and
>
> (c) is useful; and
>
> (d) was not secretly used in the patent area before the priority date of that claim by, or on behalf of, or with the authority of, the patentee or nominated person or the patentee's or nominated person's predecessor in title to the invention.

The term "invention" is defined in Schedule 1 of the Act to mean:

> … any manner of new manufacture the subject of letters patent and grant of privilege within section 6 of the Statute of Monopolies, and includes an alleged invention.

79 Section 6 of the Statute of Monopolies defined the right of the Crown to grant letters patent for "the sole working or making of any manner of new manufacture within this realm".

However, the expressions "manner of manufacture" and "manner of new manufacture" are not employed in the Act to literally describe what subject matter may qualify for patent protection. Rather, they are expressions that bring into play principles and concepts which have been developed over many years to ensure that patent law keeps up with advances in industry and technology.

80 Section 18(1A) of the Act is concerned with innovation patents. It is not necessary to set s 18(1A) out. As with standard patents, the invention the subject of a claim in an innovation patent must be a manner of manufacture. Section 18(1A) is followed by s 18(2)-(4). They provide:

> (2) Human beings, and the biological processes for their generation, are not patentable inventions.
>
> (3) For the purposes of an innovation patent, plants and animals, and the biological processes for the generation of plants and animals, are not patentable inventions.
>
> (4) Subsection (3) does not apply if the invention is a microbiological process or a product of such a process.

National Research Development Corporation v Commissioner of Patents

81 The starting point for my consideration of the legal issues that arise is the High Court's decision in the *NRDC* case. The case was described by Barwick CJ in *Joos v Commissioner of Patents* (1972) 126 CLR 611 at 616 as a "watershed" in this area of law, and in *Grain Pool of Western Australia v Commonwealth of Australia* (2000) 202 CLR 479 at para [45] Gleeson CJ, Gaudron, McHugh, Gummow, Hayne and Callinan JJ referred to it as a "celebrated judgment". As the Full Court (Spender, Gummow and Heerey JJ) explained in *CCOM Pty Ltd v Jiejing Pty Ltd* (1994) 51 FCR 260 (at 289):

> In Australia, when the 1952 Act was replaced by the 1990 Act, the new British legislation was not followed. There was in s 18(2) an express exclusion from patentable inventions of human beings and biological processes for their generation. Beyond that the legislature left the matter, in terms of s 18(1)(a), to rest with the concept of manner of manufacture within the meaning of s 6 of the *Statute of Monopolies*, as developed by the Courts, notably in the *NRDC* case. This was a matter of deliberate legislative choice.

82 There were three claims in issue in the *NRDC* case. All were method claims concerned with the use of a known chemical composition ("herbicide") in the eradication or control of weeds. The first claim was directed to the use of the herbicide in the eradication of

weeds from areas containing leguminous fodder crops of the *Trifolium* and *Medicago* families, as well as celery and parsnip. The second and third claims were directed to the use of the herbicide to control charlock, creeping thistle and annual nettle weeds in different crop varieties.

83 The examiner raised objections to these claims on the basis that none was directed to any manner of manufacture. There were two arguments relied upon by the examiner in support of that conclusion. The first was that the claims involved "the mere use of known substances" and the second was that the use of these substances did "not result in any vendible product". Both arguments relied upon by the examiner were also relied upon by the Commissioner of Patents (**the Commissioner**) in the High Court. The first was rejected by the High Court on the basis that the invention as claimed involved a new and inventive use of a known chemical composition. The second was also rejected by the High Court.

84 The Court (Dixon CJ, Kitto and Windeyer JJ) began its consideration of the argument that a manner of manufacture must result in "vendible product" by remarking that this was "the central question in the case". The Court said (at 268-270):

> The central question in the case remains. It is whether the process that is claimed falls within the category of inventions to which, by definition, the application of the *Patents Act* is confined. The definition, it will be remembered, is exclusive: invention means any manner of new manufacture the subject of letters patent and grant of privilege within s. 6 of the *Statute of Monopolies*. The Commissioner, adopting certain judicial pronouncements to which reference will be made, emphasizes the word "manufacture" and contends for an interpretation of it which, though not narrow, is restricted to vendible products and processes for their production, and excludes all agricultural and horticultural processes. On the grounds both of the suggested restriction and of the suggested exclusion he denies that a process for killing weeds can be within the relevant concept of invention. The appellant, on the other hand, urges upon us a wider view: that there is a "manufacture" such as might properly have been the subject of letters patent and grant of privilege under s. 6 of the *Statute of Monopolies* whenever a process produces, either immediately or ultimately, a useful physical result in relation to a material or tangible entity.
>
> Section 6 of the *Statute of Monopolies* provides that the declarations of invalidity contained in the preceding provisions of the Act "shall not extend to any letters patents and graunts of privelege … hereafter to be made of the sole working or makinge of any manner of new manufactures within this realme, to the true and first inventor and inventors of such manufactures, which others at the tyme of makinge such letters patents and graunts shall not use, soe as alsoe they be not contrary to the lawe or mischievous to the state by raisinge prices of comodities at home, or hurt of trade, or generallie inconvenient": *Halsbury's Statutes of England*, 2nd ed. vol. 17 (1950), p. 619. It is of the first importance to remember always that the *Patents Act* 1952-1955 (Cth), like its predecessor the *Patents Act 1903* (Cth) and corresponding statutes of the United Kingdom (see the *Patents, Designs and Trade Marks Act* 1883,

