**Patents Act 1977** **Opinion Number** **26/20**

# OPINION UNDER SECTION 74A

| | |
|---|---|
| Patent | GB 2423721 B |
| Proprietor(s) | F T Tehrani |
| Exclusive Licensee | |
| Requester | F T Tehrani |
| Observer(s) | Bristows LLP on behalf of Hamilton Bonaduz AG |
| Date Opinion issued | 19 March 2021 |

## The Request

1. The comptroller has been requested to issue an opinion on the validity of GB 2423721 (the patent). The patent was originally published as WO 2005/051280 with a filing date of 25 October 2004. It remains in force.

2. Observations were received from Bristows acting on behalf of Hamilton Bonaduz AG (Hamilton), and observations in reply were received subsequently from the requester. The observations were concerned solely with reasons for refusing the request (as provided for by Rule 96(2)).

3. The Patent was granted on 14 October 2008 and remains in force.

## Preliminary matters

4. I issued a previous opinion (09/18) on the patent regarding infringement of the patent. In that opinion I considered that the patent was infringed. Subsequently, it appears court proceedings were initiated by the patent proprietor alleging infringement. The defendant to those proceedings sought to defend the issue, at least in part, by way of a counterclaim that the patent was invalid based on certain prior art.

5. The patent proprietor now seeks a validity opinion based on the arguments and prior art put forward as part of the counterclaim.

6. The request was formed somewhat unusually, consisting essentially solely of the bundle of court documents without an explicit statement. The bundle contains both the defendant's arguments alleging invalidity and the claimant's (requester's) response to those arguments. The arguments are considered sufficiently clearly set

out that the opinion can proceed. To that end the opinion is based on the arguments set out in the claims table of Annex D of the defendant's re-amended counterclaim and the counter-arguments put forward in Annexes 1 and 2 of the claimant's re-amended response to the defendant's invalidity counterclaim. The opinion will only consider the validity of claims 1, 29, 40 and 45. In view of the fact that the request includes arguments both for and against the validity of the patent, I will refer as necessary to these being the claimant's and defendant's arguments rather than the requester's.

7. The observations only set out reasons why the opinion request should be refused. No observations relating to the validity of the patent were received. Counter-arguments regarding refusal were received as observations in reply.

8. Section 74A(3) of the Patents Act deals with refusal of opinions as follows:

> *Section 74A(3) The comptroller shall issue an opinion if requested to do so under subsection (1) above, but shall not do so –*
>
> *(a) in such circumstances as may be prescribed, or*
>
> *(b) if for any reason he considers it inappropriate to do so.*

9. Rule 94(1) of the Patent Rules sets out the prescribed circumstances:

> *Rule 94(1) The Comptroller shall not issue an opinion if –*
>
> *(a) the request appears to him to be frivolous or vexatious; or*
>
> *(b) the question upon which the opinion is sought appears to him to have been sufficiently considered any proceedings*

10. Having established that a date for a court hearing had been scheduled for July 2021, and that the opinion would issue before that date, Rule 94(1)(b) did not apply. Nevertheless, the Comptroller has wide ranging power under Section 74A(3) to refuse a request if he considers it inappropriate.

11. The observations argued that the request should be refused for the following broad reasons:

    (i) the court proceedings were at a late stage

    (ii) squeeze arguments were to apply in court

    (iii) expert witness evidence was soon to be filed

    (iv) an opinion would give rise to a risk of conflicting decisions

    (v) duplication was wasteful of resources

12. I have given very careful consideration to these arguments, especially regarding the

lateness with which this opinion has been sought. Ultimately I have decided that, as the requester is acting as a litigant in person and that there would still be several months between issue of the opinion and the hearing, it was not too late in the day to consider the request. In my view the opinion may be beneficial to the requester as it will provide her with an independent view on the merits of her case and may help her understand where the main issues lie. If the requester was not a litigant in person or the request had been received any nearer to the court date, the request would more than likely have been refused.

13. In relation to the squeeze argument raised, this relates to a common feature of infringement proceedings where a counterclaim of invalidity is raised. Typically the court will be invited by the defendant to adopt either a broad construction of the claim which results in the claim being infringed but invalid, or a narrow construction of the claim which results in the claim being valid but not infringed. Either way the defendant *wins*. However, these are not the only outcomes, and, despite the issues not being considered together I have already issued an opinion on infringement based on a particular construction of the claims. Although I am not bound to follow that construction in this opinion, the requester is not in a position to seek a different construction simply because I am now and separately considering the validity of the patent.

## The Patent

14. The patent relates to a system for controlling a ventilator, i.e. an artificial respirator for a patient. It seeks to provide an improvement on prior art open-loop control ventilators which required considerable skill and monitoring to provide effective treatment, especially of less medically stable patients. The invention provides a closed-loop feedback control system whereby the ventilator is controlled based on the measured levels of oxygen of the patient. In particular, the concentration of oxygen in the air provided to the patient and the pressure at the end of the expiration phase are controlled with the aim of achieving a target patient oxygen level. Measurements of other physical conditions of the patient, such as $CO_2$ level and lung function parameters, may additionally be included. Similarly, additional control of the ventilator to cover breathing frequency, tidal volume, etc., may be provided. Whilst the patent provides a detailed description of the closed-loop control regime, the claims define the invention more straightforwardly.

15. Figure 1 of the patent (reproduced below) provides an overview of the system. I note that the figure illustrates a digital processor (10) for analysing the inputs and computing the required outputs, and separately albeit linked, a signal generator circuit (46) for generating the signals (48) necessary to control the ventilator (56). Amongst the inputs to the digital processor is a signal from a patient oxygen sensor (30). The signal generator circuit is linked to an oxygen air mixer (62) for supplying the required concentration of oxygen to the patient.

