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PATENTS ACT 1977

APPLICANT MOHAMED MOHAMED ADEL EL-SOKKARY

ISSUE Whether patent application GB0901645.2 complies with section 1(1)(b) and section 1(2)(d) of the Patents Act 1977

HEARING OFFICER Dr L Cullen

DECISION

Introduction

1 International patent application PCT/EG2007/000028 entitled "*Establishment of a new phylogenetic system for identification of bacteria by dihydropteroate synthase gene (DHPS)*" was filed on 28 August 2007 in the name of MOHAMED MOHAMED ADEL EL-SOKKARY and claimed priority from an earlier Egyptian application, EG 2006090485 which was filed on 10 September 2006. The international application, which was published by WIPO as WO 2008/028496 on 13 March 2008 (with amended claims filed under the PCT and received by the International Bureau on 23 December 2007), entered the UK national phase as GB 0901645.2 and was re-published as GB 2455013 on 3 June 2009.

2 Following entry into the UK National Phase, the first examination report issued by the Intellectual Property Office (hereafter "the Office"), dated 2 August 2010, raised clarity and inventive step objections. I note that the inventive step objection raised in this report is essentially the same as that raised during the International Phase in a Written Opinion of the International Searching Authority (ISA) dated 22 October 2007. In this written opinion, the ISA examiner explained that although they considered the claims to define a novel invention having industrial application; this invention was not inventive, i.e. it was obvious, in the light of the disclosure in the journal article entitled "*Genetic Divergence of the Dihydrofolate Reductase and Dihydropteroate Synthase Genes in* Pneumocystis carinii *from 7 Different Host Species*", Liang Ma, Hiromi Imamichi, Antti Sukura and Joseph A Kovacs, Journal of Infectious Diseases, 2001, Vol 184, pp 1358-1362, hereafter referred to as MA et al.

3 The applicant is handling the patent application process himself. Following a further three rounds of correspondence between the examiner and the

applicant, the examiner maintained the inventive step and clarity objections (see further examination reports, dated 26 October 2010, 9 February 2011 and 20 May 2011). The examiner also considered that the amendments filed with the applicants letter dated 22 December 2010, altered the scope of the claims such that a further objection to the patentability of the claimed invention under s.1(2)(d) was raised and maintained in the examination reports dated 9 February 2011 and 20 May 2011.

4 The applicant requested an oral hearing before a Hearing Officer in their letter of 15 June 2011. An official letter dated 2 August 2011 was issued by the examiner summarising the issues to be considered at the hearing which was held by telephone on 15 August 2011. Present in the Hearing Room at the Office were myself, my assistant, Dr Graham Feeney, and a number of observers. The applicant was assisted by a colleague Professor Mohamed Adel El-Sokkary.

Technical Background

5 This patent application lies in the field of microbiology, molecular biology and bioinformatics and concerns the use of nucleic acid sequence alignments to obtain a phylogenetic tree that can be used for the classification, identification and detection of microbial species. Before I discuss the application in detail, I consider that it is necessary to provide some further explanation of the technical background.

6 A Phylogenetic tree is a diagram that is constructed to show the evolutionary relationships among different living things based upon similarities or differences in their physical and/or genetic characteristics[1]. Hence the use of the term, tree, to describe the whole diagram and, branches, to show the relationship between different parts of the tree. Such a tree is based on the premise that the more similar one organism is to another, the more closely related it is in terms of evolutionary progression and, as a consequence, the more closely located to each other, the two organisms will be in the phylogenetic tree. Such a phylogenetic tree may be constructed based on the measurement of, or the implied relationship between, physical traits or genetic sequences such that similar living organisms would share a common 'sub-branch' in the tree. For example, in a tree showing the relationship between living organisms, mice and cats would both appear on the mammal branch of such a tree, whilst fish would not, but all three would appear on the same 'parent' branch as other animals, whilst plants would appear on a separate branch. The evolutionary relationship between living organisms can be determined by a statistical analysis of sequence data, either nucleic acid or amino acid sequences, originating from a gene having an analogous function in these different living organisms. The results of this statistical analysis can be used to align the relationship between the organisms.. Based on the statistical scores, similar genetic sequences are grouped more closely together in the phylogenetic tree than more divergent sequences. As a result, a phylogenetic tree is a diagrammatic way to present,

[1] For a definition or explanation, see for example, the entry on Wikipedia at http://en.wikipedia.org/wiki/Phylogenetic_tree

and aid understanding, of the evolutionary interrelationships between living organisms.

