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PATENTS ACT 1977

APPLICANT	Population Diagnostics, Inc.
ISSUE	Whether patent applications GB0822081.6 and GB1104294.2 comply with Sections 1(1)(b) and 1(2)
HEARING OFFICER	Mrs S E Chalmers

DECISION

Introduction

1 International patent application PCT/US2007/068183 entitled "Evaluating Genetic Disorders" was filed on 03 May 2007 in the name of POPULATION DIAGNOSTICS, INC. and claimed priority from applications US60746359, US60746482, and US11421348, dated 3 May 2006, 4 May 2006, and 31 May 2006, respectively. The international application was published by WIPO as WO2007/131135 on 15 November 2007, entered the UK national phase as GB0822081.6, and was re-published as GB2452437 on 4 March 2009. Divisional application GB1104294.2 was lodged on 14 March 2011 claiming the same priority and filing dates as the aforementioned parent application GB0822081.6 and was published as GB2476007 on 8 June 2011.

2 Despite amendment of the claims, the examiner maintained his objections that the claimed inventions in both GB0822081.6 and GB1104294.2 lack an inventive step and are excluded from patentability under Section 1(2) of the Patents Act 1977 on the grounds that the claims relate to a method of performing a mental act. The applicant disagreed and requested an oral hearing in their letter dated 14 October 2011. This hearing was held before me on 21 December 2011. The applicant was represented by Dr Jon Broughton of Avidity IP, with Dr Eli Hatchwell, one of the inventors, also attending. Dr Philip Mountjoy was in attendance as hearing assistant together with the examiner Dr Jeremy Kaye.

3 Before the hearing, the examiner issued a pre-hearing report dated 28 October 2011 summarising the issues to be addressed. In response to this report, Dr Broughton filed submissions dated 8 November 2011 commenting on the

judgment in *Halliburton's Applications* ([2011] EWHC 2508 (Pat)[1] and requesting my views on the examiner's objections under Section 1(2). In my subsequent letter I explained that my preliminary view was that there was no non-mental limitation of the nature suggested in the decision in *Halliburton's Applications* in either of the main claims of applications GB0822081.6 or GB1104294.2, and that on the face of it the methods claimed could be performed mentally. I also noted that, even if the claims did not fall foul of the mental act exclusion, it did not mean that they were necessarily immune from the computer program exclusion. I therefore invited the applicant to address me on the patentability issue.

The applications

4 Copy number variants (CNVs) are modifications of a genome which result in cells having an abnormal number of copies of a particular region of the genome. Such variations can lead to modifications of gene expression in the cell. It is known in the prior art that CNVs can occur in normal (i.e. healthy) individuals and that certain CNVs are also associated with various diseases/phenotypes.

5 The applications relate to a method of identifying a relevant copy number variant (CNV) for a particular phenotype by identifying CNVs in human (GB0822081.6) or non-human (GB1104294.2) subjects with the phenotype using a high resolution method capable of achieving a resolution of 30kb to 50kb, and comparing these variants to the CNVs from genome screens of a population of at least 1000 individuals without the phenotype, thereby eliminating normal polymorphic CNVs and identifying CNVs which are relevant to a particular phenotype.

The claims

6 The latest sets of claims for each of the applications are dated 14 October 2011. Each application has one independent claim (claim 1), which for GB0822081.6 reads:

A method of identifying a relevant copy number variant for a phenotype comprising:

a) Identifying a set of copy number variants in a genome wide screen of a human subject with said phenotype, using a method capable of achieving a resolution of 30kb to 50kb;

b) Providing genome wide copy number variant frequency data from a population of at least 1000 human individuals without said phenotype obtained using a consistent method capable of achieving a resolution of 30kb to 50kb and comparing said set of copy number variants of step (a) to that data; and

[1] Halliburton's Applications ([2011] EWHC 2508 (Pat)

c) Determining a copy number variant which is present in said subject but not present in said genome wide copy number variant frequency data as being relevant to the phenotype.

7 Claim 1 of application GB1104294.2 is very similar to the above claim, with the exception that the method is limited to identifying a relevant copy number variant for a phenotype in a non-human subject, with steps a) and b) also therefore referring to non-human rather than human subjects.