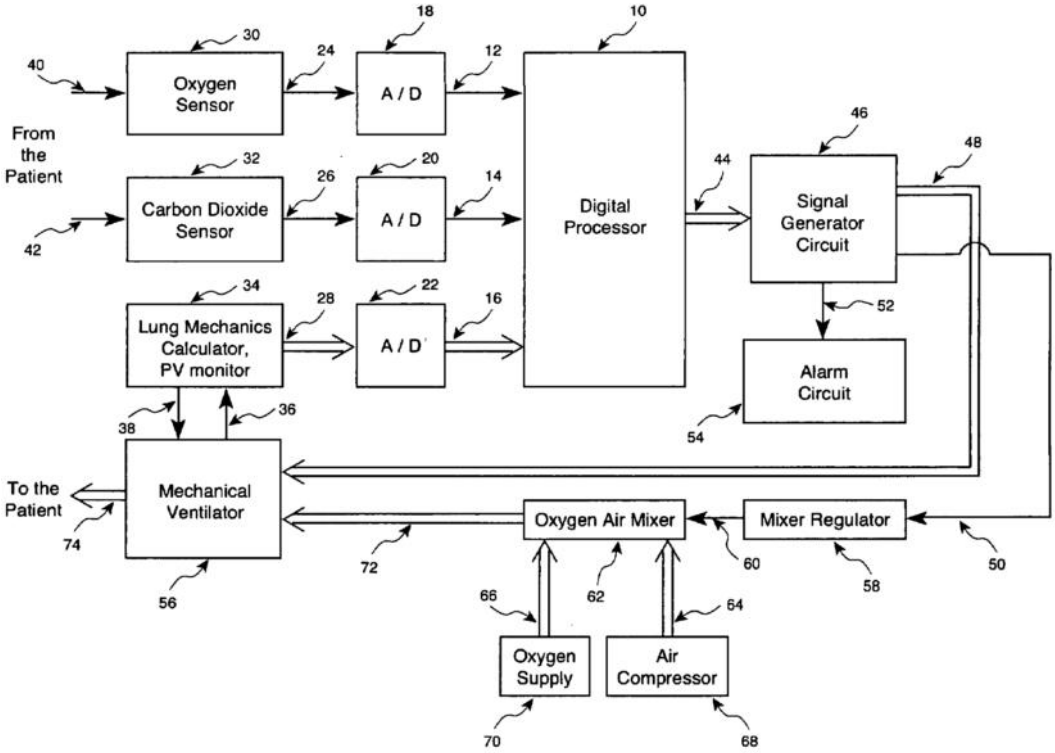


**Figure 1**

16. The patent provides the following definitions for certain terms:

> *Ventilator – a device which is used to provide total or assist ventilator treatment to patients, and includes mechanical ventilators (i.e. artificial respirators).*
>
> *PEEP – Positive end-expiratory pressure. [Typically expressed in cm $H_2O$].*
>
> *$FiO_2$ – Concentration of oxygen in a patient's inspiratory gas (fraction of inspired oxygen). $FiO_2$ for atmospheric air is 0.21 (i.e. 21% oxygen)*
>
> *I:E – ratio of inspiration time to expiration time*

17. One further important term which is used is $SpO_2$ to refer to the blood oxygen saturation percentage. It is a measurement of how much oxygen the red blood cells in the arteries of a person are carrying relative to the maximum amount they can carry. Typical levels in a healthy person are 95-99%. A similar measure used in the prior art is $PaO_2$ which is the partial pressure of oxygen in arterial blood. The normal range for healthy individuals of $PaO_2$ is 75-100 mm Hg.

18. The system primarily works by determining a value of $FiO_2$ based on the patient's $SpO_2$ level and setting this as the ventilator $FiO_2$ level accordingly. $FiO_2$ is determined either by way of a PID (proportional, integral, derivative) control regime, or, where more substantial changes in FiO2 are deemed necessary, by way of a stepwise control function. A ratio of PEEP to $FiO_2$ is then calculated based on the existing PEEP setting and the new $FiO_2$ level. If this ratio lies outside a

predetermined range then PEEP is adjusted to bring the ratio back within the predetermined range, with the proviso that PEEP is adjusted by small increments and 4 minutes is allowed to elapse between changes in PEEP.

## Claims

19. There are three independent claims (1, 29 and 45) all directed to automatically controlling a ventilator.

20. Claim 1 reads as follows. I note that the primary input to the control system is an indication of the measured oxygen level of the patient ($SpO_2$). This is used to control the $FiO_2$ level and PEEP value. I also note that the claim refers to first means, and second means operatively coupled to the first means.

> *1. An apparatus for automatically controlling a ventilator comprising:*
>
> *first means for processing data indicative of at least a measured oxygen level of a patient,*
>
> *and for providing output data indicative of required concentration of oxygen in inspiration gas of the patient (*$FiO_2$*) and positive end-expiratory pressure (PEEP) for a next breath of a patient,*
>
> *wherein* $FiO_2$ *is determined to reduce the difference between the measured oxygen level of the patient and a desired value;*
>
> *wherein PEEP is determined to keep a ratio of PEEP/* $FiO_2$ *within a prescribed range and while keeping the ratio within the prescribed range, to keep the measured oxygen level of the patient above a predefined value; and*
>
> *second means, operatively coupled to the first means, for providing control signals, based on the output data provided by the first means, to the ventilator*
>
> *wherein the control signals provided to the ventilator automatically control PEEP, and* $FiO_2$*, for a next breath of the patient.*

21. Claim 29 is set out below. It is largely equivalent to the apparatus of claim 1 save that it refers specifically to a programmable controller storing executable instructions rather than a first means.

> *29. An apparatus for automatically controlling a ventilator comprising:*
>
> *(a) means for providing a data signal indicative of the measured oxygen level of a patient;*
>
> *(b) a programmable controller storing executable instructions that when executed perform the steps of determining;*

*(i) required concentration of oxygen in an inspiratory gas of the patient,* $FiO_2$*, based on the data signal indicative of the measured level of the patient and to reduce the difference between the measured oxygen level of the patient and a desired value;*

*(ii) required positive end-expiratory pressure, PEEP wherein a ratio of PEEP/* $FiO_2$ *is maintained within a prescribed range, and to keep the measured oxygen level of the patient above a predefined value; and*

*(c) means for providing data signals indicative of the required* $FiO_2$ *and the required PEEP based upon the determining of step (b), for automatically controlling* $FiO_2$ *and PEEP for a next breath of the patient.*

22. Finally claim 45 is set out below. It is more complex than the apparatus of claims 1 and 29 in that the carbon dioxide level of the patient, the respiratory elastance and airway resistance are also measured. Furthermore, breathing frequency, ventilation, and inspiration to expiration time ratio are also controlled.

*45. An apparatus for automatically controlling a ventilator comprising:*

*(a) means for providing data indicative of the measured oxygen level of the patient;*

*(b) means for providing data indicative of the measured carbon dioxide level of the patient;*

*(c) means for providing data indicative of respiratory elastance, and respiratory airway resistance of the patient;*

*(d) a programmable controller storing executable instructions that when executed perform the steps of:*

*I) determining from the data indicative of the measured oxygen level of the patient provided by (a), a required concentration of oxygen in an inspiratory gas of the patient,* $FiO_2$*, to reduce a difference between the measured oxygen level of the patient and a desired value, and providing a data signal indicative of the required* $FiO_2$*;*

*II) determining a required positive end-expiratory pressure, PEEP, and providing a data signal indicative of the required PEEP, wherein the required PEEP maintains a ratio of PEEP/* $FiO_2$ *within the prescribed range, to keep the measured oxygen level of the patient above a predefined value;*

*III) determining, based upon the data provided by (a), (b) and (c), an optimal breathing frequency, a required ventilation, and a required adjustment in inspiration to expiration time ratio, I:E, for a next breath of the patient, and providing data signals indicative of the same; and,*

*(e) means for providing to the ventilator, based upon the data signals provided by (I), (II) and (III), final data signals for automatically controlling: (i) the required* $FiO_2$*, (ii) the required PEEP, (iii) optimal breathing frequency, (iv) the required ventilation, (v) the required adjustment in I:E ratio, for a next breath of the patient.*

23. For present purposes it should be noted that all the claims require a ratio of PEEP/ $FiO_2$ to be maintained within a prescribed range.