7 Phylogenetic analyses obtained from multiple sequence alignments are useful to biologists to measure the evolution of an individual gene as it appears in different species through the course of evolution, and as, already indicated above, the results from such analysis is usually best illustrated as a phylogenetic tree. Such analysis and the tree derived from it can be used to demonstrate species evolution in terms of genetic changes. More pertinent to the present application, the alignment of a genetic sequence from an unidentified organism (e.g., a bacterial sample obtained from a swab of an infected wound) to a series of already known sequences may be used to identify that unknown organism. A very close statistical match in the sequence database may identify the organism, whilst more distant matches might reveal the closest evolutionary relatives to a previously undiscovered organism.

8 Although the relationship between the unknown organism and known organisms may be represented diagrammatically as a phylogenetic tree, the tree diagram itself is not essential to the analysis of the data or to the interpretation of the results. The key step is the comparison, i.e. degree of homology, between the genetic sequence of the unknown sample and the known genetic sequences.

9 It is necessary to emphasize two points in relation to the use of phylogenetic trees:

(a) an unknown organism cannot be identified by sequence alignment unless a sequence for that particular species already features in the alignment database used;

(b) multiple sequence alignment analyses are not immovable and fixed; the addition, removal and even alteration of sequences in an alignment dataset as information from newly and previously analysed living organisms is being obtained and updated, inherently alters the alignment interrelationships between the sequences and thus the structure of the phylogenetic tree representing that data (the tree obtained for 100 sequences is ordinarily expected to differ from that obtained for 101 sequences).

The Application

10 The application concerns the identification of bacterial species by collecting publically available sequence data for the Dihydropteroate synthase (DHPS) gene from more than 260 bacterial species including different strains of the same bacterial species. Although it is not entirely clear from the patent specification, the sequences used were obtained both from public databases and from published journal articles. This was verified and confirmed at the hearing. The applicant also emphasised that this sequence data was nucleotide sequence data, as distinct from amino acid sequence data. The compiled sequence data was subsequently analysed using a publically available sequence alignment and phylogenetic tree generation software

package ***ClustalW***[2]. A phylogenetic tree based upon DHPS sequence alignments was disclosed by the applicant in their patent application which comprises at least 47 phylogenetic clusters (i.e. branches) and, as such, represents an extremely detailed phylogenetic analysis.

11 At page 2 of the specification, it is indicated that the data from the 'established tree' may be used subsequently as the basis for the identification of bacterial species and strains from which DHPS sequence data has been obtained by conventional molecular biology approaches. This was also confirmed by the applicant during the hearing. It would appear that bacterial identification is achieved, as referred to in the patent application (see step 4 on page 2 of the description), by performing '*examination of the…sequencing to determine it's [sic] related to different clusters'*, i.e. one uses well known molecular biology techniques to find out the genetic code of the DHPS gene in an unknown bacterial sample and then compares the result obtained with those in the phylogenetic tree that the applicant has produced, from publically available sequence data, in order to identify what bacterial species it is..

12 During the hearing, and indeed in his written response dated 25 September 2010, the applicant indicated that, for his invention, only oligonucleotide sequences may be used to obtain the sequence alignments from which the phylogenetic tree is generated (he asserted that amino acid sequences were not used). However, it is difficult to be certain that this feature is an essential feature of the invention disclosed in the application, as filed, for example see the last two lines of page 2 of the description. Notwithstanding Dr El Sokkary's arguments in writing and his oral submissions during the hearing, I remain unconvinced that the original application as filed discloses that it is, indeed, essential to the invention that it is restricted solely to the use of DHPS nucleotide sequences.