8 Given the similarity between the claims of the two applications, I will primarily direct my discussion of inventive step and patentability to the parent application GB0822081.6 in the first instance. However, I also consider my comments to be equally relevant to the divisional application GB1104294.2.

Inventive step

The law

9 The examiner has raised an objection under Section 1(1)(b) of the Patents Act 1977 that the invention does not involve an inventive step. The relevant parts of Section 1 read as follows:

1(1). A patent may be granted only for an invention in respect of which the following conditions are satisfied, that is to say:

(a) …;

(b) It involves an inventive step;

(c) …;

(d) ….

10 Section 3 of the Act, entitled Inventive Step reads:

3. An invention shall be taken to involve an inventive step if it is not obvious to a person skilled in the art, having regard to any matter which forms part of the state of the art by virtue only of Section 2(2) above (and disregarding Section 2(3) above).

11 The Office's approach to assessing inventive step is the structured approach found in *Windsurfing International Inc. v Tabur Marine (Great Britain) Ltd* ("Windsurfing")[2] as modified by Jacob LJ in *Pozzoli SPA v BDMO SA* ("Pozzoli")[3]. The modified approach involves the following steps:

(1) (a) Identify the notional "person skilled in the art";
(b) Identify the relevant common general knowledge of that person;
(2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;

[2] *Windsurfing International Inc. v Tabur Marine (Great Britain) Ltd*, [1985] RPC 59 ("Windsurfing")
[3] *Pozzoli SPA v BDMO SA* [2007] EWCA Civ 588 ("Pozzoli")

(3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
(4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

Analysis

12 I will consider each step of the *Windsurfing/ Pozzoli* approach in turn:

(1) (a) Identify the notional "person skilled in the art"

13 The examiner identified the "person skilled in the art" as a team comprising molecular biologists and cytogeneticists. The applicant has not disputed this and I agree that this is an accurate assessment of the person skilled in the art.

(1) (b) Identify the relevant common general knowledge of that person

14 The examiner asserted that the common general knowledge of this skilled team would include: the fact that DNA copy number will modify gene expression and function; that copy number variation is found among the normal population and that variation may also be associated with various diseases/phenotypes; molecular biological techniques such as the polymerase chain reaction (PCR) and array comparative genomic hybridization (aCGH) and basic statistical methods to enable assessment of the significance of results. The applicant has not disputed this view and I am content that this is an accurate assessment of the common general knowledge of the skilled team.

(2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it

15 The inventive concept identified by the examiner is a method for identifying a copy number variant (CNV) that is relevant for a phenotype by identifying CNVs in a subject (either human in GB0822081.6 or non-human in GB1104294.2) using a method capable of achieving a resolution of 30kb to 50kb and comparing these variants to the results of copy number variation in a "normal" population of at least 1000 individuals without the phenotype.

16 The applicant disagrees with the examiner's assessment of the inventive concept. The inventive concept of the claimed invention identified by the applicant and summarised by Dr Broughton at the hearing is the use of a reference set of at least 1000 individuals without a phenotype in order to eliminate all normal polymorphic CNVs from a set of CNVs obtained in a high resolution genome wide screen from an individual in order to identify a CNV associated with a phenotype in that individual i.e. you can use a reference set which is large enough to exclude polymorphic CNVs, and that reference set is 1000 individuals.

17 As referenced by Dr Broughton at the hearing, in *Generics (UK) Limited and others v H Lundbeck*[4] the inventive concept was summarised as relating to the "core (or kernel, or essence) of the invention – the idea or principle...which entitles the inventor's achievement to be called inventive".

18 In my opinion the "core" of the present invention is the use of a reference set of CNVs from a population of 1000 individuals without a particular phenotype in order to eliminate 'normal' CNVs identified as being present in a high resolution screen in an individual with a particular phenotype through a comparison of the two sets of data, thereby identifying a CNV in the individual which is relevant to the particular phenotype.

