BL O/228/11

28 June 2011

PATENTS ACT 1977

APPLICANT	INA RESEARCH INC.
ISSUE	Whether patent application GB0806669.8 complies with section 1(1)(b)
HEARING OFFICER	Dr L Cullen

DECISION

1 International patent application PCT/JP2006/322044 entitled "Animal model with induced arrhythmia" was filed on 27 October 2006 in the name of INA RESEARCH INC. and claimed priority from the earlier application JP 2005315434 filed on 28 October 2005. The international application was published by WIPO as WO2007/049821 on 3 May 2007, entered the UK national phase as GB0806669.8 and was re-published as GB2444687 on 11 June 2008.

2 The first examination report dated 26 February 2010 raised objections relating to novelty, inventive step, and the fact that the invention related to a method of surgery. The examiner maintained his inventive step objection in two subsequent examination reports dated 29 December 2010 and 21 February 2011 following amendments and arguments from the applicant.

3 The applicant requested an oral hearing before a Hearing Officer in their agent's letter of 25 February 2011. A date of 20 April 2011 was set and agreed for the hearing before me as Hearing Officer. An official letter dated 28 March 2011 was issued by the examiner to summarise the issues to be considered at the hearing in relation to the issue of inventive step. In response to this, in their agent's letter of 7 April 2011, the applicant submitted a set of claims which they referred to as the 'Main Request' for consideration at the hearing. In addition, they also submitted an alternative set of claims, referred to as the 'Auxiliary Request', and asked that they be considered at the hearing only if the Main Request was rejected. Some additional materials were also provided for consideration at the hearing; a copy of a declaration signed by Dr Sugiyama (the inventor) which had recently been filed at the US Patent and Trademark Office and a related supporting journal article (Sugiyama 2008, British Journal of Pharmacology, 154, pages 1528-1537).

4 However, on 14 April 2011, the applicant informed the Office that they would not be attending the scheduled hearing and instead requested that a decision be issued based on the papers currently on file. They requested that the application be allowed to proceed on the basis of the claims in the Main Request, referred to above; or in the event that this Main Request was rejected, on the basis of those in the Auxiliary Request referred to above. The applicant subsequently filed amended description pages for both the Main and Auxiliary claim requests with their agent's letter of 18 April 2011.

5 The decision below is thus based on the papers presently on file.

Status of the Claims in the Main Request

6 I will first consider the status of the so-called Main Request and the Auxiliary Request in order to identify which set of claims I will base my decision on. I will then go on to consider the substantive issue of inventive step in relation to these claims and the related description.

7 Given that the applicant clearly identified that they wanted the application to proceed on the basis of claims filed in the Main Request and that these and the related necessary amendments to the description to bring it into line with these claims were filed sufficiently in advance of the proposed hearing date to allow the examiner, at my request, to confirm that these claims do not add matter and so are valid claims, I am content to confirm these as the latest set of claims officially on file. I have based the decision below on these claims.

8 I note in this regard that the use of multiple possible sets of claim where the Hearing Officer is asked to consider first one set, and then if these are found not to meet requirements, to consider a second set and so on and so on, appears to be happening with increasing frequency. At least this has been my experience as a hearing officer of late at the IPO. This can produce a situation where the applicant has two or more possible sets of claims that they want considered at the hearing at a stage in the application process where the compliance date is usually imminent and time is short to get the application into order for grant. I am aware that this practice is relevant to the prosecution of cases before the EPO where, under a different set of rules and procedures, there is no compliance date and thus such prioritised alternatives may have a role in deciding what claims can be granted in a reasonable time scale. However, in cases before the IPO as in this instance, where the compliance date is imminent, it is necessary to clearly identify what claims define the invention so that one can properly decide whether the invention is in order or not at the end of the compliance period. It makes it easier to identify what deficiencies need to be addressed in order to secure a valid patent.

The Application

9 The application concerns an arrhythmia model animal that enables an evaluation of the QT interval prolongation by a drug. The QT interval is the time period which elapses between the Q wave and the T wave in the electrical cycle of the heart. The problem of drugs prolonging the electrocardiogram QT interval and inducing proarrhythmia[1], such as the fatal ventricular arrhythmia called *Torsades de pointes* (TdP), is known in the art. New drugs must be assessed for any QT interval prolongation effects, and model animals exist in the art which enable such effects to be studied. The present invention is intended to provide an improved method of evaluating the QT interval prolongation by a drug using an improved model animal.

