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# D E C I S I O N
# of 6 July 2000

**Case Number:** T 0504/98 - 3.4.2

**Application Number:** 90900765.0

**Publication Number:** 0449899

**IPC:** G01N 21/64, G01N 33/48

**Language of the proceedings:** EN

**Title of invention:**
A method of photometric *in vitro* determination of the content of oxygen in a blood sample

**Patentee:**
Radiometer Medical A/S

**Opponent:**
AVL Medical Instruments AG

**Headword:**
-

**Relevant legal provisions:**
EPC Art. 56

**Keyword:**
"Inventive step (confirmed)"

**Decisions cited:**
-

**Catchword:**
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Beschwerdekammern | Boards of Appeal | Chambres de recours

**Case Number:** T 0504/98 - 3.4.2

**D E C I S I O N**
**of the Technical Board of Appeal 3.4.2**
**of 6 July 2000**

**Appellant:** (Opponent)
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**Decision under appeal:** **Decision of the Opposition Division of the European Patent Office posted 26 March 1998 rejecting the opposition filed against European patent No. 0 449 899 pursuant to Article 102(2) EPC.**

**Composition of the Board:**

**Chairman:** E. Turrini
**Members:** A. G. Klein
V. Di Cerbo

## Summary of Facts and Submissions

I. The opposition filed against European patent No. 0 449 899 (application No. 90 900 765.0) was rejected by decision of the Opposition Division.

The opposition was founded on the ground set out in Article 100(a) EPC that the subject-matter of the patent was not patentable, in view in particular of the contents of the following documents:

D2: GB-A-2 025 065;

D4: US-Re.31 179;

D6: EP-A-0 138 152; and

D11: N. Bridges et al, "Evaluation of a new system for haemoglobin measurement" American Clinical Products Review, April 1987, pages 22 to 25.

II. The appellant (opponent) filed an appeal against the decision rejecting the opposition.

III. Oral proceedings were held on 6 July 2000 at which the appellant submitted the following further documents:

Ref. 2: G.J. Kost, "New Whole Blood Methods and Instruments: Glucose Measurement and Test Menus for Critical Care, JIFCC, Volume 3, Issue 4, September 1991, pages 160 to 172;

Ref. 3: G.P. Zaloga, "Bedside blood gas and electrolyte monitoring in critically ill patients", Critical Care Medicine, 1989, Volume 17, No. 9, pages 920 to 925; and

Ref. 5: J.B. Riley, "In Vitro Measurement of the Accuracy of a New Patient Side Blood Gases, pH, Hematocrit and Electrolyte Monitor, Journal of Extra-Corporal Technology, 19 [3], Fall 1987, pages 322 to 329.

At the end of the oral proceedings, the appellant requested that the decision under appeal be set aside and that the patent be revoked.

The respondent (proprietor of the patent) for his part requested that the appeal be dismissed and that the patent be maintained as granted, with a set of claims of which claims 1, 3 and 11, the only independent claims, read as follows:

"1. A method of photometric in vitro determination of the content of oxygen in a blood sample by means of luminescence quenching and wherein a luminophor is utilized the luminescence of which is quenched in the presence of oxygen and the content of oxygen is determined on the basis of a luminescence characteristic of the luminescence emitted from the excited luminophor,
characterized in,
that the blood sample is transferred from an in vivo locality to the sample container (23;5000) of a sampling device (2), said sample container (23;5000) having a measuring chamber (500;5007) with an at least locally transparent wall part (5003) and containing a luminophor
that the connection between the sampling device (2) and the blood circulation is broken after the filling of the sample container (23;5000) with blood sample,
that the measuring chamber (500;5007) is brought into

optical communication with an optical system (50) comprising a radiation source (501) and a radiation detector (507),
that the luminophor provided within the measuring chamber (500;5007) is excited by irradiation with radiation from the radiation source (501), and
that a luminescence characteristic of the luminescence emitted from the luminophor is determined on the basis of the luminescence detected at the radiation detector (507)."

"3. A sampling device (2) comprising a sample container (23;5000) with a measuring chamber (500;5007) having an at least locally transparent wall part (5003) and an inlet opening (21 ;5006),
characterized in,
that the sample container (23;5000) apart from the inlet opening (21;5006) is an essentially sealed container and that the measuring chamber (500;5007) contains a luminophor, the luminescence of which is quenched in the presence of oxygen."