> s. 46; the *Patents Act* 1907, s. 93; and the *Patents Act* 1949, s. 101), defines the word "invention", not by direct explication and in the language of its own day, nor yet by carrying forward the usage of the period in which the *Statute of Monopolies* was passed, but by reference to the established ambit of s. 6 of that Statute. **The inquiry which the definition demands is an inquiry into the scope of the permissible subject matter of letters patent and grants of privilege protected by the section. It is an inquiry not into the meaning of a word so much as into the breadth of the concept which the law has developed by its consideration of the text and purpose of the *Statute of Monopolies*.** One may remark that although the Statute spoke of the inventor it nowhere spoke of the invention; all that is nowadays understood by the latter word as used in patent law it comprehended in "new manufactures". **The word "manufacture" finds a place in the present Act, not as a word intended to reduce a question of patentability to a question of verbal interpretation, but simply as the general title found in the *Statute of Monopolies* for the whole category under which all grants of patents which may be made in accordance with the developed principles of patent law are to be subsumed. It is therefore a mistake, and a mistake likely to lead to an incorrect conclusion, to treat the question whether a given process or product is within the definition as if that question could be restated in the form: "Is this a manner (or kind) of manufacture?" It is a mistake which tends to limit one's thinking by reference to the idea of making tangible goods by hand or by machine, because "manufacture" as a word of everyday speech generally conveys that idea. The right question is: "Is this a proper subject of letters patent according to the principles which have been developed for the application of s. 6 of the *Statute of Monopolies*?"**
>
> **It is a very different question. A perusal of the definitions and quotations appearing in the *Oxford English Dictionary* under "manufacture" will show that the word has always admitted of applications beyond the limits which a strict observance of its etymology would suggest, and, as the present Chief Justice said in *Maeder v. Busch* [(1938) 59 CLR 684 at p. 706], a widening conception of the notion has been a characteristic of the growth of patent law.**

(emphasis added)

85 The Court then reviewed various other authorities, mostly decided in the eighteenth and nineteenth centuries, concerning the meaning of s 6 of the Statute of Monopolies and, in particular, the expression "manner of manufacture". This review led the Court to conclude (at 271):

> The truth is that any attempt to state the ambit of s. 6 of the *Statute of Monopolies* by precisely defining "manufacture" is bound to fail. The purpose of s. 6, it must be remembered, was to allow the use of the prerogative to encourage national development in a field which already, in 1623, was seen to be excitingly unpredictable. To attempt to place upon the idea the fetters of an exact verbal formula could never have been sound. It would be unsound to the point of folly to attempt to do so now, when science has made such advances that the concrete applications of the notion which were familiar in 1623 can be seen to provide only the more obvious, not to say the more primitive, illustrations of the broad sweep of the concept.

86 There are three important points that emerge from these passages. First, the Court identified the question that must be addressed for the purpose of determining whether or not subject matter is patentable, *viz*. "[i]s this a proper subject of letters patent according to the principles which have been developed for the application of s. 6 of the *Statute of Monopolies*?" Secondly, this question involves a conceptual inquiry as opposed to a consideration of the etymology of the expression "manner of manufacture". Thirdly, the concept of manner of manufacture has a "broad sweep" intended to encourage developments that are by their nature often unpredictable.

87 The High Court then turned to some more recent authority including the decision of Morton J (as his Lordship then was) in *Re GEC's Application* (1943) 60 RPC 1. The Court observed that Morton J's judgment – which drew upon the concept of the "vendible product" as a criterion of patentability – would have "a narrowing effect on the law" if it was literally applied. In a key passage of the judgment the Court held (at 277):

> **Notwithstanding the tendency of these decisions, the view which we think is correct in the present case is that the method the subject of the relevant claims has as its end result an artificial effect falling squarely within the true concept of what must be produced by a process if it is to be held patentable. This view is, we think, required by a sound understanding of the lines along which patent law has developed and necessarily must develop in a modern society.** 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; for it provides a remarkable advantage, indeed to the lay mind a sensational advantage, for one of the most elemental activities by which man has served his material needs, the cultivation of the soil for the production of its fruits.** Recognition that the relevance of the process is to this economic activity old as it is, need not be inhibited by any fear of inconsistency with the claim to novelty which the specification plainly makes. The method cannot be classed as a variant of ancient procedures. It is additional to the cultivation. It achieves a separate result, and the result possesses its own economic utility consisting in an important improvement in the conditions in which the crop is to grow, whereby it is afforded a better opportunity to flourish and yield a good harvest.

(emphasis added)

88 It is apparent from this passage that a product that consists of an artificially created state of affairs which has economic significance will constitute a "manner of manufacture". In relation to a process, the product is the state of affairs in which an effect may be observed. In the *NRDC* case, the product was the discernible effect achieved by the use of selective

herbicides which killed weeds but not particular types of crop to which they might be applied. The economic significance of the methods the subject of the patent in terms of improved crop production was virtually self-evident in that case. In the present case, the question of economic significance may be put aside because, as I have previously mentioned, the applicants accepted that this aspect of the requirements of patentability established by *NRDC* was satisfied.