10 The applicants have produced a monkey arrhythmia model in which the atrioventricular node of the heart in the monkey has been preablated. Ablation is the process whereby high-frequency electrical impulses are used to destroy or cauterise tissue: in this case, the heart tissue at the atrioventricular node.

11 The monkey arrhythmia model allows an evaluation of drug-induced prolongation of the QT interval. Unlike previous proarrhythmia model animals (e.g. dogs), the monkey model disclosed in the present application recovers from any arrhythmia which may develop following administration of the drug. Thus the same model animal can be used repeatedly. The advantage of using this model is that it will allow the evaluation of results without the need to account for differences between individual animals.

The Claims

12 As noted above, the latest set of claims for the application officially on file are those sent with the agent's letter of 7 April 2011 (the claims of the so-called Main Request referred to above). These claims contain two independent claims, claim 1 and claim 13 (as well as a further omnibus claim, claim 19).

13 Claim 1 relates to a method of evaluating the QT interval prolongation in a cynomolgus monkey[2] caused by a drug and reads:

> *"A method of evaluating the QT interval prolongation by a drug, comprising using a cynomolgus monkey model of proarrhythmia in which the atrioventricular node has been preablated."*

14 Claim 13 relates to a method of identifying a cynomolgus monkey that can be used as a model of proarrhythmia and reads:

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[1] *Proarrhythmia* is a new or more frequent occurrence of pre-existing arrhythmias, and is, paradoxically, precipitated by anti-arrhythmic therapy. It is thus a side effect associated with the administration of some existing anti-arrhythmic drugs, as well as drugs for other indications. In other words, it is a tendency of anti-arrhythmic drugs to facilitate the emergence of new arrhythmias.

[2] The *cynomolgus monkey* is also known as the Philippine monkey, the long-tailed macaque and the Crab-eating macaque. It is primarily a tree-living macaque native to Southeast Asia.

"A method of identifying a cynomolgus monkey that can be used as a model of proarrhythmia by determining whether a cynomolgus monkey possesses an atrioventricular block, and has a concentration of atrial natriuretic peptide or cerebral natriuretic peptide in the blood that is elevated compared to that for a normal cynomolgus monkey."

15 The difference between these claims and those previously considered by the examiner is that they limit the model to a specific monkey model, i.e. to that using cynomolgus monkeys, rather than referring to a monkey model in general.

The Law

16 The examiner has raised an objection under section 1(1)(b) of the Patents Act 1977 (hereafter the Act) that the invention does not involve an inventive step.

17 The relevant parts of section 1 of the Act 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) ….

18 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).

19 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;
(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?

Analysis

20 I will first consider each step of the *Windsurfing/ Pozzoli* approach in turn in relation to the claims of the applicant's Main Request:

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

21 The examiner identified the "person skilled in the art" as a team including, at least, a cardiologist and a pharmacologist with expertise in the cardiotoxic side-effects of drugs. He also suggested that the team would consider recruiting a veterinary surgeon in light of the disclosures of the closest prior art documents. The applicant does not appear to have raised any fundamental objections to such an assessment of the person skilled in the art. 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;

22 The examiner asserted that the common general knowledge of this skilled team would include the standard testing protocols to determine cardiotoxic effects, including the *in vivo* testing of drugs for their effects on the QT interval in animal models, as set out in the ICH[3] Harmonised Tripartite Guideline S7B entitled '*The Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarisation (QT Interval Prolongation) by Human Pharmaceuticals*', as referred to and discussed on pages 1-2 of the present application. The team would also be aware that suitable model animals for these tests (as set out in ICH Guideline S7B) include dogs and monkeys, but not rats or mice (see page 9 of ICH Guideline S7B). The skilled team would be aware of the relative merits (including cost and physiological relevance) of the different model systems in general use. In addition, the common general knowledge in the art would include knowledge of the link between levels of markers including atrial and cerebral natriuretic peptides and noradrenaline, and atrioventricular (AV) block.

23 The applicant also suggested that it was a common understanding in the art that fewer monkeys are available as test animals as the cost of each monkey is high, and that all previous animal models of proarrhythmia did not survive drug-induced arrhythmia.

24 I am content that the aforementioned knowledge, including the further points proposed by the applicant, would be part of the common general knowledge of the skilled team.

[3] ICH, International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use

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

25 The inventive concept identified by the examiner is the use of a monkey with an AV block in screening methods to test drugs for arrhythmic effects.