The Claims

13 The latest claims were filed on 21 March 2011, superseding those filed on 21 December 2010 and the original claims as received from WIPO. Claim 1 relates to a new phylogenetic tree or perhaps to its method of use:

> *'A new phylogenetic tree that can be used for classification, differentiation, identification and detection of a complete set of a number of 45 bacterial genera by the use of DHPS gene detection of their diseases, carriers and in biological warfare. The method also includes the phylogenetic tree for differentiation of other four bacterial genera namely Staphylococcus, Bacillus, Escherichia and mycobacterium only to their species level of differentiation, identification and detection.'*

14 Claim 2, which is dependent upon claim 1 appears to provide some clarification as to the scope of claim 1. It reads as follows:

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[2] For further details on **Multiple Sequence Alignment (MSA)** tools and, in particular, the ClustalW family of such MSA tools, the website of The European Bioinformatics Institute (EBI) part of the European Molecular Biology Laboratory (EMBL) see the http://www.ebi.ac.uk/Tools/msa/

Application or implementation of the new method in claim 1 that includes the use of DHPS gene oligonucleotides for any classification, identification and detection of the set of 45 bacterial genera to the species level through the procedure of production of any type of the already known diagnostic kit production or any new future procedures for kit product.'

This, suggests that claim 1 is intended to be to a method for use of the phylogenetic tree rather than a claim to the tree itself.

15 Claim 3, is an independent claim and concerns the use of an oligonucleotide as follows:

'*Implementation of DHPS gene oligo-nucleotide alone or within any complementary kit system or through any other mean]sic] of identification of all living beings that includes prokaryotic and eukaryotic groups of living creatures'*

The Relevant Law

16 The principle objection to this application is that the invention lacks an inventive step as required under s.1(1)(b) of the Patents Act 1977 (hereafter, the Act), which reads:

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) the grant of a patent for it is not excluded by subsections (2) and (3) or section 4A below; and references in this Act to a patentable invention shall be construed accordingly.

17 Following the amendments filed by the applicant dated 22 December 2010, the examiner also objected to the patentability of the invention under Section 1(2)(d). This latter patentability objection was maintained in relation to the latest amended claims on file, dated 21 March 2011, in addition to the inventive step objection raised against these claims.

18 Section 1(2)(d) of the Act reads:

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) …;
(b) …;
(c) …;
(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"

19 Section 3 of the Act, entitled 'Inventive Step' reads:

"*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)."*

20 The Office's approach to assessing inventive step is the structured approach found in *Windsurfing International Inc. v Tabur Marine (Great Britain) Ltd*, [1985] RPC 59 (hereafter "Windsurfing") as modified by Jacob LJ in *Pozzoli SPA v BDMO SA* [2007] EWCA Civ 588 (hereafter "Pozzoli"). The Windsurfing/Pozzoli modified approach involves the following steps:

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

(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?

21 In approaching steps 1(a) and 1(b) of this test above, I will bear in mind the comments of Sachs LJ in *General Tire & Rubber Co v Firestone Tyre & Rubber Co Ltd* (see [1972] RPC 457), that the skilled person "*is not a highly skilled expert or Nobel prize winner, nor is he some form of lowest common denominator. Instead he is best seen as someone who is good at their job, a fully competent worker*" and that "*he should be taken to be a person who has the skill to make routine workshop developments but not to exercise inventive ingenuity or think laterally*".

22 If I find that the application has an inventive step, I will then go on to consider if the invention as claimed relates to excluded subject matter using the four step assessment out in *Aerotel Ltd v Telco Holdings & Ors Rev 1* [2007] RPC 7 (Aerotel/Macrossan)[3]; i.e.

(i) Properly construe the claim;

[3] For full text of this decision from the UK courts (Court of Appeal) please see http://www.bailii.org/cgi-bin/markup.cgi?doc=/ew/cases/EWCA/Civ/2006/1371.html&query=aerotel&method=boolean

(ii) identify the actual contribution;

(iii) ask whether it falls solely within the excluded subject matter;

(iv) check whether the actual or alleged contribution is actually technical in nature.

Matters arising at the Hearing

23 During the hearing Dr El-Sokkary raised a number of queries. Firstly, he wished to know why the International Searching Authority had seemingly accepted the amendments he had made to the original claims filed with his application but to which the UK examiner subsequently objected. I indicated that it is not the role of the International Searching Authority (ISA) to examine the application to determine if a patent can be granted: this is the job of the UK patent examiner once the international application has entered the national phase[4]. The fact that the ISA did not issue any further correspondence after these amendments were made cannot be taken to mean that the amended claims filed at the International stage overcame the inventive step issue raised in the international search report. The IPO examiner, Dr Jeremy Kaye, was performing his duty as substantive examiner for the national phase of this application when he raised the inventive step objection regarding the amended claims filed in response to the written opinion of the ISA.