Products of Nature

89 Another argument relied upon by the Commissioner in the *NRDC* case, closely related to the first, was that the claims in question were for processes that were "dependent on the operation of natural laws or the natural properties of the materials involved" and that "[t]here is no process independent of the discovery itself". To put this argument in context, it is helpful to refer to what Buckley J said in *Reynolds v Herbert Smith & Co Ltd* (1903) 20 RPC 123. His Lordship said (at 126):

> Discovery adds to the amount of human knowledge, but it does so only by lifting the veil and disclosing something which before had been unseen or dimly seen. Invention also adds to human knowledge, but not merely by disclosing something. Invention necessarily involves also the suggestion of an act to be done, and it must be an act which results in a new product, or a new result, or a new process, or a new combination for producing an old product or an old result.

90 The same point was made by Whitford J in *Genentech Inc's Patent* [1987] RPC 553 where his Lordship said (at 566):

> It is trite law that you cannot patent a discovery, but if on the basis of that discovery you can tell people how it can be usefully employed, then a patentable invention may result. This in my view would be the case, even though once you have made the discovery, the way in which it can be usefully employed is obvious enough.

This statement was expressly approved by the House of Lords in *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd* [2005] RPC 169 (**Kirin-Amgen)**.

91 Similarly, in *Advanced Building Systems Pty Limited v Ramset Fasteners (Aust) Pty Limited* (1998) 194 CLR 171, Brennan CJ, Gaudron, McHugh and Gummow JJ said (at para [34]) that "… it has long been established that 'a clear distinction will be drawn between the discovery of one of nature's laws, and of its application to some new and useful purpose …'".

92 Returning then to the Commissioner's argument in *NRDC* (that the inventor had made a discovery but not an invention), the High Court said (at 263-264):

> Arguments of this kind may be answered as Frankfurter J. answered them in *Funk Bros. Seed Co. v. Kalo Inoculant Co*. [(1948) 333 U.S. 127 [92 Law. Ed. 588]]. "It only confuses the issue," the learned Justice said, "to introduce such terms as 'the work of nature' and the 'laws of nature'. For these are vague and malleable terms infected with too much ambiguity and equivocation. Everything that happens may be deemed 'the work of nature', and any patentable composite exemplifies in its properties 'the laws of nature'. Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost any patent". [(1948) 333 U.S., at pp. 134, 135 [92 Law. Ed., at p. 591]]. The truth is that the distinction between discovery and invention is not precise enough to be other than misleading in this area of discussion. There may indeed be a discovery without invention—either because the discovery is of some piece of abstract information without any suggestion of a practical application of it to a useful end, or because its application lies outside the realm of "manufacture".

93 Frankfurter J's criticism of the expressions "the work of nature" and "the laws of nature" did not involve a rejection of the proposition that "the work of nature" or "products of nature" cannot constitute patentable subject matter. The point made by Frankfurter J, and accepted by the High Court, was that there are cases in which the use of such expressions will be of little assistance because everything in some sense or another involves the work of nature.

94 Moreover, the High Court's approval in *NRDC* of Frankfurter J's remarks in *Funk Bros. Seed Co. v Kalo Inoculant Co.* (1948) 333 US 127 was particularly significant given what other members of the US Supreme Court had said in that case. The issue in *Funk Bros* was whether a new combination of different strains of bacteria was inherently unpatentable. The strains of bacteria were already known, but it was the idea of the inventor to bring them together to form a new combination. Douglas J who wrote for the majority on this issue said (at 130):

> We do not have presented the question whether the methods of selecting and testing the non-inhibitive strains are patentable. We have here only product claims. Bond does not create a state of inhibition or of non-inhibition in the bacteria. Their qualities are the work of nature. Those qualities are of course not patentable. For patents cannot issue for the discovery of the phenomena of nature. The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men.

(citations omitted)

95 In 1980, in *Diamond v Chakrabarty* 447 US 303 (1980) the US Supreme Court distinguished *Funk Bros* and held that a live, human made micro-organism was patentable. The decision in *Chakrabarty* was considered to be a landmark because it established that a patent could be obtained for something that was living, a characteristic of micro-organisms which many had assumed rendered such subject matter unpatentable because it was necessarily "the handiwork of nature" (*Funk Bros* at 131).

96 At this point, it is convenient to refer to two authorities relied upon by the applicants. The first is *American Cyanamid Company v Upjohn Company* [1971] RPC 425 (**Dann's Patent**). The second is *Kirin-Amgen* [2005] RPC 169.