26 The applicant disagrees with the examiner's assessment of the inventive concept (see for example, comments from the applicant to this effect in agent's letter dated 7 April 2011). The inventive concept of the claimed invention is, according to the applicant, the use of an animal model of proarrhythmia for evaluating drug-induced long QT syndrome, which animal recovers from arrhythmia and therefore can be repeatedly used in such studies, allowing results to be obtained with no variation due to individual differences between model animals.

27 I am not convinced that the skilled person would interpret the inventive concept of claim 1 in the manner proposed by the applicant. In *Generics (UK) Limited and others v H Lundbeck A/S, UKHL 12, [2009], RPC 13*, Lord Walker in paragraph 30, citing *Kirin-Amgen [2005] RPC 9* (paras 112-113), summarised the inventive concept in the following manner:

> *""Inventive Concept" is concerned with the identification of the core (or kernel, or essence) of the invention – the idea or principle of more or less general application...which entitles the inventor's achievement to be called inventive*".

28 Consequently, I consider that the skilled person or team would interpret the core of the presently claimed invention to be the use of a cynomolgus monkey model of proarrhythmia in which the atrioventricular node has been preablated in order to evaluate the QT interval prolongation by a drug.

29 Whilst I do not dispute that it is an advantageous consequence of the applicant's model that the animal recovers from arrhythmia, the core inventive concept of the claim in question remains the production of the cynomolgus monkey model of proarrhythmia in which the atrioventricular node has been preablated and its use to evaluate the QT interval prolongation by a drug.

(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;

30 The examiner has cited documents (b) – (d) below:

> (b) Japanese Journal of Pharmacology (2002); Vol 88, pp 341-350, "*Electrophysiological, Anatomical and Histological Remodelling of the Heart to AV Block Enhances Susceptibility to Arrhythmogenic Effects of QT-Prolonging Drugs*, A. Sugiyama et al; see whole document.
>
> (c) Folia Pharmacologica Japonica (2003); Vol 121, pp 393-400, "*Effects of clinically available drugs on the repolarization process of the heart assessed by the* in vivo *canine models*", A. Sugiyama; see esp. abstract and figures.

(d) WO 00/67839 A1 (CEDARS-SINAI MEDICAL CENTER). *"Method and Apparatus for Inducing Ventricular Arrhythmias in Test Animals";* see whole document.

together with the common general knowledge in the field as exemplified by the following two documents, (f) and (g):

(f) BIOSIS Accession No PREV200300402210 & FASEB Journal (2003); Vol 17, Abstract No 400.2; "*QTc interval in conscious cynomolgus monkey by use of telemetry*", Mow & Matz; see abstract and whole document; relevant to claims 1-21;

(g) European Journal of Pharmacology (1999); Vol 378, pp 169-175, "*Effects of terfenadine, astemizole and epinastine on electrocardiogram in conscious cynomolgus monkeys* ", T. Ohmura et al; see whole document, esp. abstract, p 174 col 2 para 2; relevant to claims 1-21.

31 In relation to independent claim 13 and dependent claims 14-18, the examiner has also cited the aforementioned prior art documents (b)-(d) when considered with the further common general knowledge as disclosed in the following two documents, (h) and (i):

(h) British Heart Journal (1991); Vol 65, pp 188-193, "*Double blind crossover comparison of the effects of dual chamber pacing (DDD) and ventricular rate adaptive (VVIR) pacing on neuroendocrine variables, exercise performance, and symptoms in complete heart block*", K.G. Oldroyd et al; see whole document, esp. p191, final paragraph.

(i) International Journal of Cardiology (2005); Vol 102, pp 259-268, "*Detection of cardiac sarcoidosis using cardiac markers and myocardial integrated backscatter*", H. Yasutake et al., see whole document, esp. discussion, page 266

32 The examiner identified documents (b)-(d) as the closest prior art documents. These documents disclose surgically ablating the AV node in dogs to produce models of Torsades de Pointes (TdP) and/or drug-induced arrhythmia. I agree that these documents represent the closest prior art of the documents cited.

33 The examiner argued that the difference between prior art documents (b)-(d) and the presently claimed invention is simply the selection of a monkey, now specifically a cynomolgus monkey, as the test animal. The atrioventricular (AV) node is ablated in the same way (using electrical stimulation from the tip of a catheter) and for the same purpose in the prior art documents as in the present application.

34 The applicant does not appear to have disputed these facts during the prosecution of the application, and I am content that this is the main difference between prior art documents (b)-(d) and the presently claimed invention.