(3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed

19 The examiner has cited three documents:

D1 Ann. Rev. Genomics Hum. Genet., Vol.6, 2005, Pinkel, D. et al., "Comparative genomic hybridization", pp.331-354.
D2 Hum. Mol. Genet., Vol.15, 2006, Wilson, G. M. et al., "DNA copy-number analysis...", pp.743-749.
D3 Hum. Mol. Genet., Vol.14, 2005, Vissers, L. E. L. M., et al., "Identification of disease genes...", pp.R215-R223.

20 The examiner identified the differences between the cited prior art and the presently claimed invention as being that the present method uses a technique capable of achieving a resolution of 30kb to 50kb whereas the prior art methods describe resolutions of ~1 Mb (documents D1 and D2) or 100kb – 1Mb (document D3) and that the number of "normal" subjects without the phenotype is at least 1000 compared to 35 in document D2 and a "reference pool" in document D3.

21 Dr Broughton did not appear to dispute these differences between the cited prior art and the claimed invention. However, he emphasised that D1 did not identify that it was possible to use a reference set to eliminate polymorphic CNVs, but instead merely identified that there is a problem with polymorphic CNVs being present. He did, however, accept that the document suggested using high resolution screens. Similarly, he asserted that D3 merely identified that there is a problem with polymorphic CNVs being present and that these CNVs need to be excluded. He noted that D3 also fails to disclose the use of high resolution genome screens, but agreed that D3 proposed methods which compare measured variations to parental samples or independent normal controls. He also explained that D2 utilised a small reference set to eliminate some more common CNVs which were not related to brain (the tissue being investigated) but failed to disclose that a larger reference set could be used to eliminate all polymorphic CNVs.

[4] *Generics (UK) Limited and others v H Lundbeck A/S UKHL* 12, [2009], RPC 13

(4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

22 Much of the argument presented by Dr Broughton at the hearing centred on the issue of whether or not the prior art disclosed or suggested a solution to the problem of eliminating polymorphic CNVs present in the normal population from genomic screens in order to identify the particular CNV associated with a particular phenotype in an individual, or to identify what he called the "needle in the haystack".

23 Dr Broughton accepted that the skilled person was aware of high resolution screening methods from the prior art and of the fact that such high resolution screens may identify more CNVs than lower resolution screens (as indicated in D1, page 343). He also accepted that they would know that polymorphic CNVs present in the normal population would complicate the analysis of results from high resolution DNA screening methods. In addition, he agreed that the prior art disclosed methods which could be used to eliminate some common CNVs (e.g. by comparing results to the parental genome or to normal controls in D3, or by using a "small" population of controls as in D2).

24 However, he argued that the skilled person had no knowledge of the number of CNVs present in the normal population. Consequently, in his opinion they would not conclude that a reference set could be used to eliminate normal polymorphic CNVs, or have any idea how big such a reference set would need to be. He also emphasised that, contrary to the examiner's suggestion, the inventors had not merely increased the number of controls to increase statistical significance. Given these facts, Dr Broughton asserted that there would be no motivation for the skilled person to derive a method as claimed in the present application, and that it would not be obvious to try as the skilled person would not know that they could succeed.

25 In considering these arguments I observe that the description of the present application as filed identifies the lowest number of individuals to be used as the normal population in the comparison step of the claimed method as being 100 individuals, an order of magnitude lower than the number of individuals specified in the claim. This figure of 100 individuals is only around three times as many as the number of individuals used in the control experiments in the prior art (e.g. see document D2). The description also fails to include any specific examples which demonstrate the use of the claimed 1000 individuals in the reference population used in the comparison step.

26 At the hearing, Dr Broughton conceded that the high resolution screen in itself was not inventive (the only mention of the resolution of 30kb to 50kb in the specification as filed is in paragraph [0082]). He also suggested – if I understood him correctly – that selecting this level of resolution leads to the problem that the present invention is proposed to solve i.e. you will identify many more CNVs at this resolution, and thus you are left with the issue of finding the "needle in a haystack".

27 Given that the resolution of the genome wide screen presently claimed is not in itself inventive, the question which I must therefore answer is whether the use of the control population of 1000 individuals without the phenotype to eliminate "normal" CNVs in order to identify a CNV which is relevant to the particular phenotype is inventive.

