IN THE HIGH COURT OF AUSTRALIA
SYDNEY REGISTRY

No. S28 of 2015

BETWEEN:

YVONNE D'ARCY

Appellant

and

MYRIAD GENETICS INC

First Respondent

GENETIC TECHNOLOGIES LIMITED
ABN 17 009 212 328

Second Respondent

FIRST RESPONDENT'S SUBMISSIONS

Part I: Suitable for publication

1. The First Respondent certifies that this submission is in a form suitable for publication on the internet.

Part II: Issues presented by the appeal

2. The Appellant erroneously formulates the question for this Court as "whether an isolated human gene is a patentable invention, being a manner of manufacture within the meaning of s 18(1)(a) of the *Patents Act 1990*?". The question does not arise on the appeal.

3. Rather, claims 1 to 3 of Australian Patent No. 686004 (**Patent**) are claims to "isolated nucleic acids". The claims in issue are not claims to "isolated human genes". Nor are they claims to the "genetic code" or to "information". The claims are to a product; that is, a chemical compound. That is the uncontroverted evidence, including that of the Appellant's expert.

4. This was expressly recognised by the enlarged Bench of the Full Court of the Federal Court of Australia (**Full Federal Court**) which defined the invention of the claims as follows: "[w]hat is claimed is an isolated nucleic acid, a chemical molecule characterised in a certain way, which is chemically, structurally and functionally different to what occurs in nature".[1]

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[1] [2014] FCAFC 115 at [194]. See also [2014] FCAFC 115 at [210] and [2013] FCA 65 at [76]-[77].

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5. Thus, the First Respondent respectfully submits that the question for this Court is whether the chemical compound the subject of claims 1 to 3 is a manner of manufacture according to the principles of patentability enunciated by the High Court in *National Research Development Corporation v Commissioner of Patents*[2] (***NRDC***), as affirmed last year by this Court in *Apotex Pty Ltd v Sanofi-Aventis Australia Pty Ltd*[3] (***Sanofi***).

6. The First Respondent notes that the Appellant has not challenged the claims in dispute on any other grounds available to her under the *Patents Act 1990* (Cth) (the ***Patents Act***). In these circumstances, the patentability of the invention the subject of each of the claims stands to be determined independently of any questions of novelty, inventiveness and utility.

Part III: *Judiciary Act 1903*

7. It is certified that the First Respondent considers that the giving of a notice pursuant to s 78B of the *Judiciary Act 1903* (Cth) is not necessary.

Part IV: Contested material facts

Claims 1 to 3

8. The Appellant's characterisation of claims 1 to 3 of the Patent as "isolated nucleic acids corresponding to all or part of a human gene" is factually inaccurate.[4] A gene is a functional unit of contiguous DNA sequence that encodes a protein (or set of proteins).[5] In contrast, the claims are to a product: an isolated nucleic acid. That isolated nucleic acid is chemically, structurally and functionally different to genomic DNA which occurs in nature.[6] In reaching this conclusion of fact, the Full Federal Court considered the evidence carefully.[7]

9. Indeed, this is expressly recognised by the Appellant's submissions that refer to the claim being to a "product", namely isolated DNA or RNA.[8]

10. The isolated nucleic acids claimed are characterised by comparison to the "BRCA1 polypeptide encoding sequence set forth in SEQ.ID No:1". As prefaced by the claim, SEQ.ID No:1 represents the sequence of a nucleic acid which encodes the BRCA1 polypeptide.[9] The contiguous sequence set out in SEQ.ID No:1 (known as cDNA) includes only exons and is generated by the process of

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[2] (1959) 102 CLR 252.
[3] (2013) 304 ALR 1.
[4] Appellant's Submissions (**AS**) at [13].
[5] Affidavit of Matthew Brown dated 21 December 2011 (**Brown**) at [30].
[6] [2014] FCAFC 115 at [194] and [213].
[7] See particularly [2014] FCAFC 115 at [174]-[178], [183] and [189]-[193].
[8] See, for example, AS at [11], [41] and [60].
[9] Patent pp 119-128 (SEQ.ID No:1).

reverse transcription from mRNA (to which it is complementary, but not identical).

11. Importantly, SEQ.ID No:1 is *an artificial sequence* which does not contain any of the intervening intronic sequences that are found in naturally occurring DNA. In addition to containing this polypeptide encoding sequence, the isolated nucleic acids claimed must contain one or more of the mutations and/or polymorphisms set out in the relevant tables of the Patent.[10]

12. The Appellant erroneously states that the trial judge rejected the argument that "the claimed nucleic acids were structurally, functionally and chemically different from those that occurred in nature".[11] The trial judge held that not every isolated nucleic acid within the scope of the claims of the Patent required the breaking of covalent bonds.[12] Nevertheless, his Honour found that "[i]t is inevitable that some bonds will be broken in the course of isolating nucleic acids ...".[13] That is, it is inevitable that there will be some differences in chemical composition between an isolated nucleic acid and DNA *in vivo* which arise directly as a result of the process of isolation.