## Claim construction

24. As a first step in determining the validity of the patent I must correctly construe the claims. This means interpreting them in the light of the description and drawings as instructed by Section 125(1). In doing so I must interpret the claims in context through the eyes of the person skilled in the art. Ultimately the question is what the person skilled in the art would have understood the patentee to be using the language of the claims to mean. This approach has been confirmed in the decisions of the High Court in *Mylan v Yeda*[1] and the Court of Appeal in *Actavis v ICOS*[2].

25. The skilled person is considered to be a team comprising a critical care consultant, familiar with medical procedures, and a designer of ventilators familiar with the operation of mechanical ventilators and their control, including such automated control as is common general knowledge.

26. I have not been provided with any argument about how the claims should be construed.

27. I note firstly that the requirement in claim 1 is that a level for $FiO_2$ is *determined*. Whilst *determined* could be interpreted narrowly, e.g. *calculated*, I do not consider a narrow construction is appropriate in this instance. In particular, the patent describes two different control regimes which are both considered to be covered by the claim. Firstly, there is a rapid stepwise control scheme (¶¶ [0043], [0044], [0045], [0051]) which sets a slightly high, moderately high or high level of $FiO_2$ based on how far $SpO_2$ falls below a threshold value. Secondly, a proportional, integral, derivative (PID) control procedure (¶¶ [0045], [0051]) is implemented for fine-tuning calculation of $FiO_2$ based on $SpO_2$ when $SpO_2$ is in a more normal range. In the rapid stepwise control scheme, changes in $SpO_2$ do not necessarily result in changes in $FiO_2$, i.e. there is no direct relationship between $FiO_2$ and $SpO_2$. The system may *determine* that $FiO_2$ is not changed. I consider that the skilled person would understand *determined* should be construed broadly in order to encompass the different schemes described in the patent.

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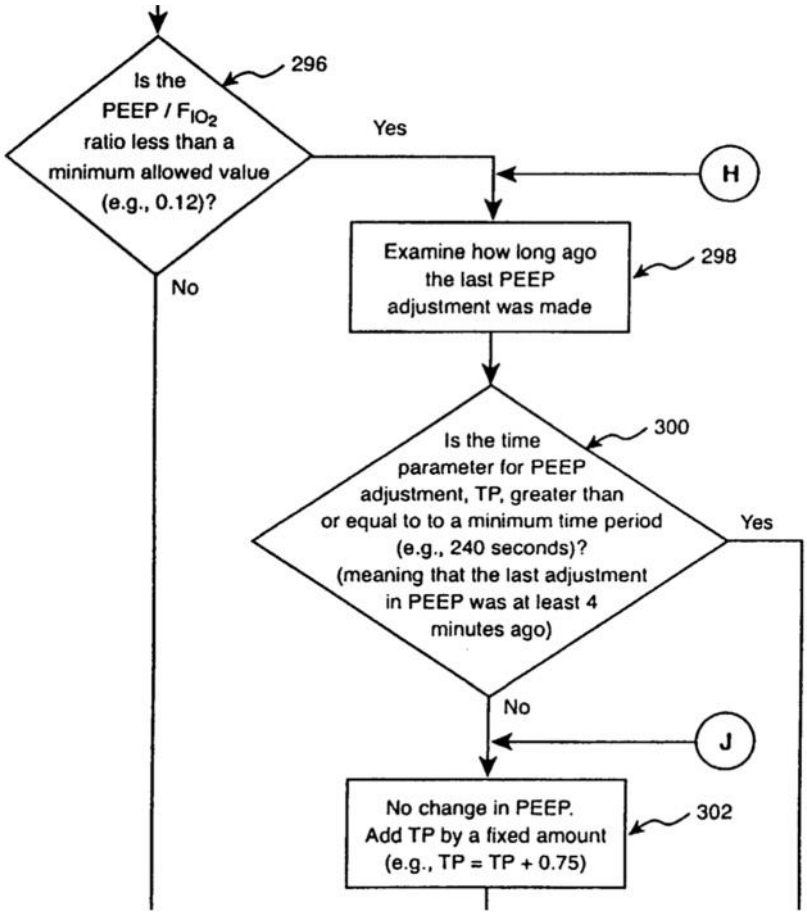
[1] *Generics UK Ltd (t/a Mylan) v Yeda Research and Dev. Co. Ltd & Anor* [2017] EWHC 2629 (Pat)
[2] *Actavis Group & Ors v ICOS Corp & Eli Lilly & Co.* [2017] EWCA Civ 1671

28. Claim 1 also requires that “PEEP is determined to keep a ratio of PEEP/ $FiO_2$ within a prescribed range and, while keeping the ratio within the prescribed range, to keep the measured oxygen level of the patient above a predefined value”. Claims 29 and 45 similarly require the ratio of PEEP/ $FiO_2$ to be maintained within a prescribed range. This phrase needs careful analysis to construe it in line with the teachings of the description.

29. As above, I consider that d*etermined* should be interpreted broadly, in line with the its interpretation for $FiO_2$.

30. The phrase specifies to “keep a ratio of PEEP/ $FiO_2$ within a prescribed range”. Yet it is evident from the specification as a whole that the ratio may lie outside the prescribed range. This is perhaps best illustrated by the flowchart of figure 3h, reproduced in part below.




31. In the steps preceding step 296, the level of $FiO_2$ is determined, e.g. by the PID controller, and a calculation is then made of PEEP/ $FiO_2$ by dividing the current value of PEEP by the new value of $FiO_2$. Then at step 296 this value of PEEP/ $FiO_2$ is compared with the lower value of the prescribed range, and if it is below the lower limit then control proceeds to steps 298 and 300. At step 300 a determination is made as to whether or not 4 minutes have elapsed since PEEP was last changed. If 4 minutes have not elapsed than at step 302 no change is made in PEEP. I.e. even though it is determined that the ratio of PEEP/ $FiO_2$ is outside the prescribed range, no attempt is made to alter it to bring it within the prescribed range. Once 4 minutes

have elapsed then PEEP is increased by a fixed incremental amount. However, that would not necessarily be sufficient to increase the PEEP/ $FiO_2$ ratio above the minimum, and the process may be repeated, including the 4 minute wait, until the ratio is above the minimum. A similar procedure exists for comparison of PEEP/ $FiO_2$ with the upper limit of the prescribed range.

32. I do not therefore consider that the embodiment of the patent can be said to *keep the PEEP/* $FiO_2$ *within the prescribed range* as that phrase might normally be understood. Instead the embodiment *aims* to keep it within the range and this phrase should be construed accordingly.