28 It is clear from the discussion above that it was well known in the prior art that polymorphic CNVs were present in the normal population, and that the presence of such polymorphic CNVs could complicate the analysis of CNVs which were relevant to a particular phenotype. The fact that high resolution screens would result in more CNVs being identified was also known, and at least some effort had been made in the prior art to eliminate some normal/common CNVs in screening experiments directed towards identifying CNVs which could cause a disease phenotype (e.g. as disclosed in documents D2 and D3).

29 In light of this knowledge from the prior art, I believe that the skilled person would have ample motivation to try increasing the number of individuals in the normal control population when using higher resolution screening methods. In my opinion, it would be obvious to them that this would filter out more of the polymorphic CNVs associated with the normal population and help them to identify CNVs which are relevant to a particular phenotype in an individual.

30 In my view, the reference in the claim to using data from 1000 individuals in the comparison step does not add an inventive step to the claimed method. Although the prior art does not specifically suggest using control populations containing this number of individuals (e.g. D2 refers to the use of a control population of 35 individuals to exclude common CNVs), as I have explained above, I believe the skilled person would be motivated to try increasing the number of individuals in the normal control population. In this regard, I note that the lower limit for the control population was specified as 100 individuals in the description of the present application as originally filed (i.e. a full order of magnitude lower than the limit now claimed). I also note the lack of any specific examples which demonstrate the use of the claimed 1000 individuals in the reference population used in the comparison step of the method. The claimed population of 1000 individuals has not therefore been shown to be any more advantageous than the other reference population sizes specified in the description.

31 I therefore conclude that the invention of claim 1 of application GB0822081.6 lacks an inventive step in light of the cited prior art documents. Furthermore, in my opinion dependent claims 2-18 of the application do not add any inventive features to the method of claim 1. For similar reasons, I also find that the invention of claims 1-19 of application GB1104294.2 lacks an inventive step.

Patentability

The law

32 The examiner also raised an objection under Section 1(2) of the Patents Act 1977 that the invention is excluded from patentability. The relevant parts of Section 1(2) read as follows:

It is hereby declared that the following (among other things) are not inventions for the purposes of this Act, that is to say, anything which consists of –

(a) ...;
(b) ...;
(c) a scheme, rule or method for performing a mental act, playing a game or doing business, or a program for a computer;
(d) ...;
but the foregoing provision shall prevent anything from being treated as an invention for the purposes of this Act only to the extent that a patent or application for a patent relates to that thing as such.

33 It is not disputed that the assessment of patentability under Section 1(2) is governed by the judgement of the Court of Appeal in *Aerotel/Macrossan*[5]. In this case the court reviewed the case law on the interpretation of Section 1(2) and approved the following four-step test for the assessment of patentability:

1) *Properly construe the claim;*
2) Identify the actual contribution;
3) Ask whether it falls solely within the excluded matter;
4) Check whether the actual or alleged contribution is actually technical in nature.

34 In *Symbian*[6] the Court of Appeal confirmed that the above test is intended to be equivalent to the technical contribution approach specified in its previous decisions. I will consider each step of the *Aerotel/Macrossan* approach in turn:

1) Properly construe the claim

35 The claims present no difficulties in construction. Claim 1 relates to a method for identifying a CNV for a phenotype by identifying copy number variants in a human (GB 0822081.6) or non-human (GB 1104294.2) subject with a particular phenotype using a method capable of achieving a resolution of 30 kb to 50kb, and comparing these variants to the results of copy number variation in a population of at least 1000 individuals without the phenotype.

2) Identify the actual contribution

36 In *Aerotel/Macrossan* Jacob LJ stated that the question to be answered in this step is "What has the inventor really added to human knowledge?". The examiner identified the actual contribution as being the comparison step which compares test data to control data since the methods used to obtain the copy number data are entirely standard.

[5] *Aerotel/Macrossan (Aerotel Ltd v Telco Holdings & Ors Rev* 1 [2007] RPC 7)
[6] *Symbian Ltd's Application* [2008] EWCA Civ 1066, [2009] RPC 1

37 The applicant disagreed with the examiner's assessment. At the hearing Dr Broughton identified the actual contribution as being the provision of a reference set that is adequate to eliminate polymorphic CNVs from a set of CNVs identified in an individual in a high resolution screen such that the "needle in the haystack" single CNV of interest can be isolated from the large number of irrelevant polymorphs, enabling the use of such high resolution techniques for that endeavour (to identify CNVs associated with the phenotype). In the applicant's opinion, the actual contribution was technical.