13. The trial judge made no findings regarding the functional differences between isolated nucleic acids and DNA *in vivo*.[14]

14. In any event, the trial judge found that patentability did "not turn upon what changes have been made to the chemical composition of such substances as a result of having been isolated".[15] Further, he noted that "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".[16] On this basis, he found the claims valid, further explaining that "naturally occurring DNA and RNA as they exist in cells 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".[17]

Part V: Applicable provisions

15. The First Respondent submits the only applicable provisions are s 18(1)(a) and the definition of "invention" in Schedule 1 of the *Patents Act*. These provisions are set out in the Appellant's submissions.[18]

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[10] Patent pp 89 (Table 12), 92 (Table 12A), 100 to 102 (Table 14) and 105 (Table 18).
[11] AS at [18].
[12] [2013] FCA 65 at [74].
[13] [2013] FCA 65 at [105].
[14] Cf. AS at [18].
[15] [2013] FCA 65 at [105].
[16] [2013] FCA 65 at [108].
[17] [2013] FCA 65 at [77].
[18] AS at [73] and [75].

16. In addition to the above provisions, the Appellant's submissions draw heavily on the decision of the US Supreme Court in *Association for Molecular Pathology v Myriad Genetics Inc*, 569 US ___ (2013), 133 S Ct 2107 (2013) ***(AMP v Myriad)***, which considers the operation of 35 USC § 101.

17. 35 USC § 101 states as follows:

> *Whoever invents or discovers any new and useful process, machine, manufacture or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.*

10 18. The limitations imported by the US Supreme Court into 35 USC § 101 differ from the provisions of the *Patents Act* especially s 18(1)(a) and the definition of "invention" in Schedule 1. Significantly, as discussed below in the context of *AMP v Myriad*, the US Supreme Court does not import into 35 USC § 101 a definition of "manner of manufacture" based on s 6 of the *Statute of Monopolies* which, as this Court has held in *NRDC* and *Sanofi*, remains the basis for determination as to the scope of patentable subject matter under the *Patents Act*.

19. The applicablity of the decision in *AMP v Myriad* is discussed further below.

Part VI: Argument on appeal

20 *The Patent*

20. The title of the Patent is "In vivo mutations and polymorphisms in the 17q-linked breast and ovarian cancer susceptibility gene".

21. The Patent at page 10, lines 29 to 31, states as follows:

> *We have discovered that there are mutations in the coding sequence of the BRCA1 locus in kindreds which are responsible for the 17q-linked cancer susceptibility known as BRCA1. This gene was not known to be in this region.*

22. The Patent describes the invention at page 8, lines 16 to 20, as follows:

> *The present invention provides an isolated polynucleotide comprising all,*
> 30 *or a portion of the BRCA1 locus or of a mutated BRCA1 locus, preferably at least eight bases and not more than about 100kb 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.*

23. As the Full Federal Court found,[19] Myriad identified the BRCA1 gene, its nucleic acid sequence and the characteristics and sites of mutations. The Full Federal Court held (and it was not in dispute) that this involved an inventive step.

Approach to question on appeal

24. The question raised by this appeal is whether the invention claimed in claims 1 to 3 of the Patent is a manner of manufacture within the meaning of s 6 of the *Statute of Monopolies* pursuant to s 18(1)(a) of the *Patents Act.*

25. The first step called for in answering this question involves determining "what is the invention claimed by the patent".

26. The second step involves considering whether the invention claimed by the patent is a "manner of manufacture". This requires an analysis as to the meaning of the phrase as used in the *Patents Act.* The application of the principles enunciated in *NRDC* (and affirmed in *Sanofi*) lead to the result that the challenged claims are patentable subject matter.

Construction of claims

27. The starting point for determining whether the invention claimed is a manner of manufacture is an analysis of the claims according to traditional principles that apply to all patent claims. There is no basis for a different approach to claims 1 to 3.

28. The term "isolated" is defined at page 26, lines 12 to 18, of the Patent as follows:

> *"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.*

29. Claims 1 to 3 appear at page 185, lines 3 to 14, of the Patent but claim 1 can be used as an exemplar:

> *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:1 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.*

[19] [2014] FCAFC 115 at [79].

30. The claims are clear on their face: the Patent claims a chemical compound, that is, *an isolated nucleic acid*. This was the effect of the expert evidence, including that of the Appellant's own expert Dr Suthers who construed the claim as "[referring] to specific DNA or RNA molecules".[20]

31. The isolated nucleic acid claimed by the Patent is made up of a number of chemical components including nitrogenous bases, sugars, and phosphate groups bonded together with covalent and hydrogen bonds. It is not merely a sequence of nucleotides.[21] This was uncontroversial.[22]

32. The claims are to a "product".[23] To assess patentability, that claimed product must be construed in the same manner as any other patented product, according to well and long established principles of patent claim construction.[24] Once that is done, it is apparent that the claimed product, a chemical compound, has no counterpart in nature.

33. Despite this, the Appellant argues that to characterise the claims as "a chemical molecule" is to approach the claim at "the wrong level of analysis".[25] The Appellant suggests that, at the "correct level of analysis", the claims are to "information".[26] She does this by equating "coding for" with "possession of the code".[27]

34. The phrase "coding for"[28] is undoubtedly an important part of the claim: it describes the sequence of nucleotide bases in the claimed chemical compound. However, the claimed chemical molecule is much more than just a sequence of nucleotides; were it otherwise it would have no utility.

35. The experts construed the phrase in this way.[29] Indeed, Dr Suthers referred to the words as a "descriptor".[30] Contrary to this evidence, the Appellant seeks to use the words not as a "descriptor" but as defining the totality of what is claimed. This proposition ought be rejected.

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[20] Annexure GKS-1 to the Affidavit of Dr Graeme Kemble Suthers dated 8 November 2011 (**Annexure GKS-1**) at [66].

[21] AS at [51]; see also [2014] FCAFC 115 at [194].