97 Lord Wilberforce suggested in *Dann's Patent* that an *isolated* strain of micro-organism was not patentable if it exists in nature. In that case, the House of Lords was concerned with a claim for a new antibiotic (Porfiromycin) and a method for its production that involved subjecting a suitable strain of a particular micro-organism to fermentation. It is apparent from the facts of the case that the production of the new antibiotic depended upon finding the right micro-organism to work with. At issue in the appeal was the sufficiency of the description of the invention, and whether the patent was invalid because the specification failed to indicate how a person seeking to practice the invention might go about obtaining the micro-organism upon which production of the new antibiotic depended. Lord Wilberforce's speech contains a clear acknowledgement of how much effort may be required to isolate a strain of a naturally occurring micro-organism. His Lordship said (at 446):

> Strains of micro-organisms have been found to be useful in various connections; but very large numbers of differing varieties are found in nature. The problem for the scientist lies in identifying and isolating the particular strains which, or mutants of which, can be made use of. These may come to light by painstaking or expensive research assisted by good fortune or by pure good fortune: once identified they represent a valuable asset. It may take years of search for other scientists, however competent, and though provided with full information as to the characteristics of the strain, to isolate the same strain for themselves, if indeed they can ever succeed in doing so.

Lord Wilberforce went on to observe (at 448) that it was the isolated strain of the micro-organism (a strain of Streptomyces verticillatus) that represented the result of the research effort of the inventors but that the strain "being something living, found in nature, cannot be patented". The question whether an isolated strain of micro-organism was a manner of manufacture (as required by the *Patents Act 1949* (UK) which was still in force at the time)

was not necessary to the decision in *Dann's Patent* nor, it appears, was the point the subject of argument.

98 The applicants also relied upon an observation of Lord Hoffmann in *Kirin-Amgen* which was said to support the proposition that a naturally occurring protein (and, *a fortiori*, naturally occurring DNA) was not patentable subject matter *even if it was isolated*. His Lordship said in *Kirin-Amgen* (para [132]):

> The result is that I would allow TKT's appeal and revoke the patent on the ground that claim 19 is insufficient (s.72(1)(c)) and claim 26 is anticipated (s.72(1)(a)). **Standing back from the detail, it is clear that Amgen have got themselves into difficulties because, having invented a perfectly good and ground-breaking process for making EPO and its analogues, they were determined to try to patent the protein itself, notwithstanding that, even when isolated, it was not new.**

(emphasis added)

99 However, it is clear that Lord Hoffmann did not say that an isolated protein (specifically, erythropoietin, otherwise known as EPO), was inherently non-patentable. The relevant sentence was plainly directed at the validity of claim 26 which Lord Hoffmann said was to something that was "not new" and therefore not patentable: see s 1(1)(a) of the *Patents Act 1977* (UK) (**the UK Act**).

100 Claim 1 in *Kirin-Amgen* was to a DNA sequence for use in the expression of certain polypeptides (rEPO) in an eukaryotic host cell. Claim 26 was to "[a] polypeptide product of the expression in a eucaryotic host cell of a DNA sequence according to any of claims 1 [and various other dependent claims]": see at 182, para [15]. The reason why claim 26 was held to be invalid turned on two findings of fact. First, natural occurring EPO (uEPO) had previously been isolated in minute quantities from large quantities of urine collected from patients suffering from aplastic anaemia. Secondly, rEPO and uEPO have the same chemical composition. It followed that rEPO, even if isolated, could not be new because uEPO had been isolated before rEPO: see generally *Kirin-Amgen* at paras [5], [86]-[87], [96]-[101].

101 Whether or not a composition of matter (including a micro-organism) is a "manner of manufacture" must be decided in accordance with the principles set out in the *NRDC* case. It follows (leaving aside any relevant statutory exception) that a composition of matter may

constitute patentable subject matter if it consists of an artificial state of affairs, that has some discernible effect, and that is of utility in a field of economic endeavour.

102 It goes without saying that the relevant state of affairs must be the result of some human intervention. After all, it is the element of human intervention that allows one to both characterise the relevant state of affairs as being artificial and to identify one or more inventors who, one way or another, must have brought such a state of affairs into existence in the first place. The real problem lies in knowing, or rather not knowing, what degree of human intervention is necessary before it can be concluded that the requisite artificial state of affairs exists. It is an especially difficult problem in the present case, not so much because the authorities provide no clear solution to it, but because the problem has an almost metaphysical dimension to it.

103 There are two further points to be made concerning *NRDC*. First, it is important to note that *NRDC* does not require the Court to ask whether a composition of matter is a "product of nature" for the purpose of deciding whether or not it constitutes patentable subject matter. *NRDC* recognises that it may be unhelpful to approach the problem in this way. I think this is especially so in the field of biotechnology in which micro-organisms play a critical role in the development, manufacture and use of diagnostic and therapeutic products and techniques. And second, *NRDC* does not require the Court to ask whether a micro-organism is "markedly different" to something that already exists in nature for the purpose of deciding whether it constitutes patentable subject matter (cf. *Chakrabarty* at 310).

Isolated nucleic acid

104 In the context of biological material, an artificial state of affairs may manifest itself in different ways. The physical properties of the naturally occurring material may have changed as a result of it having been isolated. But even if the physical properties of the material have not changed, the removal of the material from its natural environment and its separation from other cellular components may still give rise to what might reasonably be described as an artificial state of affairs.

105 In my opinion the patentability of the isolated nucleic acids referred to in the disputed claims does not turn upon what changes have been made to the chemical composition of such substances as a result of them having been isolated. In particular, the question of whether

these substances constitute patentable subject matter does not depend upon the type of chemical bond that may have been broken in the process of isolating them. It is inevitable that some bonds will be broken in the course of isolating nucleic acids, but it is not apparent from the evidence that these will necessarily include covalent bonds. As I have already explained, the disputed claims do not require that the isolated nucleic acids they describe differ from those found in the cell in this or any other respect so far as their chemical composition is concerned.