33. In relation to the scope of the *prescribed range*, it is apparent that there are certain maxima and minima associated with $FiO_2$ and PEEP. For example, minimum $FiO_2$ is 21%, corresponding to the normal level of oxygen in air, and maximum is 100%. For PEEP, the minimum is zero (PEEP being the pressure above normal atmospheric pressure) and the maximum typically ranges between 30 to 50 cm $H_2O$. These minima and maxima can be used to calculate a range of values for the PEEP/ $FiO_2$ of between 0 and about 1.4 (30/21). All ventilators will operate such that the ratio of PEEP/ $FiO_2$ is more or less within this range.

34. I do not however consider this to be a *prescribed* range, it is simply a naturally inherent range.

35. For comparison, the example upper and lower values for PEEP/ $FiO_2$ given in the patent are 0.24 and 0.12. No technical reasons are provided regarding these values. The corresponding part of the description specifies that "In performing the automatic PEEP adjustments, the PEEP/ $FiO_2$ ratio is kept within a clinically acceptable range." There is no disclosure of what constitutes a clinically acceptable range beyond the example values used. They correspond to PEEP values between 2.5 to 5 cm $H_2O$ at 21% $FiO_2$ and 12 to 24 cm $H_2O$ at 100% $FiO_2$. It is notable that the values of PEEP are clinically acceptable throughout the whole range of $FiO_2$ values, but I do not consider that the skilled person would understand the phrase "clinically acceptable range" to be restricted in this way.

36. I have to say that, without any disclosure of what constitutes a clinically acceptable range, then, unless the patent lacks sufficiency, the skilled person must understand what the clinically acceptable range is.

37. I consider that when construing what constitutes a *prescribed* range of the ratio PEEP/ $FiO_2$, the skilled person would not expect an explicit statement that this ratio is maintained within precise boundaries. That would amount to unacceptable parametritis, i.e. attempting to define an invention by reference to inherent parameters. What I consider is required is some disclosure that lower values of $FiO_2$ are only associated with low values of PEEP and high values of $FiO_2$ are only associated with high values of PEEP, and that the prescribed range of the ratio of PEEP/ $FiO_2$ should be construed accordingly.

## Prior art

38. The following are the main prior art documents referred to:

*Waisel D. B., Fackler J. C., Brunner J. X. & Kohanne I. "PEFIOS: An Expert Closed-Loop Oxygenation Algorithm"; MEDINFO 95 Proceedings; 1995. (**Waisel**).*

*Anderson J. R. & East, T. D. "A closed loop controller for mechanical ventilation of patients with ARDS"; Proceedings of the Annual Rocky Mountain Bioengineering Symposium, Vol. 39, pp. 289-294; 2002. (**Anderson**).*

*Tehrani, F. "A Dual Control System for Ventilatory Treatment of Premature Infants"; Proceedings of the 5th International Conference on Information Systems, Analysis and Synthesis; Volume 8, Concepts and Applications of Systemics, Cybernetics and Informatics; 31 July – 4 August 1999. (**Tehrani**).*

39. These documents were all published before the filing date of the patent.

40. I shall consider each of these documents in turn below.

## Waisel

41. Waisel describes a closed-loop, computer controlled, expert algorithm for controlling a ventilator. It adjusts levels of PEEP and $FiO_2$ based on a patient's measured oxygen levels. Although the paper refers to measuring a patient's arterial oxygen saturation ($SaO_2$), it specifies that these measurements are made using a pulse oximeter and references to $SaO_2$ are therefore considered to be $SpO_2$. The two are of course very closely related and whichever is used makes no difference to the issues being considered.

42. The algorithm, known by the acronym PEFIOS, controls the ventilator by decreasing therapy ($FiO_2$ and/or PEEP lowered) if measured $SaO_2$ is above a target level or increasing therapy ($FiO_2$ and/or PEEP raised) if $SaO_2$ is below a target level. For each of the decreasing or increasing therapy regimes there are two levels of change, a rapid change when measured $SaO_2$ deviates significantly from target and a slow change when the difference between $SaO_2$ and target is less.

43. Figure 1 of Waisel, reproduced below, illustrates a look-up table which shows how PEEP and $FiO_2$ are changed by PEFIOS. Although the caption refers to therapy slowly decreasing, this appears to be an error and it is meant to refer to slowly increasing therapy.

| $FiO_2$ | PEEP | ≥5 ≤8 | >8 ≤12 | >12 ≤15 | >15 ≤20 | >20 ≤25 |
|---|---|---|---|---|---|---|
| =1 | PEEP | 2 | 1 | 1 | 1 | 1 |
| | $FiO_2$ | 0 | 0 | 0 | 0 | 0 |
| <1 | PEEP | 2 | 1 | 1 | 1 | 0 |
| ≥0.8 | $FiO_2$ | 0 | 0 | 1 | 1 | 1 |
| <0.8 | PEEP | 1 | 1 | 1 | 0 | 0 |
| ≥0.6 | $FiO_2$ | 0 | 0 | 1 | 1 | 1 |
| <0.6 | PEEP | 1 | 0 | 0 | 0 | 0 |
| ≥0.4 | $FiO_2$ | 0 | 1 | 2 | 2 | 2 |
| <0.4 | PEEP | 0 | 0 | 0 | 0 | 0 |
| ≥0.21 | $FiO_2$ | 1 | 2 | 3 | 3 | 3 |

Figure 1. Level 2: Therapy Slowly Decreasing

Number from PEFIOS Table

| $FiO_2$ | Action |
|---|---|
| -4 | decrease $FiO_2$ by 0.1 every 15 minutes |
| -2 | decrease $FiO_2$ by 0.1 every 30 minutes |
| -1 | decrease $FiO_2$ by 0.05 every 15 minutes |
| 1 | increase $FiO_2$ by 0.1 every 15 minutes |
| 2 | increase $FiO_2$ by 0.2 every 15 minutes |
| 3 | increase $FiO_2$ by 0.3 every 15 minutes |

| PEEP | Action |
|---|---|
| -3 | decrease PEEP by 3 $cmH_20$ every 2 hours |
| -2 | decrease PEEP by 2 $cmH_20$ every 2 hours |
| -1 | decrease PEEP by 1 $cmH_20$ every 2 hours |
| 1 | increase PEEP by 2 $cmH_20$ every 30 minutes |
| 2 | increase PEEP by 4 $cmH_20$ every 30 minutes |
| 3 | increase PEEP by 6 $cmH_20$ every 30 minutes |

44. Based on this table it can be seen that a patient receiving very little oxygen ($FiO_2$ < 0.4) and at low pressure (PEEP >5 <8; i.e. bottom left of table) but with a measured $SaO_2$ below target, will receive slowly increasing levels of oxygen (increase $FiO_2$ by 0.1 every 15 minutes) until $FiO_2$ reaches 0.4. At that point the algorithm starts slowly increasing PEEP until PEEP >8, at which point $FiO_2$ is increased again whilst maintaining constant PEEP. The therapy will continue to increase based on the table until the patient's $SaO_2$ level is above the target level. The control algorithm will then switch to a slowly decreasing therapy mode to slowly reduce the levels of $FiO_2$ and PEEP based on the equivalent look-up table for slowly decreasing therapy.