[22] Affidavit of Professor John Rasko dated 23 September 2011 (**Rasko**) at [42]-[50] and [84]-[87]; Cross-Examination of Dr Graeme Kemble Suthers (**Suthers XXN**) at T 95.35-96.13.

[23] See, for example, AS at [11], [41] and [60].

[24] See, for example, *Australian Mud Co Pty Ltd v Coretell Pty Ltd* (2011) 93 IPR 188 at [63]-[69]; *H Lundbeck A/S v Alphapharm Pty Ltd* (2009) 177 FCR 151 at [118]-[120]; *PAC Mining Pty Ltd v Esco Corporation* (2009) 80 IPR 1 at [26]-[29]; *Jupiters Ltd v Neurizon Pty Ltd* (2005) 65 IPR 86 at [67]; *Sachtler GmbH & Co KG v RE Miller Pty Ltd* (2005) 221 ALR 373 at [43]-[67].

[25] AS at [30].

[26] AS at [38]-[39].

[27] AS at [53].

[28] AS at [51]-[57].

[29] Brown at [110]; Suthers XXN at T 93.39-42.

[30] Suthers XXN at T 93.39-42.

36. The Full Federal Court expressly rejected the contention that '"encode" equates to "code for"', noting the use of the different words in the claim.[31] The Full Federal Court correctly distinguished between "code for" – "(passive; having the **potential** to produce the polypeptide)", and "encode" – "means actually to produce the polypeptide (the active)" [emphasis in original].[32] This is consistent with the expert evidence, including that of the Appellant's own expert, that the claimed isolated nucleic acids are not capable of actually producing the polypeptide. As Dr Suthers said, isolated nucleic acid is "inert".[33]

37. The Appellant further argues that the only relevant attribute of the claimed chemical compounds is that they contain "the same sequence of nucleotides, carrying the same information [as the BRCA1 gene]".[34] The Appellant submits that as this "information" is the same, "[t]he information claimed is not artificial in the required sense".[35] The First Respondent submits that, not only is this proposition made without any jurisprudential basis, the proposition is contrary to the expert evidence as recognised by the Full Federal Court.

38. First, as noted above, and as held by the primary judge and the Full Federal Court, the claim is not to information. The Full Federal Court noted correctly that:[36]

> *To identify the invention as lying in the concept of information said to be embodied in a sequence of nucleotides ignores the language of the claim.*

39. Contrary to the Appellant's submission, the fact of isolation *does* in fact change "that attribute" (i.e. information). The evidence is that an isolated nucleic acid of the claim cannot by itself produce the BRCA1 proteins (and corresponding mRNA) produced by the naturally occurring BRCA1 gene *in vivo*.[37] Further, when manipulated, in a way that does not occur in nature, the isolated nucleic acid can produce polypeptides that are *not produced* in the human body.[38] This was clearly articulated by the Full Federal Court:[39]

> *Isolated DNA cannot code, in the sense of being operated on by ribosomes to produce a protein or polypeptide, this being a function that occurs naturally within the cell. Isolated DNA cannot itself produce a polypeptide. In that sense it is inert, although it is capable of being manipulated to produce a protein but in a different way, by a different process to production from non-isolated genomic DNA.*

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[31] [2014] FCAFC 115 at [172].
[32] [2014] FCAFC 115 at [175].
[33] Suthers XXN at T 126.4-5.
[34] AS at [39].
[35] AS at [40].
[36] [2014] FCAFC 115 at [194].
[37] See, for example, Suthers XXN at T 123.46-124.6, T 126.4-5 and T 126.30-40; Annexure GKS-1 at [96].
[38] Brown at [124].
[39] [2014] FCAFC 115 at [176].

40. Indeed, as the undisputed evidence at trial demonstrated, any polypeptide that may be produced from isolated nucleic acid (via human manipulation) "may be recognised as foreign and rejected by the body".[40]

41. The Full Federal Court recognised this as follows:[41]

> *The genetic code is not functionally a static sequence of nucleotides. It is a template for dynamic processes that result in the production of the polypeptide. The evidence is that the question of what polypeptides would be produced in the cell and in what quantity depends upon more than the sequence in which particular nucleotide bases are arranged.*

42. The flaw in the Appellant's argument is demonstrated by applying the "correct level of analysis" to cDNA (which falls within the scope of the disputed claims). cDNA contains all of the "information" that is present in genomic DNA *in vivo*, but differs insofar as particular intronic sequences have been removed. Despite the "sameness" in information content, the Appellant appears to concede that cDNA is a "manner of manufacture".[42]

43. This inconsistency in principle was recognised by the Full Federal Court:[43]

> *Ms D'Arcy does not challenge the claimed uses in later claims of polynucleotides with partial sequences as primers, probes, vectors and transformed cells. These consist of sequences that also, on her argument, exist in nature but do not code for the entire polypeptide. This seems to recognise that despite sequence identity, use and function differences from the naturally occurring genomic sequence are relevant to patentability. She submits that there cannot be a manner of manufacture because the sequence is a naturally occurring sequence. Recognising that cDNA, the sequence of SEQ.ID No:1, is an artificial construct, she points out that claim 1 is not so limited. She recognises that it encompasses a sequence that may be as short as five codons and submits that if it is a manner of manufacture, it is the coding sequence that equates to the naturally occurring coding sequence and is therefore unpatentable. This seems to conflict with her recognition that short sequences that equate to naturally occurring sequences and are used as probes are patentable. This makes her challenge to cDNA, an artificial sequence, more difficult to sustain.*

44. The only basis upon which the Appellant apparently says that cDNA can be distinguished from an isolated genomic DNA (or RNA) is on the basis that the latter is a "product of nature".[44] For the reasons discussed below, this is not a proper basis to exclude subject matter from patentability pursuant to the principles in *NRDC*.