38 I am not convinced that the step of actually identifying CNVs in an individual with a particular phenotype using high resolution screening methods is the contribution in the sense that this is what has been added to the stock of human knowledge. As I have indicated above, the use of high resolution screening methods had already been suggested in the prior art. In my opinion, the substance of the claimed method, and what has actually been added to the stock of human knowledge, is the comparison step involving the use of the reference set comprising data from a normal population of at least 1000 individuals without a particular phenotype to eliminate normal polymorphic CNVs from a set of CNVs identified in an individual with a phenotype, such that a CNV associated with the particular phenotype can be identified.

3) and 4) Ask whether it falls solely within the excluded matter and check whether it is technical

39 Referring to the decision in *Halliburton's Applications* ([2011] EWHC 2508 (Pat), Dr Broughton argued that the mental act exclusion should be applied narrowly such that it applies in situations where a claimed method can be performed only by purely mental means. In his opinion, the method of claim 1 is not performed by purely mental means due to presence of step a) of the claim, which involves identifying a set of copy number variants in a genome wide screen of a human subject with a phenotype.

40 Whilst I acknowledge that the mental act exclusion is to be applied narrowly following the *Halliburton* decision, I note that the exclusion must be applied to the actual contribution of a claimed invention (see paragraphs 67 and 70 of *Halliburton*, for example). Given my interpretation of the actual contribution, I am not convinced that step a) of claim 1 takes the claimed method outside of the mental act exclusion. Furthermore, dependent claim 2 of the application specifies that the comparison step b) is computer implemented, thereby suggesting that the actual contribution which I have identified for the method of claim 1 could indeed be performed mentally. I do note, however, that in light of the decision in *Halliburton's Applications,* the mental act exclusion for claim 1 could be overcome by specifying that step b) is computer implemented as in claim 2 of the parent application, and this would be consistent with the teaching of the application. Similarly, in GB 1104294.2, the incorporation of claim 6 would overcome the mental act objection.

41 Dr Broughton went on to argue that the claimed method did not fall foul of the computer program exclusion. Referring to paragraph 22 of *Aerotel/Macrossan,* he reminded me of the warning that just because a computer was used in an invention, it did not mean that the method was excluded as a computer

program as such. He also asserted that the actual contribution identified by the applicant was technical but did not elaborate.

42 Looking for example at paragraphs [201] to [207] and Figure 4 of GB0822081.6, there is no doubt that the Knowledge Management Tools used to carry out the comparison step involve the use of a computer program to analyse the data. Whilst I agree that the invention is technical in the broadest sense in that it involves a computer, the enquiry is whether the contribution relates solely to excluded matter and whether it is technical or not. On this occasion however, I am clear that the contribution made by the invention does relate to excluded matter as such and does not have a relevant technical effect.

43 I have found that the contribution lies wholly in excluded fields and that there is no technical contribution. The invention claimed in application GB0822081.6 is therefore excluded from patentability under Section 1(2)(c) as a method for performing a mental act and as a computer program as such. For the same reasons, the invention claimed in application GB1104294.2 is also excluded from patentability under Section 1(2)(c).

Conclusion

44 I find that the inventions claimed in applications GB0822081.6 and GB1104294.2 lack an inventive step and are excluded from patentability because they relate to a method for performing a mental act and to a program for a computer as such. After considering the specification of these applications as a whole, I have not been able to identify any amendment to the claims which could overcome the inventive step or patentability objections outlined above.

45 The extended compliance period for putting the application in order expired on 14 October 2011. As the applications were not in order at that date and there are no saving amendments, the applications are refused under Section 18(3) for failing to meet the requirements of inventive step under Section 1(1)(b) and patentability under Section 1(2)(c) of the Patents Act 1977.

Appeal

46 Under the Practice Direction to Part 52 of the Civil Procedure Rules, any appeal must be lodged within 28 days.

Mrs S E Chalmers
Deputy Director acting for the Comptroller