106 Accordingly, the issue in this case turns upon whether an isolated nucleic acid, which may be assumed to have precisely the same chemical composition and structure as that found in the cells of some human beings, constitutes an artificial state of affairs in the sense those words should be understood in the present context. There are three considerations which lead me to think that it does.

107 First, in explaining the concept of manner of manufacture as one involving the creation of an artificial state of affairs, it is apparent that the High Court in *NRDC* was deliberate in its use of very expansive language. Not only did the High Court emphasise the "broad sweep" of the concept involved, it also made clear that metaphorical analysis may not be helpful in determining whether or not something constitutes patentable subject matter.

108 Secondly, in the absence of human intervention, naturally occurring nucleic acid does not exist outside the cell, and "isolated" nucleic acid does not exist inside the cell. Isolated nucleic acid is the product of human intervention involving the extraction and purification of the nucleic acid found in the cell. Extraction of nucleic acid requires human intervention that necessarily results in the rupture of the cell membrane and the physical destruction of the cell itself. And purification of the extracted nucleic acid requires human intervention that results in the removal of other materials which were also originally present in the cell. It is only after both these steps are performed that the extracted and purified product may be properly described as "isolated" in the sense that word is used in the disputed claims.

109 Thirdly, as *Dann's Patent* demonstrates, the isolation of a particular micro-organism may require immense research and intellectual effort. In that case, it was only as a result of an intensive research effort that the isolated micro-organism in question could be made available for use in the manufacture of the new antibiotic. It was fortuitous for the patentee

that it was its employees who were first to isolate the new micro-organism and first to deploy it in the manufacture of the new drug. That will not always be so. It would lead to very odd results if a person whose skill and effort culminated in the isolation of a micro-organism (*a fortiori*, an isolated DNA sequence) could not be independently rewarded by the grant of a patent because the isolated micro-organism, no matter how practically useful or economically significant, was held to be inherently non-patentable. In my view it would be a mistake, and inconsistent with the purposes of the Act, not to give full effect in such situations to the broad language used by the High Court in *NRDC*.

110 The applicants argued that what the High Court said in *NRDC* should not be taken too literally. In support of this argument they referred to the observation of Lord Walker in *Kirin-Amgen* [2005] RPC 169 where his Lordship said (at para [138]):

> There is always a danger that any judicial summary of principle may, precisely because it is concise, practical and repeatedly cited, take on a life of its own, as if it were a statutory text with its own problems of construction to be resolved …

At the most general level, one cannot but agree with this statement. Here, however, I am not concerned with the construction of statutory text. The present case is to be resolved not by reference to statutory language in any conventional sense, but by the application of principles and concepts developed by the Courts as explained in *NRDC* and other relevant authorities. The High Court's decision in *NRDC* is a definitive statement on the question of what constitutes patentable subject matter, and unless some good reason exists to distinguish it, it should be applied in a manner that gives effect to the broad language that was used.

RECENT AMENDMENTS AND THEIR HISTORY

111 It is useful to look to the legislative history of some recent amendments to the Act for the purpose of determining whether the conclusion I have come to might for some reason be seen to be inconsistent with Parliament's intentions.

112 It is important to observe, even though it may go without saying, that the Act does not include any provision that specifically precludes the grant of a patent for an isolated DNA or RNA sequence. In particular, s 18(2) of the Act provides only that "human beings, and biological processes for their generation" are not patentable. A proposal that the *Patents Bill 1990* (Cth) be amended to include a similar provision that would have treated DNA and RNA in the same way was not adopted. The inference to be drawn is that it was not the intention

of Parliament at the time the Act was passed to deal with the issue of "gene patenting" by way of express statutory exclusion along the lines of s 18(2), but to leave it to the Courts to apply the law as settled in the *NRDC* case and other relevant authorities.

Early decisions of the Australian Patent Office on the patentability of isolated DNA sequences

113 Until now, there have been no judicial decisions in this country which have considered the patentability of isolated DNA or RNA sequences. However, there have been a number of decisions issued by the Australian Patent Office which have referred to the point. The first reported decision of the Australian Patent Office allowing a claim to isolated DNA was made in the context of an opposition proceeding in the matter of *Kirin-Amgen Inc v Board of Regents of University of Washington* (1995) 33 IPR 557. In that matter, the Deputy Commissioner of Patents (Mr D Herald) noted that no objection had been taken by the opponent to various claims in the opposed patent application on the ground that their subject matter involved the "mere discovery" of the DNA sequence encoding erythropoiten. Nevertheless, Mr Herald, having raised the issue himself, said (at 569):