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[40] Brown at [124].
[41] [2014] FCAFC 115 at [194].
[42] AS at [65].
[43] [2014] FCAFC 115 at [179]; see also [2014] FCAFC 115 at [218]; cf. AS at [65].
[44] AS at [38]-[50].

Chemical, structural and functional differences

45. The First Respondent submits that this Court ought construe the claim as it would for any other chemical compound. There is no jurisprudential basis or normative principle upon which claims to isolated nucleic acids should be treated differently from any other technology. The First Respondent respectfully submits that the Court must look to the subject matter claimed and determine the question of patentability according to the principles in *NRDC* (affirmed in *Sanofi*).

46. As the Full Federal Court held,[45] and as discussed above, the claims require comparison with SEQ.ID No:1, the cDNA which does not exist in nature. In nature, a continuous exon sequence of DNA coding for the polypeptide does not exist. Thus, the claimed nucleic acid is not simply "cut out" of the genome. The claimed RNA is different to that in nature, including because it lacks the same start and end.

47. The isolated nucleic acid molecule is chemically, structurally and functionally different from naturally occurring nucleic acids. The First Respondent does not understand this to be in issue as a matter of science, only as a matter of the "correct level of analysis".

48. By definition, the isolated nucleic acid claimed by the Patent is "chemically cleaved" from the surrounding components of the cell, including other genome sequences.[46] Further, the experts agreed that the process of isolation necessarily requires the breaking of bonds, including covalent bonds.[47] As a consequence, the isolated nucleic acids are chemically different from naturally occurring nucleic acids. As the Full Federal Court held, treating the claim to a chemical entity, the isolated nucleic acid is not the same as genomic DNA; "[t]hey have different beginnings and different ends".[48]

49. Similarly, the experts agreed that isolated nucleic acids are structurally different from naturally occurring nucleic acids. Unlike the claimed isolated nucleic acids, naturally occurring DNA has a 3D looped structure which is essential to its function in the cell.[49] Further, the claimed isolated nucleic acid is devoid of the cap and poly(A) tail present on mRNA *in vivo* which prevents genetic degradation and assists in other cellular functions.[50] These structural differences are not understood to be in dispute on the science.

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[45] [2014] FCAFC 115 at [191].
[46] See, for example, the definition of "isolated" at Patent, p 26, lines 12 to 18.
[47] Brown at [109] and [138]; Suthers XXN at T 96.41-44 and T 97.10-43; Annexure GKS-1 at [66(b)], [83] and [85].
[48] [2014] FCAFC 115 at [191].
[49] Suthers XXN at T 107.33-108.11.
[50] Rasko at [126]-[128]; Brown at [84].

50. Finally, and importantly, with respect to function, the expert evidence was that, unlike a naturally occurring nucleic acid, an isolated nucleic acid cannot, by itself, produce a polypeptide and cannot undergo replication.[51]

51. Although the ability to produce protein and replicate is lost through the process of isolation, the claimed isolated nucleic acids can be put to *new applications*. These include use as a probe, use in gene therapy and use in diagnostic testing.[52] Importantly, these uses cannot be carried out using naturally occurring nucleic acids.

52. The First Respondent submits that any one of these differences support the conclusion that the claimed invention is an artificially created state of affairs.

Manner of manufacture

53. In *NRDC*, the Court considered the principles underpinning patentability under Australian law. The Court considered the ambit of the phrase "manner of new manufacture the subject of letters patent and grant of privilege within section six of the *Statute of Monopolies*". This statute of course, was enacted in 1623 and provided an exception to the prohibition on monopolies.

54. In *NRDC*, this Court undertook a comprehensive survey of UK and Australian authorities and thereby identified the guiding principle underpinning the application of s 6 of the *Statute of Monopolies 1623* as:[53]

> *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 Monoplies?"*
>
> [emphasis added]

55. This Court in *NRDC* answered that question by applying the principle in the following terms:[54]

> *... 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 ... [a]nd the significance of the product is economic;*** *...*
>
> [emphasis added]

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[51] Brown at [119]-[120]; Suthers XXN at T 123.46-124.6; T 126.30-40; Annexure GKS-1 at [96].
[52] Brown at [122]-[127].
[53] *NRDC* at 269; cited by French CJ in *Sanofi* at (2013) 304 ALR 1 at [9].
[54] *NRDC* at 277; see also *Sanofi* at [307] (per Gageler J) and at [283] (per Crennan and Kiefel JJ).