35 The applicant does note, however, that document (b) (page 341, first 7 lines) states that "*The dog with chronic AV block has been used as a very suitable large animal model for the study of TdP*".

36 At this stage I believe it is also useful to summarise the content of the other documents cited by the examiner. Documents (f) and (g) disclose the use of cynomolgus monkeys to assess QT intervals in cardiotoxicity testing of drugs. The documents do not disclose the model of proarrhythmia in which the atrioventricular (AV) node has been preablated, but they are cited by the examiner as examples of the common general knowledge in the field.

37 Documents (h) and (i) disclose the association of elevated levels of atrial natriuretic peptide or cerebral natriuretic peptide with atrioventricular (AV) block. Documents (h) and (i) do not disclose the monkey model of proarrhythmia in which the atrioventricular (AV) node has been preablated, but again they are cited by the examiner as further evidence of the common general knowledge of the skilled person or team.

(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?

38 Much of the discussion in the correspondence between the examiner and the applicant focussed on the whether it was "obvious to try" to carry out the procedures disclosed in documents (b)-(d) on monkeys in order to produce monkey models analogous to the dog models already known. The examiner argued that it was part of the common general knowledge of the skilled team that cynomolgus monkeys could be used in cardiotoxicity testing (see documents (f) and (g), and the ICH's S7B Guidelines on the Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarisation (QT Interval Prolongation) by Human Pharmaceuticals), and that the skilled person would also be aware of the closer relationship of monkeys with humans and their greater physiological relevance. The examiner asserted that this common general knowledge would provide the skilled person with the motivation to try to produce a monkey model of proarrhythmia.

39 The applicant, in their agent's letter of 7 April 2011, as well as in previous letters (see letters dated 24 August 2010 and 31 January 2011), argued that the skilled person would have been dissuaded from attempting to produce a cynomolgus monkey model of proarrhythmia because of a lack of any perceived benefit of using cynomolgus monkeys compared with established dog models of proarrhythmia. It was also argued in these letters, and in Dr Sugiyama's Declaration which accompanied the letter of 7 April 2011, that the skilled person would not have been motivated to try to produce a monkey model analogous to the existing dog models for a variety of reasons, such as:

(a) the high cost of cynomolgus monkeys compared with dogs;

(b) the significant size difference between dogs and monkeys used for such experiments, e.g. beagles v cynomolgus monkeys, including differences in body weight, heart size and shape;

(c) the lack of any suggestion in the prior art that the electrophysiological profile of the cynomolgus monkey is a better model for the human heart than the electrophysiological profile of the dog; and

(d) prior art animal models of proarrhythmia died after suffering drug-induced arrhythmia.

40 I am not persuaded by these arguments. Whilst the dog model may have been seen as a suitable large animal model of proarrhythmia, the skilled person would certainly have been aware of the close physiological relationship between monkeys and humans. Furthermore, cynomolgus monkeys were already being used in cardiotoxicity testing in the prior art as shown in documents (f) and (g). In addition, page 9 of the ICH's S7B Guidelines on the Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarisation (QT Interval Prolongation) by Human Pharmaceuticals clearly identifies monkeys as well as dogs as being suitable animals for such testing.

41 I do not believe that the cost implications of attempting to use monkeys rather than dogs in proarrhythmia models have any material effect on the inventiveness of the claimed method. The examiner cited *Brugger & Ors. v Medic-Aid Ltd* [1996] RPC 635 to highlight the fact that a route may still be obvious even if it may not be commercially worthwhile[4]. If the model worked, the cost of using the monkeys would not be an issue. In *Pfizer Ltd's Patent* [2001] FSR 16, Laddie J provided further guidance in this respect when stating that "*whether something is obvious to try depends to a large extent on balancing the expected rewards if there is success against the size of the risk of failure*".[5] Given that the rewards of successfully producing a monkey model of proarrhythmia were substantial, i.e. a monkey model that would be more physiologically relevant to humans, I do not believe that the skilled team would be dissuaded from trying to produce such a monkey model. As indicated above, documents (f) and (g) indicate that monkeys, specifically cynomolgus monkeys, were already being used for cardiotoxicity testing. This confirms, in my view, that the cost of monkeys did not dissuade researchers from using them in this area of research, and, as such, the skilled team would have been aware that this was the case.