45. The equipment used by the Waisel system comprises an Amadeus ventilator, a pre-processor and a host computer. The Amadeus ventilator operates either in a manual mode or an automated mode. In the automated mode the host computer has control over the Amadeus ventilator. The pre-processor analyses the analog signals from the ventilator and patient sensors, and communicates with the host computer.

46. The requester has provided argument in the form of the defendant's claim comparison chart, arguing that the claims lack validity, and the claimant's counter-arguments.

47. On the whole I have not found the counter-arguments particularly helpful. For example, the claimant has denied that the apparatus of the prior art documents is for automatically controlling a ventilator. There is no basis for such a denial. There is also much irrelevant argument, for example arguing that the prior art documents are not refereed publications. This is immaterial for present purposes; the skilled person reads and considers all prior art. There are also irrelevant arguments comparing how the prior art works with how the embodiment of the patent works which do not take account of the scope of the claims.

48. One argument put forward is that Waisel does not disclose outputting data for controlling a *next breath* of the patient on the basis that adjustments are made only periodically. I do not agree with this reasoning. Firstly, it seems that the $FiO_2$ and PEEP data are sent continuously to the ventilator irrespective of whether or not there are any changes. In Waisel it states (paragraph 2.1) "PEFIOS is designed to provide

continuous and total management of … routine ventilatory care." Secondly, at least for PEEP, the embodiment disclosed in the patent works similarly, and requires 4 minutes to elapse between changes in PEEP.

49. There is also an argument that because the $FiO_2$ levels in Waisel are determined by means of a look-up table, it is not being determined to "reduce the difference between the measured oxygen level of the patient and a desired value". The fact that a look-up table is used is considered immaterial. It is the goal of all ventilator therapies to raise an unhealthily low oxygen level to a healthy one. Waisel is no different. In particular, Waisel specifies that "Therapy never plateaus; it either increases or decreases in small steps." Thus the PEFIOS system increases $FiO_2$ and/or PEEP when $SaO_2$ is below target and decreases $FiO_2$ and/or PEEP when $SaO_2$ is above target, such that it is always seeking to reduce the difference between measured and target $SaO_2$ levels as required by claim 1. Even if $FiO_2$ is not being changed, in preference to a change in PEEP, I consider that it is still being *determined* to reduce the difference.

50. As set out below, I agree largely with the defendant's claims table, that the Waisel system has most of the features required to fall within the scope of claim 1. There is however no explicit disclosure of maintaining the ratio of PEEP/$FiO_2$ within a prescribed range.

| **Claim 1** | **Waisel 95** |
|---|---|
| An apparatus for automatically controlling a ventilator comprising: | **2.1** …<br>*PEFIOS is designed to provide continuous and total management of non-emergent, routine ventilatory care.* |
| first means for processing data indicative of at least a measured oxygen level of a patient, | **2. Materials and Methods**<br>PEFIOS is driven with input from a pulse oximeter …<br><br>**2.3 Equipment**<br>VW#1 operates in … automated mode, in which a host computer has control over Amadeus. |
| and for providing output data indicative of: required concentration of oxygen in inspiratory gas of the patient ($FiO_2$) and positive end-expiratory pressure (PEEP) for a next breath of the patient; | **2. Materials and Methods**<br>Associated with each level is a table of $FiO_2$ and PEEP adjustments based on the current $FiO_2$, PEEP, and distance of the level from the goal saturation. |
| wherein $FiO_2$ is determined to reduce the difference between the measured oxygen level of the patient and a desired value; | **2. Materials and Methods**<br>A measured $SaO_2$ greater than the goal saturation decreases therapy and $SaO_2$ less than the goal saturation increases therapy. Two levels of decreasing therapy and two levels of increasing therapy flank the goal saturation… Associated with each level is a table of $FiO_2$ and PEEP adjustments based |

| | |
|---|---|
| | on the current $FiO_2$, PEEP, and distance of the level from the goal saturation. |
| wherein PEEP is determined to keep a ratio of PEEP/$FiO_2$ within a prescribed range and, while keeping the ratio within the prescribed range, to keep the measured oxygen level of the patient above a predefined value; and | |
| second means, operatively coupled to the first means, for providing control signals, based on the output data provided by the first means, to the ventilator; | **2.3 Equipment**<br>The ventilator workstation (VW#1) is a fully programmable, mechanical ventilator based on the Amadeus, a microprocessor controlled ventilator. The VW#1 consists of three parts: a remote controllable Amadeus, a pre-processor to analyse analog data … and the arbiter host. |
| wherein the control signals provided to the ventilator | **1. Introduction**<br>*We describe our preliminary experience with a closed-loop, computer-controlled, expert algorithm that allows automated changes in positive end expiratory pressure (PEEP) and fraction of inspired oxygen (*$FiO_2$*) based on arterial oxygen saturation (PEFIOS).* |
| automatically control PEEP, and $FiO_2$, for a next breath of the patient. | **2.3 Equipment**<br>VW#1 operates in … automated mode, in which a host computer has control over Amadeus. |

51. Figure 1 of Waisel indicates a minimum PEEP of 5 cm $H_2O$ and a maximum of 25 cm $H_2O$. Although values of PEEP/$FiO_2$ are constrained to lie in a range, this seems no different to the inherent range discussed earlier.

52. I have also previously set out that the phrase "wherein PEEP is determined to keep a ratio of PEEP/ $FiO_2$ within a prescribed range" should be construed as requiring low values of $FiO_2$ to be associated with low values of PEEP and vice versa. At first glance, this is inconsistent with the look-up table provided as figure 1 which also associates low values of $FiO_2$ with high values of PEEP and high values of $FiO_2$ with low values of PEEP.