56. Thus, the High Court did not leave the question of the ambit of the patentable subject matter at large. Rather, it is clear from the highlighted words, that the High Court identified a guiding principle underpinning the application of s 6 of the *Statute of Monopolies*. The High Court clarified its basis as follows:[55]

> *It is, we think, only by understanding* ***the word "product" as covering every end produced****, and treating the word "vendible" as pointing only to the requirement of utility in practical affairs, that the language of Morton J.'s "rule" may be accepted as wide enough to convey the broad idea which the long line of decisions on the subject has shown to be comprehended by the Statute.*
>
> [emphasis added]

57. This guiding principle has been applied across a breadth of subject matter for over 40 years.[56]

58. This Court, in *Sanofi*, affirmed this approach. In *Sanofi*, this Court considered the patentability of a method of human treatment, that is, a method claim. In doing so, it reiterated that the test in *NRDC* is to be applied in assessing patentability.[57]

59. Gageler J, agreeing with the reasoning of Crennan and Kiefel JJ, commented as follows:[58]

> *[NRDC] held that a process must have "two essential qualities" to be recognised as a manner of manufacture within the meaning of s 6 of the Statute of Monopolies 1623 (21 Jac I c 3). First, the process* ***must result in an "artificially created state of affairs"****. Secondly, that resultant state of affairs must have "its own economic utility".*
>
> [emphasis added]

60. The majority referred to this as the "general principle" to be applied in determining patentability of both product and process/method claims.[59]

61. What is clear from these authorities is that the question of patentability is to be determined by asking whether a product constitutes an artificially created state of affairs of economic utility.

62. On the uncontroverted science, the claimed nucleic acid is "artificial" in that it is chemically, structurally and functionally different to genomic DNA. The "human intervention" of Myriad has led to this artificial "end", a product, a chemical compound. Economic utility is conceded.

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[55] *NRDC* at 276.

[56] See, for example, *CCOM Pty Ltd v Jiejing Pty Ltd* (1994) 51 FCR 260 at 291, 295; *International Business Machines Corporation v Commissioner of Patents* (1991) 33 FCR 218 at 223-224; *Austal Ships Pty Ltd v Stena Rederi Aktiebolag* (2005) 66 IPR 420 at [211]; *Dynamite Games Pty Ltd v Aruze Gaming Australia Pty Ltd* (2013) 100 IPR 86 at [158], [162].

[57] *Sanofi* at [283] (per Crennan and Kiefel JJ).

[58] *Sanofi* at [307] (per Gageler J).

[59] *Sanofi* at [247] and [283] (per Crennan and Kiefel JJ).

63. Applying *NRDC* and *Sanofi*, the First Respondent respectfully submits that the question is not whether the claimed invention has come from cutting of the genome. It is whether through the intervention of Myriad in isolating the nucleic acids claimed, an artificial state of affairs has been created with conceded economic utility. Having regard to the chemical, structural and functional differences, the answer to that must be yes.

64. The Appellant seeks to recharacterise the test for patentability as requiring that a product "effects an artificially created improvement in something".[60] This formulation was used by Justices Crennan and Kiefel specifically in relation to a claim for a *method* of human treatment. Likewise, Gageler J's formulation of the test was specfic to a method claim by contrast with the product claim here. As the Full Federal Court discussed, this submission represents an unwaranted narrowing of the reasoning in *NRDC*.

65. In any case, even such a narrow formulation of the test for patentability is met in the circumstances of this case. In the human body, genomic nucleic acid sequences cannot function as probes, cannot be used in diagnostic testing and cannot be used in gene therapy. It is the intervention of Myriad that has unlocked the undisputed economic utility of the isolated nucleic acids, that is, Myriad's intervention has led to the artificial improvement on genomic DNA, to produce an isolated nucleic acid.

66. A number of the other aspects of the reasons of the majority of this Court in *Sanofi* support the reasoning of the Full Federal Court in this case. First, the majority of the High Court in *Sanofi* endorsed the "broad concept" or "widening conception" of "manner of manufacture" discussed in *NRDC*.[61] The primary judge in this case correctly reasoned that the "broad sweep" of the concept of manufacture emphasised in *NRDC* did not permit a narrow interpretation of what constitutes an "artificially created state of affairs". By contrast, a finding by this Court that the claimed isolated nucleic acid is not an artificially created state of affairs because it may have one characteristic in common with naturally occurring nucleic acid (i.e. a segment of nucleotide sequence) will materially narrow the scope of patentable subject matter at the very least in the field of biotechnology and potentially in a wider class of pharmaceutical materials.

67. Secondly, one of the bases relied upon by Crennan and Kiefel JJ (with whom Gageler J concurred) in support of the patentability of methods of human treatment is that the Act contains no express exclusion from patentability of such subject matter, nor could one be implied. Likewise, here, as the primary judge noted, the Act "does not include any provision that specifically precludes the

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[60] AS at [59].

[61] *Sanofi* at [9] (per French CJ), [224] (per Crennan and Kiefel JJ) and [309] (per Gageler J).

grant of a patent for an isolated DNA or RNA sequence"[62] nor, it is submitted, could any such exclusion be implied in light of the legislative history. It is respectfully submitted that it is not, even for this Court, to "legislate" for such an exclusion.

68. That legislative history involves a more than decade long exploration of the question of patentability of nucleic acid sequences. Parliament has *expressly declined* to enact any such exclusion on more than one occasion. This making of a conscious decision not to act sets this area apart from mere silence by the legislature, which might be characterised as the legislature leaving the field to the Courts for resolution.

69. The patentability of "genetic materials" was addressed directly by the legislature when an amendment to the Patents Bill 1990 (Cth) was proposed by the Australian Democrats to specifically exclude "genes, whether derived from cells or chemically synthesised". The proposed amendment was expressly rejected by the Senate.[63] In the course of debating the proposed amendment in the House of Representatives, the legislature expressed the view that the amendment would exclude a range of genetic materials that were the proper subject matter for a patent including, for example, "vaccines and antibiotics which are based on live genetic material".[64]

70. In 2004, the Australian Law Reform Commission published a report on gene patenting which concluded that "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".[65] The reasons for this conclusion are set out in full by both the Full Federal Court and the primary judge.[66]

71. Again, in late 2010, a Private Members' Bill was introduced to the Australian Senate which proposed exclusion of "biological materials [such as RNA or DNA] 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".[67] In rejecting the proposed amendment, the Legal and Constitutional Affairs Legislation Committee stated as follows:[68]

> *... the committee is concerned that proposed amendments in the Bill,*

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[62] [2013] FCA 65 at [112].