42 In their agent's correspondence, the applicant also argued that for an invention to be considered "*obvious to try*", there must be a fair expectation of success, as held by the House of Lords in *Conor Medsystems Inc v Angiotech Pharmaceuticals Inc* [2008] RPC 28. The agent suggested that, in the present case, there was no fair expectation of success of obtaining an animal model of proarrhythmia **that recovers from drug-induced arrhythmia** (emphasis added**)**. In contrast, the examiner argued that the skilled person would have a reasonable expectation that a monkey with an ablated AV node would be capable of use as a model of TdP and drug-induced arrhythmia, and that this alone would make the step of producing a monkey model of proarrhythmia obvious.

[4] See for example, comments by Laddie J on page 653, lines 28-40; page 654, lines 16-31 and page 661, lines 6-21.
[5] See especially paragraphs 106 & 107

43 It seems to me that this is the crux of the issue in this case. I agree that it is an unexpected advantage of the cynomolgus monkey model of the present invention that each monkey recovers from arrhythmia such that it can be used repeatedly for evaluation studies, and, as a consequence, there is no need to account for differences between individual test animals when evaluating the drugs being tested.

44 However, I consider that this unexpected advantage is, in effect, a discovery which would have been revealed by the skilled team had they attempted to produce the cynomolgus monkey model of proarrhythmia in an analogous manner to the models already known in dogs.

45 The question which must therefore be answered is whether it would have been obvious for the skilled team to attempt to produce a cynomolgus model of proarrhythmia in an analogous manner to those already known in dogs. Given the disclosures in documents (b)-(d) of surgically ablating the atrioventricular node in dogs to produce models of TdP and/or drug-induced arrhythmia, and the common general knowledge (see above) that cynomolgus monkeys were already being used in cardiotoxicity testing in the prior art (as shown in documents (f), (g), and in the ICH's S7B Guidelines), I consider that it would be a logical and obvious step for the skilled team to try and produce a cynomolgus monkey using the methods which had already been successfully utilised in dogs. In taking this obvious step, the skilled person would automatically identify the fact that the cynomolgus monkey model recovered from arrhythmia and could be used again.

46 I find support for this interpretation in *Bristol-Myers Squibb Co v Baker Norton Pharmaceuticals Inc* [1999] RPC 253 where Jacob J,(as he was then) held that an unexpected result found by following an obvious course of action does not render that action inventive. Whilst the exact facts of *Bristol-Myers Squibb* and the present application may well be different, I am satisfied that the general principle outlined by Jacob J is applicable to the present case. The obvious course of action of producing a cynomolgus monkey model of proarrhythmia in an analogous manner to those already known in dogs would have led to the unexpected advantage that the monkey model survived any drug-induced arrhythmia. Therefore, I do not consider the invention of claim 1 (see above) to involve an inventive step over any one of documents (b)-(d) when combined with the common general knowledge of the skilled team.

47 The applicant's agent also suggested that the skilled person would not have expected the methods disclosed in documents (b)-(d) for dogs to be successful in the cynomolgus monkey as these monkeys are smaller than dogs, have smaller blood vessels and have hearts which differ in shape to those of dogs. It was therefore proposed that the skilled person would have had no expectation that it would be possible to successfully perform the same method on a cynomolgus monkey that is used to obtain dog models of proarrhythmia in the prior art.

48 I am not persuaded by these arguments. It would be entirely within the capabilities of the skilled team to account for such differences when attempting to use the methods disclosed in documents (b)-(d) to produce a monkey model

of proarrhythmia, and, in my view, they would have had a reasonable expectation that the prior art methods could be successfully utilised in monkeys.

49 Given the above conclusions, and taking account of the common general knowledge summarised in documents (h) and (i), which disclose the association of elevated levels of atrial natriuretic peptide or cerebral natriuretic peptide with atrioventricular block, I also consider that claim 13 of the application lacks an inventive step in light of the disclosures of any one of documents (b)-(d) and the further common general knowledge summarised in documents (h) and (i).

The Auxiliary Request

50 As mentioned briefly above, the applicant also included a further set of claims, the so-called Auxiliary Request, with their agent's letter of 7 April 2011 and asked that these be considered in the event that the claims in the so-called Main Request were deemed to be unacceptable. As I have indicated above, I consider that the claims of the so-called Main Request are those that are the latest currently on file, and these are the claims that I have considered as the basis for my decision. In the normal course of events, I would have to consider whether such an additional set of claims filed at or very close to hearing can be treated as anything other than an informal suggestion from the applicant to identify a possible fruitful course of action. If so, such an informal suggestion would have to be filed formally at the Office in order for consideration by the examiner dealing with the case. However, given that this so-called Auxiliary Request was filed in good time before the scheduled hearing date (which was later abandoned by the applicant – see above) and that related necessary amendments to the description to bring it into line with these claims were also filed sufficiently in advance of the proposed hearing date to allow the examiner, at my request, to confirm that these claims do not add matter, I am content in this instance to consider whether or not these claims address the problem identified above in relation to the obviousness of the invention.