53. However, Waisel includes a further figure which shows the PEFIOS display screen. Figure 2 (below) is accompanied by the further text:

> *The PEFIOS software displays the graph of the trajectory of PEFIOS control along with designating the patients current state (Figure 2). A clinician can look at the graph and immediately know about the last therapy change and where the patient is in the therapy adjustment level (rapid v. slow, increase*

*v. decrease); she can also understand PEFIOS goals for $FiO_2$ and PEEP.*

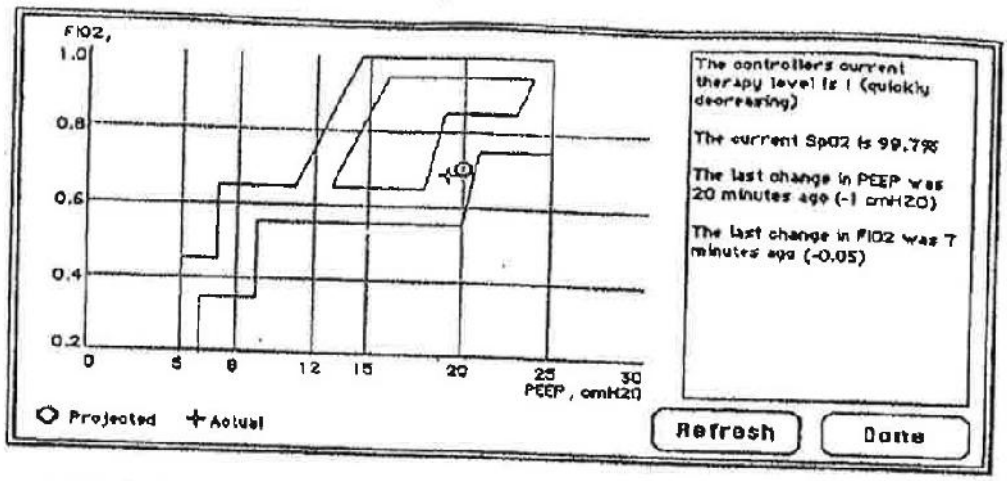



Figure 2. The PEFIOS Location Screen. The graph shows the location of the patient within the therapy continuum, and the dialogue announces the therapy level, current saturation, and last therapy adjustments.

54. Of particular note is the reference to the therapy continuum in the caption to the figure. The skilled person would understand that this is a reference to the zig-zag track superimposed on the graph which represents the ideal zone within which $FiO_2$ and PEEP should be maintained. This track, at least in part, broadly correlates with the figure 1 look-up table. As outlined previously, for low $FiO_2$ (< 0.4) and low PEEP (<8) FiO2 only is increased. This is followed by increases in PEEP only, then increases in FiO2 only until FiO2 is between 0.6 and 0.8 and PEEP is between 12 to 15. At this point $FiO_2$ and PEEP are increased simultaneously, and this corresponds to the long diagonal on the track.

55. Based on this graph I consider that the skilled person would understand that, whilst the look-up table includes combinations of low $FiO_2$ and high peep, and vice versa, the aim of the look-up table is to keep values of $FiO_2$ and PEEP within the therapy continuum illustrated in figure 2. The values in the look-up table which lie outside the continuum are intended to bring FiO2 and PEEP back within the continuum as quickly and safely as possible.

56. This therapy continuum defines a range of values of PEEP/$FiO_2$ within which the therapy is intended to be maintained. At least for the look-up table of figure 1 and the slowly increasing therapy regime, PEFIOS *aims* to keep the ratio of PEEP/$FiO_2$ within a prescribed range of values

57. Ultimately however, the figure 1 look-up table of Waisel is the only look-up table provided. There are no similar tables for rapidly increasing therapy or either of the decreasing therapy regimes. As this table only represents a part of the therapy regime, it is not possible, based on this table alone, to say that PEEP/$FiO_2$ is maintained at a prescribed range across the whole of the therapy regime.

58. To an extent, the disclosure of the therapy continuum illustrated in figure 2 is similarly limited. The text in the display indicates that the current therapy level is *quickly decreasing.* It also broadly correlates with the slowly increasing therapy regime illustrated in the look-up table. There is however no disclosure of whether or

not the same or even any similar therapy continuum applies to the other therapy regimes.

59. Waisel is therefore considered to lack disclosure of PEEP and $FiO_2$ values for at least the rapidly increasing and slowly decreasing therapy regimes. It similarly lacks disclosure of whether or not these regimes operate to a similar therapy continuum to that illustrated in figure 2. I do not see that it discloses maintaining a ratio of PEEP/$FiO_2$ within a prescribed range across the whole range of therapies.

60. Given this lack of disclosure, I consider that Waisel does not anticipate claim 1.

61. Nevertheless, I consider that it would be obvious to the skilled person to adopt a similar therapy continuum and a correspondingly similar look-up table for all the therapy regimes of Waisel. In particular, it would be obvious to the skilled person that the therapy continuum of figure 2 applies across all therapy regimes and corresponding suitable look-up tables would also be obvious. The PEFIOS system so implemented would aim to keep values of PEEP and $FiO_2$ within the therapy continuum across all therapy regimes, such that it is considered to meet the claim 1 requirement of "wherein PEEP is determined to keep a ratio of PEEP/$FiO_2$ within a prescribed range" as I have construed it. The PEFIOS system is also considered to possess all the other features of claim 1 as outlined in the claims chart.

62. On the basis therefore that it would be obvious to the skilled person to implement the PEFIOS system so that it aims to maintain PEEP and $FiO_2$ within the therapy continuum of figure 2 (or similar) for each of the therapy regimes, I consider that claim 1 lacks an inventive step based on Waisel and common general knowledge.

63. Claim 29 is considered sufficiently similar to claim 1 that it too is considered to lack an inventive step based on Waisel and common general knowledge.

64. Claim 40, which is also alleged to be invalid, reads as follows:

> *40. The apparatus of claim 29*
>
> *wherein in use the required concentration of oxygen in the inspiratory gas of the patient (FIO2) is calculated using a stepwise control scheme and/or by using a proportional-integral-derivative technique.*

65. I consider the control of $FiO_2$ indicated in figure 1 of Waisel, and in particular the instruction to raise or lower $FiO_2$ by, for example, 0.1 every 15 minutes comprises a stepwise control scheme. This claim is therefore also considered to lack an inventive step.

66. In common with claims 1 and 29, independent claim 45 requires that PEEP is determined to maintain a ratio of PEEP/$FiO_2$ within a prescribed range. It also requires additional sensors, for determining further clinical parameters of the patient, and controls additional functions of the ventilator.

67. I suspect that the additional sensors and functions of the ventilator system of this claim may form part of the skilled person's common general knowledge. However, I have not been provided with any evidence. In view of a lack of evidence and

insufficient argument I decline to reach an opinion on the inventiveness of this claim.

## Anderson

68. Anderson describes a closed-loop control system for mechanical ventilation of patients. The system comprises a patient arterial oxygenation monitor, a computer and a Hamilton Amadeus ventilator as illustrated in figure 1 (reproduced below).

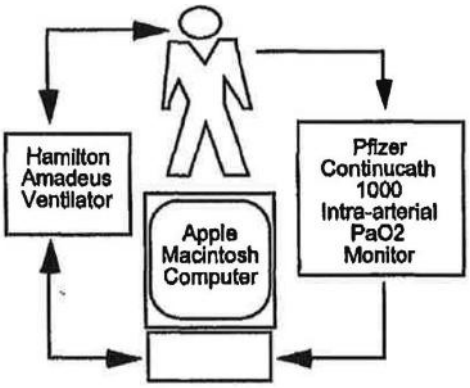



Figure 1. Hardware components of closed-loop control system.