[63] Commonwealth, *Parliamentary Debates*, Senate, 17 September 1990, 2478-2482 (John Coulter, Peter Baume, Bob Collins, Brian Archer).

[64] Commonwealth, *Parliamentary Debates*, Senate, 17 September 1990, 2479 (John Coulter) and Commonwealth, *Parliamentary Debates*, House of Representatives, 16 October 1990, 2945 (Geoff Prosser).

[65] Australian Law Reform Commission, *Genes and Ingenuity: Gene Patenting and Human Health*, Report No 99 (2004) at [6.53].

[66] [2014] FCAFC 115 at [158]; [2013] FCA 65 at [116].

[67] Patent Amendment (Human Genes and Biological Materials) Bill 2010 (Cth).

[68] Senate Legal and Constitutional Affairs Legislation Committee, *Patent Amendment (Human Genes and Biological Materials) Bill 2010*, (2011) at 64 [5.25]-[5.26].

> *which are focused on addressing a specific issue, could have a large number of unintended consequences across the entire patent system with indeterminate impacts on a range of industries and sectors.*
>
> *... Despite the need for further reform to the patent system, the committee agrees that* ***removing an area of patentable subject matter****, as proposed by the Bill, is not an appropriate solution to this complex set of issues.*
>
> [emphasis added]

72. As noted by the Full Federal Court, these deliberations make plain that "Parliament has considered, and has expressly declined, to exclude purified and isolated gene sequences from the scope of patentable subject matter".[69] The legislative intention was not to leave the matter for the Courts but to include genetic materials (including isolated nucleic acids) within the scope of inherently patentable subject matter under the *Patents Act*.

73. Thirdly, a further factor relied upon in the reasoning of Crennan and Kiefel JJ (with whom Gageler J concurred) was the practice of the Australian Patent Office since *Joos v Commissioner of Patents* (1972) 126 CLR 611 in granting patents for methods of human treatment. Here, the primary judge, noted the "longstanding practice of the Australian Patent Office" in granting patents for isolated nucleic acids on the basis that no manner of manufacture objection can be taken to such claims.[70] The practice of the Australian Patent Office is discussed in more detail below.

Product of nature

74. The Appellant submits that the claims in issue ought be denied patentability on the basis that they constitute a "product of nature".[71] Such a proposition ought be rejected for a number of reasons.

75. First, there is simply no place for a "product of nature" exemption in the light of *NRDC* and the Appellant's "carve out" relies on the type of "verbal formula" that this Court rejected in *NRDC* (affirmed in *Sanofi*).[72]

76. Second, the ambit of the "product of nature exception" is unclear and undefined as demonstrated by the difficulties of such formulas recognised in *NRDC*.

77. If it is the case (as the Appellant apparently proposes here), that the carve out captures inventions where there is a single attribute in common between that which is claimed and that which occurs in nature, the application of such a threshold test would raise the threshold for patentability for all "biological

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[69] [2014] FCAFC 115 at [161].
[70] [2013] FCA 65 at [114].
[71] AS at [38]-[50].
[72] NRDC at 271; *Sanofi* at [224] (per Crennan and Kiefel JJ) and [309] (per Gageler J).

inventions" in a manner antithetical to the scope of patentability endorsed by this Court in *NRDC* and *Sanofi*.

78. The Full Federal Court recognised this as follows:[73]

> *The isolated DNA can be characterised as material derived from naturally occurring material. This is not excluded from patentability within the reasoning of NRDC. The use of a living organism to produce a substance such as an antibiotic is patentable. It is not a question whether there is any overlap between what occurs in nature and that which is claimed. If so, all biological material would be inherently unpatentable.*

79. Third, the suggestion that such an exclusion was not expressly rejected in *NRDC* does not withstand scrutiny.[74] A close of analysis of the decision in *NRDC* demonstrates that this is exactly what the High Court did.

80. It is important to recall that one of the grounds upon which the Commissioner of Patents rejected the patent considered in *NRDC* was that it was "dependent on the operation of natural laws or the natural properties of the materials involved" and that there was "no process independent of the discovery itself".[75] In rejecting this argument, the High Court explained:[76]

> *... 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 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'.*

81. Importantly, in this context this Court endorsed the words of Frankfurter J in *Funk Bros Seed Co v Kalo Inoculant Co*:[77]

> *It only confuses the issue, however, 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 every patent.*
>
> [emphasis added]

82. The Appellant wrongly suggests that the Court's observations are of no relevance to the question of pateantability in this case as they were made in the

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[73] [2014] FCAFC 115 at [196].

[74] AS at [42].

[75] *NRDC* at 259.

[76] *NRDC* at 264.