> The present invention fundamentally relies upon the discovery of the DNA sequence encoding erythropoietin. In my view a claim directed to naturally occurring DNA characterised by specifying the DNA coding for a portion of that molecule would likely be claiming no more than a discovery per se and not be a manner of manufacture.
>
> The present specification contains claims to DNA sequences, in two categories:
>
> - Claims 14, 17, 18, and 55, which claim a "purified and isolated" sequence limited to that specified in tables V or VI, or limited to being "essentially" the sequence encoding erythropoietin. These claims are directed to a molecule which is a fragment of the full chromosome. They do not claim the naturally occurring chromosome, or any other naturally occurring entity. By being directed to a purified and isolated DNA sequence they claim "an artificially created state of affairs''.
> - Claim 33 claims:
>
> > A DNA sequence coding for a polypeptide analogue of naturally-occurring erythropoietin.
>
> and claim 34 claims:
>
> > A DNA sequence coding for …
> >
> > > specifying human erythropoietin with a range of substitutions or deletions.
> > >
> > > Both claims include within their scope a full length chromosome containing the relevant sequence, because they are not restricted to

> a "purified and isolated" sequence. However, both claims are directed to molecules which have been deliberately changed from the naturally occurring form - ie they are directed to artificially created states of affairs.
>
> I also observe that an objection of manner of manufacture might arise if the claims were directed to a mere chemical curiosity; but that is plainly not the case with this invention.
>
> Accordingly, I am satisfied that an objection of manner of manufacture does not apply to any of the claims.

114 Mr Herald's reasoning and conclusion are succinctly expressed but they are consistent with the view I have reached in the present matter. What is more important for present purposes, is that this decision reflected what is now the long standing practice of the Australian Patent Office in relation to claims to isolated DNA sequences so far as the requirements of s 18(1)(a) of the Act are concerned.

The Australian Law Reform Commission's Report into Gene Patenting

115 The patentability of gene sequences has received close attention from the Australian Law Reform Commission (**ALRC**) after it received a reference in December 2002 from the then Attorney General. The ALRC provided its detailed report on the topic to the Attorney General more than 13 years ago.

116 In its report dated 29 June 2004 entitled *Genes and Ingenuity: Gene Patenting and Human Health* (ALRC 99, 2004) (**the ALRC Report**), the ALRC recognised that legitimate concerns could be raised in relation to patents for isolated biological materials that occur in nature. But on the basis that there was a settled practice of granting patents in respect of such materials the ALRC did not favour any change to the law aimed at curtailing the practice. The ALRC said (at paras 6.51-6.53):

> 6.51 It is clear that the *processes* for identifying, isolating and purifying naturally occurring materials, including biological material such as genetic sequences, should be patentable when those processes satisfy the other requirements of patentability – namely, when they are novel, inventive, useful and fully disclosed. However, legitimate concerns have been raised about the patenting of biological *materials* that occur in nature, but have been isolated and purified by humans. Isolated biological materials may, in some cases, replicate exactly the composition and characteristics of material that occurs in nature. Although one cannot deny the legitimacy of patenting processes for isolating and purifying naturally occurring materials, or the legitimacy of patenting new chemical substances that are the product of human ingenuity, there are attractive arguments for the view that such materials should not

have been treated as patentable subject matter.

6.52 However, the time for taking this approach to the patenting of products and materials has long since passed. For decades, naturally occurring chemicals have been regarded by patent offices in many jurisdictions as patentable subject matter, when they are isolated and purified. This principle has been applied by analogy to biological materials, including genetic sequences, on the basis that they are 'merely' complex organic compounds. This development was certainly not foreseen when the modern patent system was established, and a different approach might have been available when the issue first arose for consideration.

6.53 Nonetheless, the ALRC considers that a new approach to the patentability of genetic materials is not warranted at this stage in the development of the patent system, for the following reasons:

- It would represent a significant and undesirable departure from accepted international practice with respect to genetic inventions, and may adversely affect investment in the Australian biotechnology industry.
- It may fail to deliver the anticipated benefits because many pure and isolated genetic sequences do not exist in exactly the same form in nature–for example, patented sequences may not contain the introns that are found in the naturally occurring material.
- Claims to genetic materials in their natural form (that is, *in situ*) do not constitute patentable subject matter.
- Arguments that genetic materials are not patentable inventions do not always take adequate account of the fact that – in addition to the threshold requirement of 'patentable subject matter' – a number of statutory requirements must be satisfied for patent protection to be obtained. In particular, patent protection cannot be conferred over genetic materials unless a use for such materials has been identified and fully disclosed.
- It would be difficult, on any rational basis, to confine reform to genetic materials and technologies, yet the extension of the reform to other fields – where the patenting of pure and isolated chemicals that occur in nature is uncontroversial – may have unknown consequences.

117 The ALRC Report went on to suggest that the test for patentable subject matter may warrant reform. It recommended (at para 6.58) that the responsible Minister initiate an independent review of the appropriateness and adequacy of the "manner of manufacture" test. In 2008 the Minister for Innovation, Science and Research (Senator Kim Carr) initiated such a review which resulted in the Advisory Council on Intellectual Property releasing a report entitled *Patentable Subject Matter* (December 2010) (**the ACIP Report**). Around the same time that the ACIP Report was released, another report prepared by the Senate Community Affairs References Committee entitled *Gene Patents* (November 2010) (**the SCA Report**) was also tabled in the Senate.