24 Secondly, Dr El-Sokkary expressed some frustration that, should his invention now be found to lack an inventive step, his patent application had been allowed to progress through several rounds of examination and amendment involving time, effort and expense that will in effect have been wasted. Whilst I appreciate that the patent process can take time, nonetheless the total time period for putting a patent application in order for grant is fixed (see, for example, s.20 of the Act). This process does give the applicant a number of opportunities to decide if and how to proceed with their application before a final determination is made as to whether it is in order for grant or not. For example, the applicant has an opportunity to amend the application and/or to convince an examiner by argument that his application complies with the Patents Act 1977 in response to each official examination report. It is also possible for the applicant to decide at any time that they no longer want to proceed with an application.

25 Thirdly, Dr El-Sokkary, both in his correspondence prior to the hearing (see, for example, his letters dated 22 December 2010 and 21 March 2011) and during the hearing, questioned why an objection to the patentability of his invention as a method of presentation of information was raised when it was, i.e., at a very late stage in the examination process. This I believe is the meaning behind the applicants question as to why no objection to his application had been made "*for its unsuitability to be invention as it is a kind of simple software and known*" (see, for example, page 2 of applicants letter dated 22 December 2010). As

[4] For an explanation of how & when the PCT application enters the national phase in the UK, please see the IPO website at http://www.ipo.gov.uk/types/patent/p-applying/p-apply/p-natphase.htm and/or the WIPO website at http://www.wipo.int/pct/guide/en/gdvol2/pdf/gdvol2.pdf.

explained in the official report from the Office, dated 9 February 2011, this objection first arose because of the amendment to the claims made by the applicant in his letter of 22 December 2010 and was maintained after the amendments made to the claims by the applicant in his letter dated 21 March 2011 as these changes claim 1 from a method claim to a claim to the phylogenetic tree itself (see claim 1 as published in GB 2455013 as compared to claim 1 as amended on 22 December 2010 and as currently on file). He queried why such an objection had not already been raised by the ISA before the application entered the national (UK) phase. I indicated that this was because the issue did not arise until he had amended his claims on 22 December 2010, i.e. when the application was already part of the national phase in the UK.

Analysis

26 I will first consider whether or not this invention has an inventive step. If I find that this is not the case, there is no need to go on to consider if the invention relates to excluded matter.

27 I will first consider each step of the *Windsurfing/ Pozzoli* approach in turn in relation to the presently amended claims:

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

28 The examiner identified the "person skilled in the art" as a molecular biologist. During the hearing Dr El-Sokkary indicated that he considered that the "person skilled in the art" is a microbiologist or genetic engineer. Given the considerable overlap and blurring between these areas of technology, for example, between molecular biology and genetic engineering, I am satisfied that that there is no fundamental divergence of opinion on this matter. The skilled person is thus someone who is skilled in the art of molecular biology/microbiology/genetic engineering and would be familiar with micro-organisms, such as bacteria, and their role in causing disease, and with techniques for identifying such micro-organisms, using both laboratory-based and computer-based methods.

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

29 The examiner stated that the common general knowledge of this skilled person is considered to include knowledge of how to undertake genetic sequencing and how to find specific nucleotide sequences from a publically available sequence database. The skilled person would be aware that sequence alignments can be used to construct phylogenetic trees based on either nucleotide or amino acid sequences. Indeed, the applicant has indicated in the application itself, and also at the hearing, that it is known to use the Gyrase B gene sequence or the 16s rRNA nucleotide sequence as the basis to compare and identify bacteria and their interrelationships. The applicant did not contradict this assessment and I consider that this is a correct assessment of the common general knowledge.

30 I also consider that the skilled person would be capable of finding publically available bioinformatics software for sequence alignment and phylogenetic tree generation. Comparing sequence data using software tools such as those publically available from EMBL is well known[2]. The applicant has acknowledged, both in the application as filed and at the hearing, that these conventional approaches for determining and comparing sequence data would be known or available to the skilled person who is directed in the application thus: "*All of the data concerning the isolation, detection and sequencing of nucleotides concerning 16S and gyraseB are available everywhere and we follow the same procedures in concern with the newly suggested gene"* (see page 2 of the description). At the hearing, there was no fundamental divergence of opinion as to the common general knowledge of the skilled person.