69. The computer reads information from both the $PaO_2$ monitor and the ventilator and uses this information to calculate target values for PEEP and $FiO_2$. The closed loop controller is implemented in software on the computer and the basic elements of it are illustrated in Figure 2 of Anderson.

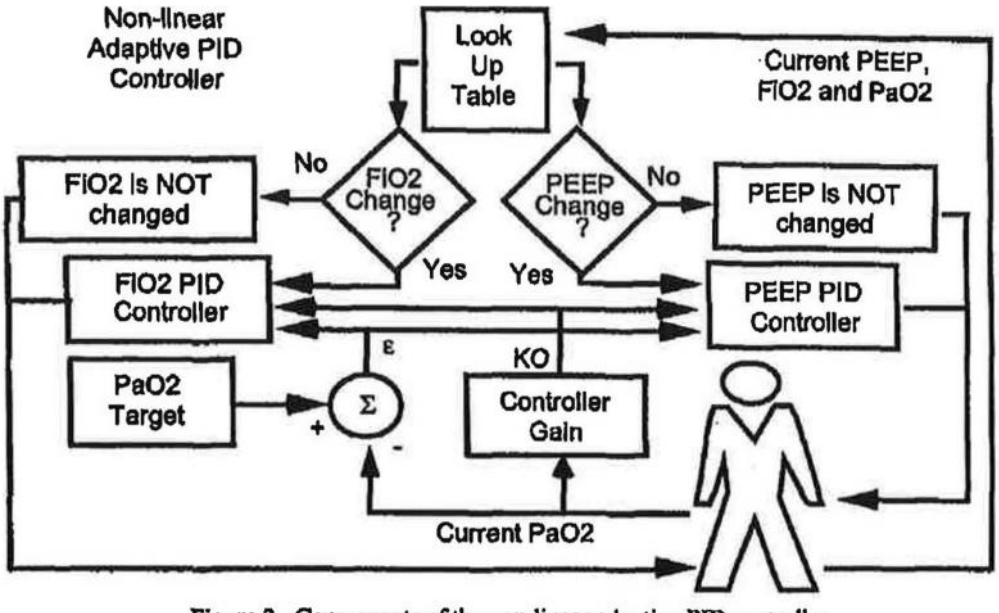



Figure 2. Components of the non-linear adaptive PID controller.

70. A look-up table is provided which monitors the current values of PEEP, $FiO_2$ and $PaO_2$ and determines if changes to PEEP and/or $FiO_2$ are necessary. An example of the look-up table for a *threatening* situation is provided as figure 3 (below). It will be noted that the look-up table indicates only whether PEEP (P), $FiO_2$ (F) or both (B) are to be changed with no indication of the manner of the change. I note also that

other look-up tables are indicated for *marginal*, *acceptable*, *satisfactory* and *supersatisfactory* situations. If any changes are considered necessary then a pair of PID controllers are provided which calculate new values based on a difference between the target $PaO_2$ and measured $PaO_2$. The controller gain is variable so that more aggressive changes are made when there is a large difference between measured and target $PaO_2$, conservative changes for a small difference and the gain turns negative when measured $PaO_2$ is above the target level.

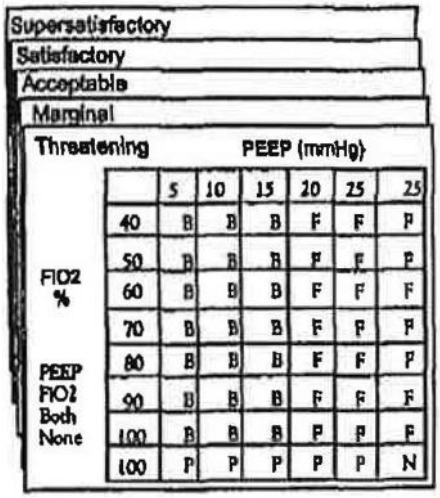



**Figure 3. Look Up Tables determine the therapy parameters to be changed based on current PEEP, FiO2 and PaO2 category.**

71. Figure 7 of Anderson illustrates a typical plot of $PaO_2$, $FiO_2$ and PEEP values over time for a patient ventilated with the Anderson system.

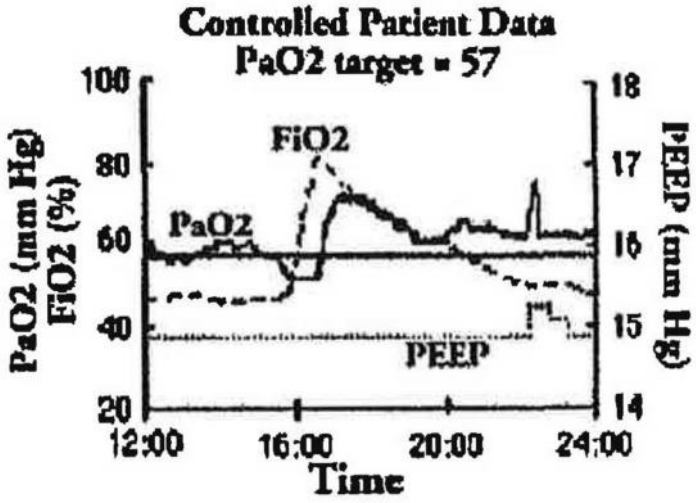



**Figure 7. Typical patient data showing the controller's maintenance of PEEP and FiO2.**

72. The graph of figure 7 shows $FiO_2$ increasing from about 50% to 80% in response to a drop in the patients $PaO_2$, followed by a gradual decline in $FiO_2$ as the patient improves. PEEP during this period remains constant. There is a small rise in PEEP at a much later time, which appears to be related to a brief increase in the patients $PaO_2$ level, but there does not appear to be any corresponding change in $FiO_2$. The

changes in PEEP and $FiO_2$ in this graph do not appear to match the example look-up table provided.

73. Based on the above graph, I do not consider that a ratio of PEEP/ $FiO_2$ is being maintained within a prescribed range. For a significant increase in $FiO_2$ there is no accompanying change in PEEP. Furthermore, I see nothing in Anderson to indicate that a ratio of PEEP/$FiO_2$ is of any interest. The look-up tables provide for independent changes of PEEP and $FiO_2$ in certain situations. The magnitude of any change to these values is calculated by the PID controller based only on the difference between the measured $PaO_2$ and a target $PaO_2$. There is no suggestion that the changes need be limited based on a ratio of PEEP/$FiO_2$.

