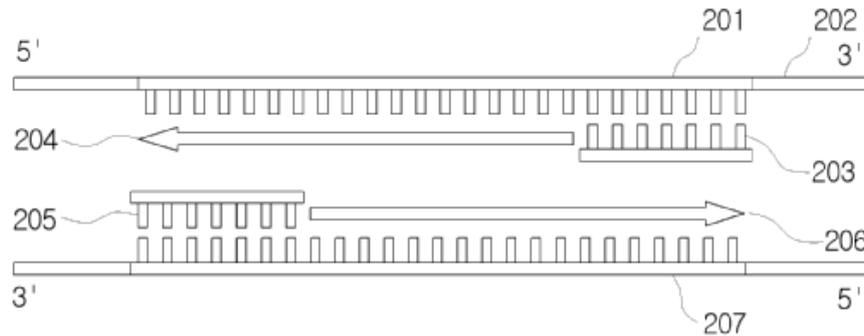




FIG. 1



- 4 Typically primers are used in polymerase chain reaction (PCR) experiments, which provide a method of rapidly amplifying a target DNA region, creating multiple copies of it over the course of multiple cycles of DNA synthesis. As the length of a DNA strand is potentially long (up to 3 billion individual bases in the human genome), and a primer is relatively short (approximately 20 bases or less), there is the potential for a primer to be non-specific to a target region, amplifying the wrong region of DNA. While most primer design programs take this into account and attempt to exclude degenerate or off-target primers, the methods used may not be entirely comprehensive in terms of identifying these off-target primers, or may take too much time to operate on large-scale data.
- 5 There are additional criteria that are required for primer design to be successful, which are again frequently incorporated into primer design methods. Such criteria generally relate to properties such as melting temperature (the temperature required to dissociate the primer from the DNA strand) or to potential issues such as self-complementarity, which will interfere with the primer successfully binding to the target strand.
- 6 What is described in the application is a method of identifying primer pairs within large-scale sequence data, subject to specific input criteria. As the method is implemented in a single program, it allows both the initial primer generation and off-target estimation, and the additional criteria, to be tested and incorporated into the designed primers at the same time such that the primer set generated includes all the limitations normally designed at separate steps. Additionally, the method can be performed efficiently over a large amount of sequence data, such that it can identify all potential primer pairs for that dataset.
- 7 The application has a single independent method claim 1. This claim, as filed, is set out below:
  1. A method for designing all coverage of valid primers which satisfies the conditions for specificity to large-scale DNA sequences in a large-scale DNA sequence database, comprising:

receiving a given DNA sequence database to extract partial sequences for candidate primers having all possible lengths between the minimum length and the maximum length (operation 1);

excluding the primers which do not satisfy input single filtering conditions when the candidate primers extracted in operation 1 are subjected to the single filtering conditions (operation 2);

pair-joining Map1, which includes all the possible partial sequences obtained in operation 1, and Map2, which includes candidate primer sets satisfying the single filtering conditions obtained in operation 2, and removing the primers for Map2 when the primers for Map1 and Map2 have the same sequences other than the 5' termini thereof (operation 3);

pair-joining Map1, which includes all the possible partial sequences obtained in operation 1, and Map2, which includes candidate primer sets satisfying the single filtering conditions and 5' cross-hybridization filtering conditions obtained in operation 3, and removing the primers for Map2 when the primers for Map1 the same sequences as the primers for Map2 except the sequences having a given mismatch number (#mismatch) (operation 4);

removing false-positive primers which still remain from the results of operation 4 and do not satisfy general cross-hybridization filtering conditions (operation 5);

dividing the primers remaining from the results of operation 5 into forward primer sets and reverse primer sets and excluding the primers which do not satisfy the filtering conditions for self-join calculation when the divided forward and reverse primer sets are subjected to the filtering conditions (operation 6); and

calculating penalty scores for the primer pairs passing operation 6, and sorting the primer pairs in the same sidset group according to the calculated penalty scores (operation 7).

## **The law**

- 8 Section 1(2) lists certain categories of subject-matter which are not considered to be inventions. These categories of subject-matter are conventionally known as excluded subject-matter:

*1(2). 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) a discovery, scientific theory or mathematical method;*
- (b) a literary, dramatic, musical or artistic work or any other aesthetic creation whatsoever;*
- (c) a scheme, rule or method for performing a mental act, playing a game or doing business, or a program for a computer;*
- (d) the presentation of information;*

*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.*

9 The Court of Appeal in *Symbian*<sup>1</sup> stated that the question of whether a computer-implemented invention is patentable has to be resolved by answering the question whether it reveals a technical contribution to the state of the art. It proceeded to answer the question with the aid of the four-step test set out in its earlier judgment in *Aerotel*<sup>2</sup>, namely:

- (1) construe the claim;
- (2) identify the actual (or alleged) contribution;
- (3) ask whether it falls solely within the excluded subject matter;
- (4) check whether the actual or alleged contribution is actually technical in nature.