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

31 The scope of each of the claims currently on file is different and, as discussed above, not entirely clear. Claim 1 can be construed as the phylogenetic tree suitable for use as a tool to classify, differentiate, identify and detect bacteria at the species level from any of the bacterial genera or clusters in the tree. It is suitable for use to detect these bacterial species when involved in disease or biological warfare and/or when present as carriers (of disease, even if not infective). The specification on file describes how a phylogenetic tree is generated, refers to a '*newly established system'* and in the opening paragraphs states that '*the present studies suggest[s] that use of DHPS gene…*' as an alternative to 16s rRNA which is '*often not very convenient to resolve bacterial strains at the species level*'.

32 During the hearing it was discussed whether the applicant considered that the invention was (a) the principal of using DHPS sequences for alignment and tree generation and subsequently identification of new bacterial species based on their DHPS gene sequence; or (b) the alignment data itself obtained from the analysis of the DHPS gene sequence data or (c) the single and detailed phylogenetic tree produced from this alignment data and disclosed in the specification. The applicant indicated that he considered that the invention was the use of the tree as a means to identify, classify and detect bacterial species based on their DHPS gene sequence. He also stated that the compiling the tree itself was a significant achievement in bringing all this data together - over 260 bacterial species and strains which were organising it into 47 bacterial genera, i.e. clusters – to provide a tool to identify unknown bacterial species.

33 I agree that the inventive concept of this application is the use of the tree as a tool to identify bacteria rather than the tree itself. I am satisfied that this was the purpose that the applicant had in mind in collecting the sequence data in the first place, analysing it and presenting the outcome from this analysis as a phylogenetic tree. The data the applicant used was publically available data and the important thing was to obtain as many examples of DHPS gene sequences from bacterial species as possible to produce as useful tool as

possible – more examples would improve the chance that one will be close enough to that of an unknown bacterial species to provide a clear indication of what the unknown bacterial species is.

34 Keeping in mind the comments[5] of Pumfrey J in *Halliburton v Smith* [2006] RPC 2, in particular those in paragraphs 68 and 69, where relate to the correct approach to the construction of claims, and taking account of the above, it is my view that the most straightforward construction of the inventive concept in this application is '*the use of dihydropteroate synthase (DHPS) gene sequence alignments (i.e. nucleotide sequences), or the phylogenetic tree resultant therefrom, for the 'classification, identification and detection' of bacterial species*.'

Step (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:

35 As already indicated above, the article by MA et al., has been cited by the examiner to show that the inventive concept of this application was already known and formed part of the knowledge available to the skilled man from the state of the art. This document describes the PCR amplification and sequencing of two genes, one of which is DHPS, from *Pneumocystis carinii* strains from various mammalian host species, including humans. *Pneumocystis carinii* is the causative pathogen of pneumonia in humans and strains of this pathogen from one host, such as mouse or monkey, do not cross-infect another, such as humans. The purpose of this study was to determine the genetic sequences of both genes in *Pneumocystis carinii* isolated from different host species, study the phylogenetic relationship between these sequences and consider the relevance of any differences in the sequences of the various *Pneumocystis carinii* strains on drug development to treat pneumonia. The article also shows that the phylogenetic analysis of this pathogen in comparison to a range of bacterial, protist (Alveolatae) and fungal species provides strong support for the classification of *Pneumocystis carinii* as a fungus. In Table 1 on page 1359 of MA et al. the results of amino acid sequence alignments and of nucleic acid sequence alignments of the DHPS (lower left part of the table) for a range of species are depicted. It is clear therefore that DHPS nucleic acid sequences obtained from public databases for a range of *Pneumocystis carinii* strains were analysed and aligned. Subsequent studies using *P. carinii* nucleic acid sequences obtained by PCR and sequencing experiments were translated into amino acid sequences and subjected to sequence alignment using PHYLIP software[6] alongside a selection of additional DHPS amino acid sequences obtained from the GenBank sequence database. The right-hand side of Figure 1 on page 1360

[5] For full text of this decision from the UK courts (The Patents Court), please see http://www.bailii.org/cgi-bin/markup.cgi?doc=/ew/cases/EWHC/Patents/2005/1623.html&query=halliburton+and+v+and+smith&method=boolean.