118 Also in late 2010 the *Patent Amendment (Human Genes and Biological Materials) Bill 2010* (Cth) was introduced into the Senate as a Private Members' Bill. The Bill sought to exclude patents of "biological materials including their components and derivatives, whether isolated or purified or not and however made, which are identical or substantially identical to such materials as they exist in nature." The term "biological materials" was defined to include DNA and RNA. The Bill was referred to the Legal and Constitutional Affairs Legislation Committee (**LCAC**) for inquiry and its report was tabled in the Senate on 21 September 2011. In its report the LCAC recommended (by majority) that the Senate not pass the Bill which eventually lapsed.

119 The Australian Government issued a response to the SCA Report in November 2011 (**the Australian Government Response**). In fact the Australian Government Response responded not merely to the SCA Report but also to the ACIP Report and, most relevantly, the ALRC Report. The Australian Government Response specifically accepted the ALRC's recommendation that the Act *not* be amended to exclude (inter alia) genetic materials and technologies from patentable subject matter (see the Australian Government Response at p 17). At the same time it accepted a range of recommendations calling for amendments to the Act that would impose stricter tests in relation to the other patentability requirements referred to in s 18(1)(b)(i) (novelty), s 18(1)(b)(ii) (inventive step) and s 18(1)(c) (usefulness). The Australian Government Response also accepted a number of other significant recommendations including the recommendation calling for the introduction of a new "experimental use" defence.

Intellectual Property Laws Amendment (Raising the Bar) Act 2012 (Cth)

120 Many of the recommendations that were accepted in the Australian Government Response were implemented by the *Intellectual Property Laws Amendment (Raising the Bar) Act 2012* (Cth) (**the Amendment Act**). In particular, the Amendment Act introduced into the Act a new experimental use defence, which took effect on 16 April 2012 (see now s 119C of the Act) and a new definition of "useful" which will take effect from 15 April 2013 (which will be s 7A of the Act).

121 Section 119C is significant in the present context. This is because one of the main arguments that has been advanced against the patentability of isolated DNA sequences (as well as other biological materials) is the impact that patents for such materials may have on

future research into previously undiscovered genetic mutations and research and the development of new diagnostic and therapeutic technologies that may only take place using patented biological materials.

122 The introduction of s 7A is also significant in the present context. Section 7A will make it more difficult for patent applicants to obtain patent protection for expressed sequence tags (**ESTs**). ESTs are short nucleotide sequences that represent a fragment of a cDNA "clone" that have proven especially controversial in circumstances where their principal use is as a research or experimental tool. (For a detailed discussion of the controversy surrounding ESTs, including references to the ALRC's consideration of them, see Dr Matthew Rimmer, *The New Conquistadors: Patent Law and Expressed Sequence Tags* (2005) 16 J. L. Inf. & Sci. 10.)

123 Of course, the history to the Amendment Act, including the Australian Government Response to the ALRC Report, does not bear directly on the proper scope of the "manner of manufacture" requirement. This is because the question whether isolated nucleic acid is within the broad sweep of the concept of manner of manufacture is to be decided in accordance with the principles developed for that purpose, rather than the legal principles or statutory provisions that are concerned with the proper interpretation of a statute. Even so, these are not matters that can be completely ignored. I think it is important to recognise that the recent and imminent changes to the Act address at least some of the problems that opponents of the Australian Patent Office's long standing practice have previously identified.

THE PATENT LAWS OF THE EUROPEAN UNION AND THE UNITED STATES

124 Both parties referred me to the legal position in the European Union (**EU**) including, in particular, the United Kingdom (**UK**) and the United States (**US**). I will briefly summarise the legal position in these jurisdictions.

The European Union

125 On 12 May 1998 the European Parliament approved the Directive on the Legal Protection of Biotechnological Inventions (**the BPD**). The BPD came into force on 6 July 1998 as Directive 98/44/EC. The EU States were given until July 2000 to implement the directive though not all did so. However, the BPD has now been implemented by all current

members of the EU. See generally Philip W Grubb, *Patents for Chemicals, Pharmaceuticals and Biotechnology* (4th ed, Oxford University Press, 2004) at 278 and Andrew Stewart, Phillip Griffith and Judith Bannister, *Intellectual Property in Australia,* (4th ed, LexisNexis Butterworths Australia, 2010) at 392.

126 In the UK, the BPD was implemented by an amendment made in 2000 to the UK Act which introduced s 76A. It provides:

> (1) Any provision of, or made under, this Act is to have effect in relation to a patent or an application for a patent which concerns a biotechnological invention, subject to the provisions of Schedule A2.
>
> (2) Nothing in this section or Schedule A2 is to be read as affecting the application of any provision in relation to any other kind of patent or application for a patent.

127 Schedule A2 is entitled "Biotechnological Inventions". Articles 1 and 5 of Schedule A2, which are most relevant, provide:

> 1 An invention shall not be considered unpatentable solely on the ground that it concerns –
>
> (a) a product consisting of or containing biological material; or
>
> (b) a process by which biological material is produced, processed or used.
>
> …
>
> 5. 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.

128 It is clear from these provisions that in the UK, as in many other parts of Europe, isolated DNA and isolated RNA may be patentable even though they are identical in their chemical composition to DNA and RNA found in the cell.