[77] *NRDC* at 263-264. *Funk Bros Seed Co v Kalo Inoculant Co*, 333 US 127 (1948) was a US case concerning a patent for inoculants of leguminous plants comprising multiple species of Rhizobia bacteria. The claimed invention was the combination of mutually non-inhibitive strains of certain species of Rhizobia bacteria to give a culture capable of inoculating plants belonging to several leguminous groups.

context of a *Microcell* challenge.[78] The context of the observations is a discussion by the Court of "inventiveness which is essential for the grant of a patent". Indeed it was in this section of *NRDC* that this Court identified that if:[79]

> *the new use that is proposed consists in taking advantage of a hitherto unknown or unsuspected property of the material ... there may be invention ... provided that a practical method of so using it is disclosed and that the process comes within the concept of ... the words 'manner of manufacture'.*

83. The Court in *NRDC* then considered this phrase reaching the conclusion at page 277 cited in paragraph 55 above that the proper analysis is whether there is an artificially created state of affairs.

84. Thus the emphatic rejection by this Court in *NRDC* of a "laws of nature" exception lay at the heart of its analysis and is at the very heart of this appeal. What the Court did in *NRDC* is reject notions such as the laws of nature as guides as to patentability. This is consistent with its rejection of "verbal formulae".

85. Further, and significantly, the Appellant is unable to point to any basis or normative principle for a "product of nature" exclusion whatever that may mean. There is no decision of this Court that provides any such foundation. There is nothing in the history of the development of the *Statute of Monoplies* that supports such a distinction. That history was analysed in some detail by this Court in *NRDC* and by the trial judge.[80]

86. Of course, there can be no doubt that isolated DNA and RNA was not within the contemplation of the legislature in 1623. But that is hardly the end of the matter.

87. Relevantly, prior to 1990, a number of cases in the United Kingdom established that the use of living organisms to produce a substance, such as an antibiotic, could be the subject of a patentable claim.[81] In such cases, according to the High Court in *NRDC*, the microorganism could be considered analogous to a chemical reagent in a chemical process.[82] Their patentability was not rejected as just applying "the laws of nature".

88. The Appellant's reference to cases regarding the definition of "vendible product" do not assist her.[83] *Boulton v Bull* considered the patentability of a method of

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[78] AS at [45]-[46].
[79] *NRDC* at 262.
[80] [2013] FCA 65 at [89]-[103].
[81] See *NRDC* at 279 (citing *Commercial Solvents Corporation v Synthetic Products Co Ltd* (1926) 43 RPC 185, *Adhesives Pty Ltd v Aktieselskabet Dansk Gaerings-Industri* (1935) 55 CLR 523, *Virginia-Carolina Chemical Corporation's Application* (1958) RPC 35 and *Re Joseph Szuecs Application* (1956) 73 RPC 25).
[82] *NRDC* at 279.
[83] AS at [47].

using an old fire engine to lessen the consumption of steam and fuel.[84] The issue before the Court was whether the alleged invention was a method or a principle.

89. The quoted statement from Eyre CJ does not support the exclusion sought.[85] The challenged claims cannot on any level of analysis be said to relate to a "principle". They are a thing, a chemical compound. Indeed, they might be said even on the Appellant's case to constitute a corporeal substance that "embodies" the principle, which for Eyre CJ was sufficient for patentability. Further, according to Buller J "[m]echanical and chemical discoveries all come within the description of manufactures".[86] Heath J also specfically recognised the patentability of "substances (such as medicines) formed by chemical and other processes".[87]

90. Consistent with the dicta in *NRDC*, at least as early as July 1984, it was the practice of the Australian Patent Office to grant patents for "naturally-occurring things" such as "living organisms". In this respect, the Patent Examiner's Manual stated as follows:[88]

> *Applications dealing with products containing living organisms (e.g. vaccines or starter cultures for yoghurt production) or processes which use living organisms to produce useful products (e.g. fermentation processes) clearly are capable of satisfying the requirements of patentability.*

91. Indeed, this view is consistent with the current practice of the Australian Patent Office:[89]

> *A chemical substance or micro-organism which is discovered in nature without any practical application is a "mere chemical curiosity" and not patentable subject matter.*
>
> *More commonly, a specification will provide some practical application for an isolated substance or micro-organism. Although such subject matter is potentially patentable, examiners should consider whether the claims distinguish the micro-organism or substance from those forms which already exist in nature.*
>
> *Thus, a micro-organism, protein, enantiomer or antibiotic discovered in nature can be claimed in its isolated form, or as substantially free of (specified) impurities. Similarly, a gene can be claimed in its recombinant or isolated or purified form (see Ranks Hovis McDougall*

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[84] *Boulton v Bull* (1795) 2 H BL 463; 126 ER 651.

[85] AS at [47].

[86] *Boulton v Bull* (1795) 2 H BL 463 at 487; 126 ER 651 at 663 (per Buller LJ).

[87] *Boulton v Bull* (1795) 2 H BL 463 at 482; 126 ER 651 at 660 (per Heath J).

[88] Australian Patent Office, *Patent Examiner's Manual* (July 1984) at [35.76].

[89] IP Australia, *Patent Manual of Practice and Procedure* at [2.9.2.5], available online at: http://www.ipaustralia.gov.au/pdfs/patentsmanual/WebHelp/Patent_Examiners_Manual.htm (accessed on 23 March 2015); see also, for example, *Kirin-Amgen Inc v Board of Regents of University of Washington* (1995) 33 IPR 557 and *Genentech Inc v Celtrix Pharmaceuticals Inc* (1995) 34 IPR 162.

Ltd's Application (1976) AOJP 3915).

92. The Appellant also points to comments in *NRDC* regarding drawing a distinction between a discovery of a principle of nature or information about a product of nature and the practical application of that discovery.[90] That is apposite here.