74. The defendant refers in the claims table to figures 5 and 6 being of interest to the PEEP/$FiO_2$ ratio. However, these graphs are based on open-loop bench testing of the system. There is no measurement of $PaO_2$ which is fed back to the controller and the difference between measured and target $PaO_2$ is constant. These are not therefore realistic portrayals. Despite this there is some support in the graph of figure 6, which shows a ratio of PEEP/$FiO_2$ being held within a narrow range. This is merely a result of the PID controller using the same information to change both PEEP and $FiO_2$ when instructed to do so by the look-up table. It does not apply when the look-up table requires only one of these values to be changed. Furthermore, these graphs are based on only two of the treatment scenarios, *threatening* and *supersatisfactory*. There is no information on how the system responds in the other treatment scenarios. If the system is to meet the requirement of claim 1 that the PEEP/FiO2 ratio is maintained within a prescribed range, then it must do so across the whole range of automatic treatment protocols.

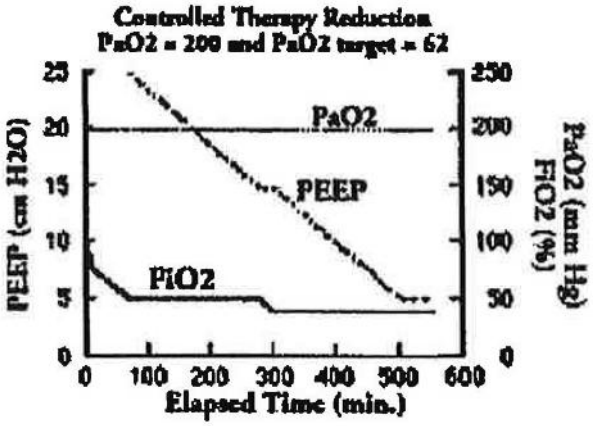



Figure 5. Controller's open loop response to "Supersatisfactory" patient PaO2.

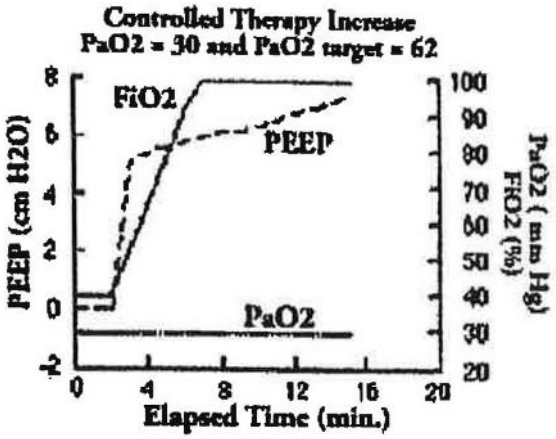



Figure 6. Controller's open loop response to "Threatening" patient PaO2.

75. On the basis that Anderson does not disclose maintaining the PEEP/$FiO_2$ ratio within a prescribed range I consider that it does not anticipate claim 1 of the patent.

76. Furthermore, based on the manner in which values of PEEP and $FiO_2$ are calculated by the PID controller, I do not consider it obvious to introduce some means for maintaining the PEEP/$FiO_2$ ratio within a prescribed range. I therefore consider that claim 1 is also inventive in relation to Anderson.

77. As I consider that Anderson is distinguished from the patent by virtue of its lack of disclosure of maintaining the PEEP/$FiO_2$ ratio within a prescribed range, claims 29 and 45 are also not anticipated by Anderson. Similarly, claims 29 and 45 are considered to be inventive in relation to it.

78. Although I consider that the claims are novel and inventive based on Anderson by virtue of the above, I shall briefly consider some of the requester's other arguments.

79. On the face of it, aside from the lack of disclosure regarding maintaining the PEEP/$FiO_2$ ratio, Anderson discloses all the other features of claim 1 as set out in the defendant's claim table.

80. As with Waisel, the claimant's counter-arguments are not on the whole particularly helpful. There are similar claims that the paper is not refereed and also claims that the results are inconsistent with other results, but these do not preclude the skilled person from considering its content.

81. The claimant also maintains that the PID control is inconsistent with the look-up table. The claimant seems to be suggesting that because PID is supposed to operate continuously, it cannot be used on an intermittent basis in conjunction with the look-up table. I see no reason why the PID controllers cannot be bypassed or ignored when no adjustment is required as is ably illustrated in figure 2 of Anderson. I see no basis for such inconsistency.

82. The claimant also argues that the PID equations used are incorrect and there is no description of the coefficients used. The PID equations are written in a very vague manner such that it is not apparent they are incorrect. There may be an argument that this aspect of the disclosure is not enabling. However, even if not enabling the appropriate PID equations to use may be obvious. In view of the conclusion I have already reached, I do not need to decide this point. Further evidence would probably be required relating to the skilled person's knowledge at the priority date before a decision on this point could be satisfactorily reached.

83. Further counter-argument has been made based on the immediacy of changes to PEEP by the PID controller of Anderson. The claimant suggests that this would not work as changes in PEEP require time to have a measurable impact on patient's oxygenation level as set out in the patent, which requires a period of 4 minutes between making changes. This delay is not a feature of claim 1 so the argument is not relevant in determining whether or not the Anderson system falls within the scope of the claims. In any event, I consider that there would be no issue provided an appropriate PID equation for PEEP was implemented.

## Tehrani

84. I shall deal very briefly with this document.

85. Tehrani discloses a model for controlling a ventilator for premature infants. A dual control system is used. The mechanical aspects of the ventilator are controlled by a first controller which measures $PaO_2$, $PaCO_2$, respiratory compliance, airway resistance, metabolic rate and barometric pressure. The oxygen mixture $FiO_2$

supplied to the ventilator is controlled by a PID controller which adjusts levels of $FiO_2$ based on a difference between target $PaO_2$ and measured $PaO_2$. There is no mention of PEEP in this document, nor does there appear to be any direct analogue for PEEP. It is possible that PEEP is controlled by the first controller as part of the mechanical control of the ventilator, although this is not discussed. It seems more likely that PEEP is not controlled, and it would be fixed by a doctor for premature infants as it typically only varies between 5-7 cm $H_2O$ in such cases. It is nevertheless clear that, even if PEEP is controlled, it is entirely independent of $FiO_2$. Consequently there is no disclosure of maintaining a $PEEP/FiO_2$ ratio within a prescribed range. For this reason, claims 1, 29 and 45 are not anticipated by this document. Furthermore, it is not considered obvious to add control of PEEP based on $FiO_2$ to the system of this document. Claims 1, 29 and 45 are also considered to be inventive in relation to this document.

## Opinion

86. Based on the evidence and arguments provided, I consider that claims 1, 29 and 40 of the patent lack an inventive step based on Waisel in combination with the skilled person's common general knowledge.

87. The inventiveness of the remaining claims has not been considered.

## Application for review

88. Under section 74B and rule 98, the proprietor may, within three months of the date of issue of this opinion, apply to the comptroller for a review of the opinion.

Matthew Jefferson
Examiner

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**NOTE**

*This opinion is not based on the outcome of fully litigated proceedings. Rather, it is based on whatever material the persons requesting the opinion and filing observations have chosen to put before the Office.*