[6] PHYLIP is the tree output software used in the *ClustalW* package, see footnote 2 above for further details

of this article shows the results of the DHPS amino acid sequence alignments in the form of a phylogenetic tree. This tree shows that the different *Pneumocystis carinii* strains are all closely related (not surprisingly) and that *Pneumocystis carinii* is more closely related to the other fungi than to the bacterial species and in turn is even less closely related to the protist species included in the tree. The contrast of the relative phylogenetic closeness of the different *Pneumocystis carinii* strains with the relative distance of bacterial species indicates that the alignments from which the tree is generated is a suitable approach for the 'classification, identification and detection' of any of one of the species or strains which featured in the alignment analysis.

36 During the hearing the applicant argued that this prior art is not relevant to the obviousness of his invention for two reasons. Firstly, no phylogenetic tree obtained from DHPS nucleotide sequences is disclosed and, secondly, MA et al. starts from a different perspective than the present application in that the analyses of the DHPS nucleic acid and amino acid sequences from different *P. Carinii* strains were intended to investigate one aspect of the differential resistance of these fungal strains to 'sulpha' drugs (the sulphonamide antibacterial drugs). Consequently it was argued that the prior art did not teach the skilled person that DHPS sequences might be used for bacterial classification, differentiation and identification.

37 Although I agree that the MA et al. article does not disclose a phylogenetic tree obtained from DHPS nucleotide sequences, I do not consider that this is a real difference. Both sets of data were available, i.e. the DHPS amino acid sequences and the nucleotide sequences for the different *P. Carinii* strains (see NOTE at end of Table 1 on page 1359). It is noted at p1359, column 1, paragraph 3, that these sequence alignments are publically available. The DHPS nucleotide sequences were obtained and were used for multiple sequence alignments to compare *P. Carinii* strains (hence the data in Table 1). The nucleotide based sequences were longer than the amino acid based sequences and this may have been the reason why the authors used the DHPS amino acid sequences for preparing the phylogenetic tree in Figure 1. Thus, I consider that it is simply a matter of convenience which data to use for compiling the tree. However, the nucleotide sequence alignments do differ in so much that it was only different *P. Carinii* strains that were analysed, i.e. the sequences relate to fungal species and so are not of direct relevance to bacterial classification and identification.

38 With respect to the second point made by the applicant, i.e., that there is a different starting point in the MA et al. study, in comparison to the invention in question, the question to be answered is would the disclosure in MA et al. be available to the skilled man in this case and what does this document teach the skilled person when considered in the light of the common general knowledge? In my view, the MA et al. document demonstrates the classification, in a phylogenetic tree, of *P. carinii* strains in context with other known disease causing pathogens - bacterial, protist and fungal, identifies them as being most closely related to the fungi and demonstrates their evolutionary classification and identity in relation to one another. New information regarding the phylogenetic classification of *P. carinii* is obtained by aligning DHPS amino acid

sequences (translated *in silico* from nucleic acid sequences) and representing them in a phylogenetic tree. As a by-product of this analysis, the document further shows that the DHPS amino acid sequence may be used to classify various bacterial pathogens as well as fungi and Alveolatae protists.

39 I note that in compiling the phylogenetic tree in Figure 1 of MA et al., the amino acid sequences for all the organisms analysed are deduced, i.e. are translated *in silico* from nucleic acid sequences of the various bacteria, fungi and protists (see legend for Figure 1 on page 1360). This is clearly indicative that there is no significant difference between using nucleotide sequences or amino-acid sequences for the purpose of comparing DHPS genes from different pathogenic micro-organisms

40 Overall, I consider that the prior art differs from the present inventive concept in two respects: firstly whilst the prior art discloses alignment using both DHPS nucleic acid and amino acid sequences, only amino acid sequences, (and not nucleic acid sequences) of bacterial origin have been used to construct a phylogenetic tree. However, the amino acid sequences used have been deduced from the nucleotide sequence. Secondly the prior art differs from the present inventive concept in that a much smaller number of sequences has been actually been aligned, the result being that the prior art alignments and phylogenetic tree would be expected to be considerably less refined than the present invention. A consequential difference is that the prior art analyses and phylogenetic tree would be of use only for the 'classification, identification and detection' of *B. subtilis, S. pneumoniae, E.coli, N. meningitidis, M. tuberculosis* and *M. leprae*.