93. In any case, the suggestion that claims 1 to 3 "are claims to the same genetic information as occurs in nature" and do not "tell people how [the discovery of the coding sequence of the BRCA1 gene] can be usefully employed"[91] is without foundation. The patentee's "discovery" of the location of the BRCA1 gene and the mutations that result in a predisposition to certain cancers has *not* been claimed. Rather, the patentee claims the *practical application* of that discovery through an isolated nucleic acid which can be used, for example, in diagnostic testing and gene therapy.

94. It is not to the point that the challenged claims do not use the words "utilised".[92] There is no contest that the claimed nucleic acids can be used in a number of applications (the economic utility of which is conceded). The patent specification discloses such applications. On the Appellant's approach, all claims to chemical compounds *per se* would be bad.

95. Consistently with the approach in Article 5.2 of the *EC Directive on the Legal Protection of Biotechnological Inventions*, where "[a]n element isolated from the human body ... including the sequence or partial sequence of a gene, may constitute a patentable invention",[93] the patent specification here discloses such a patentable element and such use as required by Article 5.3 of the Directive.

96. Thus, under Article 5 of the EC Directive, claims 1 to 3 would be patentable in the EU.

AMP v Myriad

97. The Appellant erroneously seeks to rely upon the decision of the US Supreme Court in *AMP v Myriad*, notwithstanding significant differences in the statutory context.

98. As the US Supreme Court itself confirmed in *AMP v Myriad,* 35 USC § 101 contains an important implicit exception as follows: laws of nature, natural phenomena and abstract ideas are not patentable.[94] As discussed above, this Court in *NRDC* eschewed such an exception in Australia.[95]

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[90] AS at [49].
[91] AS at [50].
[92] AS at [49].
[93] AS at [67] but note that AS at [68] misapplies Article 5.3.
[94] *AMP v Myriad* at 2116.
[95] *NRDC* at 263-4.

99. The US Supreme Court held that Myriad's claims in the US were not patentable subject matter because they fall within the "law of nature exception" apparently because they have their origins in nature.[96]

100. The law in the US does not reflect the law in Australia.[97] There is no "laws of nature exception" neither should there now be one implied into the *Patents Act*. The "relevant level of analysis" under Australian jurisprudence is that set out in *NRDC* (and affirmed in *Sanofi*).[98] The relevant question in this case is whether there is an artificially created state of affairs of economic utility. As economic utility is conceded here by the Appellant, the only issue is whether the claimed subject matter is an "artificially created state of affairs".

101. In *Sanofi*, Crennan and Kiefel JJ noted the application of the "laws of nature" exception in *AMP v Myriad* to deny patentability to the claimed nucleic acids "even though such important and useful genes had never before been located, or isolated from surrounding genetic material".[99] This observation was expanded upon by the Full Federal Court:[100]

> *Their Honours did note that in Association for Molecular Pathology v Myriad Genetics, Inc, 596 US 12-398 (2013), the United States Supreme Court had focussed on the genetic information encoded into genes associated with certain cancers, and had held that composition claims to a naturally occurring DNA segment fell within the exception to patentability. However, their Honours added the observation that this conclusion was reached 'even though such important and useful genes had never before been located or isolated from surrounding genetic material'.* ***With respect, that observation draws the important distinction between the newly isolated gene and the information it contains.***
>
> [emphasis added]

102. It is also important to recall that in the US, the question that underpins the analysis is whether the thing claimed is "new 'with markedly different characteristics from any found in nature'".[101] That clearly directs attention to any *similarity* between naturally occurring and isolated nucleic acids. As noted by the Full Federal Court, that is not the question to be answered under the *Patents Act* applying the approach in *NRDC*.[102]

103. In Australia, the approach of this Court in *NRDC* (affirmed in *Sanofi*) emphasises difference, not sameness, in looking to whether there is an artificially created state of affairs. Indeed, this was the approach correctly adopted by the Full

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[96] *AMP v Myriad* at 2117.
[97] *Sanofi* at [264]-[268] (per Crennan and Kiefel JJ); cf. AS at [66].
[98] [2014] FCAFC 115 at [217].
[99] *Sanofi* at [269] (per Crennan and Kiefel JJ).
[100] [2014] FCAFC 115 at [129].
[101] *AMP v Myriad* at 2117, citing *Diamond v Chakrabarty*, 447 US 303 at 310 (1980).
[102] [2014] FCAFC 115 at [215].

Federal Court who noted that, consistent with Australian law, "the analysis should focus on differences in structure and function effected by the intervention of man and not on the similarities".[103]

104. Further, and significantly, the question in the US is not determined by reference to the concept of manner of manufacture according to the *Statute of Monopolies*.

105. Finally, the factual findings made by the US Supreme Court, if they were to be applied in Australia, in fact support the patentability of the claimed subject matter. Indeed, the US Supreme Court accepted that "isolating DNA from the human genome severs chemical bonds and thereby *creates a nonnaturally occurring molecule*" [emphasis added].[104] That is, as the First Respondent submits, an isolated nucleic acid is chemically different from that which occurs in nature – it is an "artificially created state of affairs".

Part VII: Argument on notice of contention/notice of cross-appeal

106. Not applicable.

Part VIII: Estimate of time

107. The First Respondent estimates that approximately 3.5 hours will be required for the presentation of its oral argument.

DATED: 24 March 2015

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[103] [2014] FCAFC 115 at [155].
[104] *AMP v Myriad* at 2118.