The United States

129 The parties made detailed submissions in relation to the decision of the United States Court of Appeals for the Federal Circuit in the matter of *The Association for Molecular Pathology & Ors v United States Patent and Trademark Office and Myriad Genetics Inc* 653 F3d 1329 (2011). However, after the present case was argued, the *Myriad* case was re-argued before the Court of Appeals for the Federal Circuit which delivered it most recent decision in

the matter on 16 August 2012 (*The Association for Molecular Pathology & Ors v United States Patent and Trademark Office and Myriad Genetics Inc* 689 F3d 1303 (2012)). The re-argument occurred as a result of a decision of the US Supreme Court vacating the earlier *Myriad* decision and remanding the case for further argument in light of the US Supreme Court's own decision in *Mayo Collaborative Services v Prometheus Laboratories Inc* 132 SCt 1289 (2012).

130 The *Myriad* litigation concerned a US patent that is closely related to the Patent in issue in the present case. It involved a challenge by the plaintiffs to the validity of the first respondent's (ie. Myriad Genetics Inc's) US patent including claims to isolated DNA (claims 1 and 2) in these terms:

> 1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID No:2.
>
> 2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

131 By majority the Court of Appeals for the Federal Circuit upheld the validity of these claims in the *Myriad* appeal. One member of the majority (Lourie J) placed emphasis upon the smaller size of isolated DNA compared to the size of a naturally occurring DNA molecule, and that an isolated DNA molecule was different to a naturally occurring DNA molecule as a result of having had covalent bonds in its backbone chemically severed (at 1328).

132 The other member of the majority (Moore J) also upheld the validity of the claims to isolated DNA sequences. However, Judge Moore placed much greater emphasis upon the long-standing practice and guidelines of the US Patent Office in granting patents for isolated DNA molecules that have the same sequence as a naturally occurring gene on the basis that the DNA molecule does not occur in nature in isolated form. Her Honour said that this practice had given rise to "exceedingly valuable property rights" and "settled expectations of the biotechnology industry". Her Honour referred to US Supreme Court authority suggesting that "the courts must be cautious before adopting changes that disrupt the settled expectations of the inventing community" (at 1344) citing *Festo Corp. v Shoketsu Kinzoku Kogyu Kabushiki Co.* 535 US 722, 739 (2002).

133 The third member of the Court in the *Myriad* appeal (Bryson J) delivered a forceful dissent in relation to the patentability of isolated DNA (but not cDNA). Judge Bryson was not persuaded by either of the different approaches favoured by the majority. As to the first of these, his Honour said (at 1355):

> Neither isolation of the naturally occurring material nor the resulting breaking of covalent bonds makes the claimed molecules patentable. We have previously stated that "isolation of interesting compounds is a mainstay of the chemist's art," and that "[i]f it is known how to perform such an isolation doing so 'is likely the product not of innovation but of ordinary skill and common sense.'" Similarly, the structural changes ancillary to the isolation of the gene do not render these claims patentable. The cleaving of covalent bonds incident to isolation is itself not inventive, and the fact that the cleaved molecules have terminal groups that differ from the naturally occurring nucleotide sequences does nothing to add any inventive character to the claimed molecules. The functional portion of the composition–the nucleotide sequence–remains identical to that of the naturally occurring gene.

(citations omitted)

As to the approach adopted by Judge Moore, his Honour gave several reasons which lead him to conclude that the US Patent Office's long standing practice and guidelines should not be given significant weight (at 1357-1358).

134 On 30 November 2012, the US Supreme Court announced that it would hear an appeal in the *Myriad* case. The US law in relation to the patentability is therefore not likely to be settled until the Supreme Court reaches it own decision on the issue.

135 In any event, it seems to me that the *Myriad* decision does not provide any direct assistance to either side in the present case. I say this for two reasons. First, the law in Australia is different. I must apply the law as explained in *NRDC*. It must also be recognised, especially as the *Myriad* case heads to the US Supreme Court, that the constitutional setting in which patent legislation operates in the US is quite different to that in which patent legislation operates in this country: *Grain Pool of Western Australia v Commonwealth of Australia* (2000) 202 CLR 479 at paras [28]-[32]. Secondly, the evidence in the *Myriad* case was not the same as the evidence in the present cast. And at least in relation to the matter of covalent bonds, I have taken a different view of the facts to that taken by Judge Lourie.

CONCLUSION

136 There is no doubt that naturally occurring DNA and RNA as they exist inside the cells of the human body cannot be the subject of a valid patent. However, the disputed claims do not cover naturally occurring DNA and RNA as they exist inside such cells. The disputed claims extend only to naturally occurring DNA and RNA which have been extracted from cells obtained from the human body and purged of other biological materials with which they were associated.

137 The applicants contended that each of the disputed claims was invalid on the sole ground that it was not a claim to a manner of manufacture and therefore did not comply with the requirements of s 18(1)(a) of the Act. That contention should be rejected for the reasons previously given. In my opinion each of the claims is to a manner of manufacture as that expression should now be understood. My reasons have nothing to say about the possible invalidity of the disputed claims on any other ground.

138 In the result, the amended application will be dismissed with costs. I will stay the costs order under such time as any appeal that may be brought has been heard and determined.

I certify that the preceding one hundred and thirty-eight (138) numbered paragraphs are a true copy of the Reasons for Judgment herein of the Honourable Justice Nicholas.

Associate:

Dated: 15 February 2013