10 The fourth step of the test is to check whether the contribution is technical in nature. In paragraph 46 of *Aerotel* it is stated that applying this fourth step may not be necessary because the third step should have covered the question. This is because a contribution which consists solely of excluded matter will not count as being a "technical contribution" and thus will not, as the fourth step puts it, be "technical in nature". Similarly, a contribution which consists of more than excluded matter will be a "technical contribution" and so will be "technical in nature". In the present case, which concerns a computer-implemented invention, I shall consider whether the contribution is excluded alongside the question of whether the contribution is technical in nature, i.e. I will consider the third and fourth steps of *Aerotel* together.

### Argument & analysis

11 While there may be some minor clarity issues, I do not consider there to be any difficulty in construing the various features of the claim. As set out by the examiner in his examination report dated 24 July 2017, and reproduced by the applicant in their letter dated 2 April 2019, the method of claim 1 can be summarised as:

- i) extracting from the sequence data all partial sequences between a specified minimum and maximum length, giving a set of candidate primers. The output of this step is or forms the basis of Map1.
- ii) excluding candidate primers which do not satisfy the 'input single filtering conditions'. The output of this step is or forms the basis of Map2.
- iii) pair-joining Map1 and Map2, which appears to involve examining every possible pairing of sequences from Map1 and Map2, and in a given pair excluding sequences from Map2 which have the same sequence as that from Map1, apart from at the 5' terminal region.
- iv) pair-joining Map1 and the Map2 obtained from step iii, and in any given pair excluding the Map2 sequence which does not fulfil a mismatch criterion.
- v) removing false positives from step iv which do not otherwise fulfil general cross-hybridisation filtering conditions.
- vi) dividing these results into forward and reverse sets, and excluding primers which do not fulfil self-join filtering conditions. This step appears to identify suitable forward/reverse primer pairs that will amplify a region of suitable

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<sup>1</sup> *Symbian Ltd. v Comptroller-General of Patents* [2008] EWCA Civ 1066

<sup>2</sup> *Aerotel Ltd v Telco Holdings Ltd and Macrossan's Application* [2006] EWCA Civ 1371

length for a PCR experiment, and which both have otherwise similar properties.

vii) calculating penalty scores for each pair, and sorting based on this score.

- 12 In his letter dated 19 February 2019, the examiner considers the contribution to reside “in the provision of the parallelised algorithm that allows the implementation of the primer search and filtering on a computer cluster”. The applicant does not appear to dispute this assessment. I am also content to proceed to the third and fourth steps of *Aerotel* on the basis of this contribution.
- 13 The applicant’s main argument is that the method of claim 1 provides a technical contribution for the same or similar reasons to those on the basis of which the invention in *Halliburton*<sup>3</sup> was found to provide a technical contribution. In *Halliburton*, a method of designing a drill bit was not considered to relate to excluded matter. In his letter dated 19 February 2019, the examiner acknowledged that “primer design can be a technical task”. However the examiner concluded that the particular method of claim 1 does not provide a technical contribution - as the end product of the method is a database of all potential pairs for a given series of sequence data, which is an abstract and extensive list of all possible primer pairs (e.g. a list of possible primer pairs in the tens of millions for a genome) which is not a narrow result or set of results as per *Halliburton*. The examiner also notes that there is no basis in the application for a more specific method, such as the use of a particular subset of primers obtained for a qPCR (quantitative polymerase chain reaction) experiment.
- 14 The applicant suggests that the invention in *Halliburton* is not limited to producing a “narrow result or set of results”. In particular, the result of the drill bit design method of *Halliburton* was “at least one drill bit design parameter” which cannot be said to be a “narrow result or set of results”. Furthermore, characteristics of the drill not determined by this parameter(s) would need to be determined by subsequent steps of the design process. Therefore, the applicant argues, because no unique primer is defined by the method of the present invention, and subsequent steps may be required to select a particular primer do not provide distinctions over *Halliburton*.
- 15 The applicant also notes that, while the present invention is not connected to any specific downstream use of a primer, such a requirement is not necessary in light of the drill bit design method of *Halliburton* – which did not need to be ‘tethered’ to a particular manufacturing step in order to be patentable. Furthermore, just as designing drill bits is a technical task irrespective of the effectiveness of the design, designing primers is a technical task whether or not the end result is a ‘better’ primer.
- 16 In determining whether or not the method of the present application is excluded as a computer program as such, the applicant considers paragraphs 38, 70 & 71 of *Halliburton* to be instructive:

*38. What if the task performed by the program represents something specific and external to the computer and does not fall within one of the excluded areas? Although it is clear that that is not the end of the enquiry, in my judgment that circumstance is likely to indicate that the invention is patentable. Put in other language, when the task carried out by the computer program is not itself something within the excluded categories then it is likely*

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<sup>3</sup> *Halliburton Energy Services Inc's Patent Application* [2012] RPC 12

*that the technical contribution has been revealed and thus the invention is patentable. I emphasise the word "likely" rather than "necessarily" because there are no doubt cases in which the task carried out is not within the excluded areas but nevertheless there is no technical contribution at all.*

...

*70. Approached on the correct, narrow basis, the mental act exclusion is irrelevant in this case. The claimed method cannot be performed by purely mental means and that is the end of the matter. Put another way, the contribution is a computer implemented method and as such cannot fall within the mental act exclusion.*

*71. That does not mean it is necessarily immune from the computer program exclusion but that is a different matter. Is it more than a computer program as such? The answer is plainly yes. It is a method of designing a drill bit. Such methods are not excluded from patentability by Art 52/s1(2) and the contribution does not fall solely within the excluded territory. Drill bit design is not a business method, nor a scheme for playing a game nor (as I have held) is this claim a scheme for performing a mental act.*

- 17 The applicant thus concludes that designing primers is clearly a technical task and using a computer to do so does not make it any less so.
- 18 I would agree that a method of designing valid primers does not require a connection to a downstream experiment in order to be technical. This is clear from the reasoning in *Halliburton*. What matters is whether the task itself being performed by the design method or program is technical. Looking at the method of the invention, what it achieves as a matter of practical reality is the filtering of sequences and primers to provide a database which covers all valid primer pairs. Such a task is characterised by processing sequence data to provide a reduced, but still large, dataset of sequences for primer pairs. I do not consider this to represent something specific and external to the computer, as discussed in paragraph 38 of the *Halliburton*. While I note that the applicant states in their letter dated 22 September 2017 that filtering is precisely the type of process which may be used as part of a design process, in contrast to *Halliburton* - which determined particular features of cutting elements for a roller cone drill bit - the present method determines a database of possible primer pairs, which is extensive in nature and does not provide what could reasonably be defined as a design for a particular technical artefact. Thus, I do not consider the task performed by claim 1 to be technical in nature.
- 19 Both the examiner and applicant have referred to the 'AT&T signposts' that Lewison J considered to be helpful when considering whether a computer program makes a technical contribution. He reconsidered the signposts in *HTC/Apple*<sup>4</sup> in light of the decision in *Gemstar*<sup>4</sup>. The signposts are:
- i) whether the claimed technical effect has a technical effect on a process which is carried on outside the computer;

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<sup>4</sup> Gemstar-TV Guide International Inc v Virgin Media Ltd [2010] RPC 10

ii) whether the claimed technical effect operates at the level of the architecture of the computer; that is to say whether the effect is produced irrespective of the data being processed or the applications being run;

iii) whether the claimed technical effect results in the computer being made to operate in a new way;

iv) whether the program makes the computer a better computer in the sense of running more efficiently and effectively as a computer;

v) whether the perceived problem is overcome by the claimed invention as opposed to merely being circumvented;

20 Looking at the first signpost, the method clearly does not have a direct effect outside the computer on which it is run. Nevertheless, the applicant considers that the first signpost accommodates more than this – such as found in *Halliburton* – where processes run on a computer are part of a broader technical process which it ultimately affects. However, as discussed above the task performed by the computer is not specific and external to the computer, such that the contribution does not extend beyond processing data to provide all valid primers for a DNA sequence database.

21 Furthermore, the contribution made by the invention is not in making the computer operate in a new or more reliable way and does produce a technical effect at the level of the computer's architecture. Nor does the contribution allow the computer to work faster or solve any technical problem. In my view, the contribution made by the invention lies in a computer program.

### **Conclusion**

22 I find that the claimed invention is excluded under section 1(2) because it relates to a computer program as such. I have read the specification carefully and I can see nothing that could be reasonably expected to form the basis of a valid claim. I therefore refuse the application under section 18(3).

### **Appeal**

23 Any appeal must be lodged within 28 days after the date of this decision.

**H JONES**

Deputy Director, acting for the Comptroller