Step (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?

41 The person skilled in the art of microbiology/genetic engineering/molecular biology having the common general knowledge concerning how nucleic acid sequences for a particular gene from a micro-organism such as a bacteria might be obtained (by PCR and sequencing) and compared with that from others with the aid of computer-based techniques, is taught by MA et al. that the DHPS gene has some utility in phylogenetic classification, identification and detection because it worked for the *P. carinii* strains. The skilled person is further taught that this principle will also work at least for some of the more common bacterial pathogens relevant to human health as demonstrated in Figure 1 of MA et al., for example *Neisseria meningitidis, Bacillus subtilis, Mycobacterium leprae* and *Mycobacterium tuberculosis*. Sequence alignments using both amino acid sequences translated from nucleic acid sequences and experimentally obtained nucleic acid sequences are performed by MA et al. and it appears to the skilled person that either nucleotide or amino acid sequences might be used such that the choice of nucleic acid alignments is entirely arbitrary: there is a difference, but it is one that is an obvious modification for the skilled person to make.

42 It should be noted that even if I had been convinced that the choice of nucleic acid alignments was deliberate and non-arbitrary, given the choice of only two alternatives (amino acid or nucleic acid sequences), in my view, it would be obvious for the skilled person to use nucleic acid alignments.

43 The skilled person reading the prior art MA et al. document would appreciate that a more refined analysis might be completed should further sequences be added to the alignment analysis. Indeed an inherent part of sequence alignment and the resultant phylogenetic trees is that each additional sequence added to the analysis both refines the result obtained and changes the relationship between each sequence and thus, also alters, the spacing and branch arrangements of the phylogenetic tree representing that analysis.

44 From the prior art it is clear that MA et al. have already shown the use of the DHPS gene to classify and distinguish closely related fungal *P. carinii* pathogen strains and to demonstrate their phylogenetic relationship in a phylogenetic tree in context with other microbial pathogens including bacteria. The result is a phylogenetic tree obtained from DHPS amino acid alignments which is suitable for the identification of bacteria.

45 The differences in the use of nucleic acid rather than polypeptide sequences for the analysis and in the use of many more sequences than are taught by the prior art are both ones which would fall within the scope of the skilled person's common general knowledge. While I can acknowledge the considerable effort that has been expended by the applicant in compiling and analysing this, albeit publically available, data and, also, that the resultant phylogenetic tree has utility for identifying bacterial strains that cause disease, such labour does not of itself mean that the work is inventive. Merely including a much larger number sequences to produce a more refined or accurate tool for identifying an unknown bacterial species is not inventive. The earlier disclosure in MA et al. had already indicated that this was approach was likely to succeed.

46 Taking account of all of the above, I consider that the invention as claimed lacks an inventive step.

Subject matter excluded under s.1(2)(d) of the Act

47 As I indicated above, the examiner has also reported that the invention is excluded from patenting as it relates to the presentation of information as such. However, having found the claimed invention lacks an inventive step, it is not necessary for me to decide this point.

Conclusion

48 I conclude that the invention defined in claims 1-3 does not involve an inventive step. Furthermore, after a consideration of the specification and the application I have not readily been able to identify any possible amendments which could overcome the inventive step objection outlined above.

49 The period for putting the application in order expired on 2 August 2011. The option is still available to the applicant, upon filing the correct form and payment

of the appropriate fee, to seek an as-of-right extension of 2 months to this date i.e. until 2 October 2011, according to rule 108(2) of the Patents Rules 2007 (as amended). This is a matter for the applicant.

50 However, given that I have not been able to identify a possible amendment that would render this invention non-obvious, the application is refused under section 18(3) of the Act for failing to meet the requirements of inventive step under section 1(1)(b) of the Act.

Appeal

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

Dr L CULLEN

Divisional Director, acting for the Comptroller