51 Independent claim 1 of the Auxiliary Request reads:

> *A method of evaluating the QT interval prolongation by a drug, comprising: administering the drug to a cynomolgus monkey model of proarrhythmia in which the atrioventricular node has been preablated; waiting for 1 day to 2 weeks for the monkey to recover from any arrhythmia that develops and then administering another drug to the monkey.*

52 Thus, in addition to the requirement that the monkey model is a cynomolgus monkey model, this claim also includes the additional feature that the monkey must be allowed to recover from any arrhythmia and then it is tested with another drug.

53 I note also that claims 10-12 of the Auxiliary Request relate to screening methods for candidate substances involving administering substances to the cynomolgus monkey models defined in claim 1 (or in specified dependent claims 2-9), waiting for 1 day to 2 weeks for the monkey to recover from any arrhythmia that develops and then administering another drug to the monkey.

54 Following the same approach as indicated above in assessing inventive step and taking account of the additional features in claim 1 of the so-called Auxiliary Request, I conclude that these additional features also do not render this claim inventive.

55 The nature of the skilled team and their common general knowledge is the same as that described above in my analysis of the claims of the so-called Main Request.

56 The inventive concept of claim 1 of the so-called Auxiliary Request is a method of evaluating the QT interval prolongation by a drug, comprising administering the drug to a cynomolgus monkey model of proarrhythmia in which the atrioventricular node has been preablated; waiting for 1 day to 2 weeks for the monkey to recover from any arrhythmia that develops and then administering another drug to the monkey.

57 The difference between prior art documents (b)-(d) and the invention of this claim 1 is the selection of a cynomolgus monkey as the test animal (rather than a dog), and the fact that after waiting for the specified period for the monkey to recover from any arrhythmia, another drug is administered to the monkey.

58 The agent argues that as it is surprising that the monkey model of the invention recovers from drug-induced arrhythmia, it would not have been obvious that it would be possible to repeatedly use the same monkey in drug evaluation studies even if arrhythmia occurs.

59 I accept that the prior art documents do not disclose or suggest animal models which recover from drug-induced arrhythmia.

60 However, in assessing the claims of the applicant's Main Request above I have already concluded that the production of a cynomolgus model of proarrhythmia in an analogous manner to the models already known in dogs would be an obvious and logical step for the skilled team. In producing such a model, the skilled team would inevitably identify the fact that the monkey model survived drug-induced arrhythmia, and it would be obvious that the monkey model could be used for tests of further drugs.

61 Given that *Bristol-Myers Squibb Co v Baker Norton Pharmaceuticals Inc* [1999] RPC 253 directs that an unexpected result found by following an obvious course of action does not render that action inventive, and the fact that I can find no other features in claim 1 of the so-called Auxiliary Request which require an inventive step, I therefore consider this claim to be obvious in light of the disclosures of any one of documents (b)-(d) when considered with the common general knowledge of the skilled team.

62 I also find that the screening methods of claims 10-12 of the Auxiliary Request are obvious for similar reasons.

Conclusion

63 I conclude that the invention of independent claims 1 and 13 and omnibus claim 19 of this application lack an inventive step as required under section 1(1)(b) of the Patents Act 1977 for the reasons identified above.

64 In addition, I also conclude that the amendments as suggested in claim 1 and in claims 10-12 of the so-called Auxiliary Request as a means to address any problems with the claims filed in the so-called Main Request also lack an inventive step as required under section 1(1)(b) of the Patents Act 1977 for the reasons identified above.

65 I also note that after considering the specification of this application, and the various dependent claims, I have not readily been able to identify any possible amendments which could overcome the inventive step objections outlined above.

66 The period for putting the application in order, which was extended as-of-right by the applicant, according to rule 108(2) of the Patents Rules 2007 (as amended), expired on 28 April 2011. The applicant has the option to seek a further discretionary extension to the period for putting the application in order, under rule 108(3), but this request must be filed by today, 28 June 2011; i.e. before expiry of the period of two months beginning with the date on which the period for putting the application in order expired. This is a matter for the applicant.

67 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

68 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