"11. A system (10) for photometric in vitro determination of the content of oxygen in a blood sample,
characterized in,
that the system comprises a sampling device (2) with a sample container (23;5000) which apart from an inlet opening (21) is essentially sealed and wherein a measuring chamber (500;5007) with an at least locally transparent wall part contains a luminophor the luminescence of which is quenched in the presence of oxygen, and that the system (10) further comprises an analyzer (11) with an optical system (50) comprising a radiation source (501) and a radiation detector (507),

said analyzer further comprising means for providing optical communication between the optical system and the measuring chamber of the sampling device and means for registering the luminescence detected at the radiation detector."

IV. In support of his requests the appellant submitted that document D6 disclosed a sampling device from which the sampling device set out in claim 3 was distinguished only in that it contained a luminophor so as to permit measurement of oxygen in blood by luminescence quenching. Document D6 however explicitly pointed at the possibility of using the device disclosed there in routine blood chemistry such as glucose, blood urea nitrogen, albumine, bilirubine, total protein, etc., and numerous other analytical tests. Since the monitoring of blood oxygen by luminescence quenching was a well-know analytical test, as was acknowledged in the patent in suit, and since the only other standard method available at the filing date for blood oxygen measurements was the electrochemical method using electrodes, selecting the former method could not be considered to involve an inventive step.

Alternatively, document D4 related to the *in vivo* measurement of oxygen concentration by luminescence quenching, using a measuring cell disposed in the patient's blood flow. The alleged invention in effect consisted in an obvious improvement of the technique disclosed in document D4 so as to allow the measurements being performed at a location separate from the patient's blood flow. The use for that purpose of a substantially closed container was know e.g. from documents D6 or D11.

In respect of the documents Ref. 2, Ref. 3 and Ref. 5 submitted at the oral proceedings, the appellant insisted that they were not to be considered as disclosing additional prior art. They had been filed only to show that the relevant skilled person did not make any difference of principle between techniques aiming at establishing routine blood chemistry on the one hand and the monitoring of oxygen in blood on the other, contrary to what had been stated by the respondent in his most recent submission. These late submissions should therefore be admitted into the procedure.

V. The respondent in particular contested that luminescence quenching was the only optical alternative to the measurement of blood oxygen via electrodes. For instance, optical oxygen blood measurement techniques were known at the filing date which were based either on chemiluminescence, on immobilized hemoglobin or on light transmission.

Since the sampling device of document D6 was specially dedicated to light transmission measurements, there was no obvious reason for the skilled person to adapt it for the particular luminescence quenching technique in accordance with the patent in suit, if not with the benefit of hindsight.

## Reasons for the Decision

1. The appeal is admissible.

2. The documents quoted Ref. 2, Ref. 3 and Ref. 5 were filed by the appellant only during the oral proceedings

held before the Board, which is long after the expiry of the time delay for filing an opposition as defined in Article 99(1) EPC.

The appellant acknowledged that these documents were not submitted as prior art citations anticipating certain features of the claim, and the documents Ref. 2 and Ref. 3 were indeed published after the priority date of the present patent. The documents were cited merely to provide evidence that the monitoring of oxygen in a patient's blood and the analysis of routine blood chemistry pertained to the same art.

In the Board's opinion, however, this issue is not of particular relevance for the present decision, which, as will be apparent from the following, would not be different if the point which the appellant tried to make by relying on the documents was admitted.

For these reasons, the late-filed documents Ref. 2, Ref. 3 and Ref. 5 will not be considered further in accordance with the provisions of Article 114(2) EPC.

3. *Patentability of the subject-matter of independent claim 3*

3.1 Novelty

Document D2 discloses a sampling device for biological fluids such as blood, which forms a syringe-like device comprising a hollow cylindrical measuring chamber with an inserted cylindrical piston. The end face of the piston comprises a set of exposed sensors to be contacted with the fluid in the container, which are connected via electrical leads to data processing and

displaying means (see the abstract and Figure 2). The document does not expressly specify that the measuring chamber has an at least locally transparent wall, as is set out in present claim 3, and the device does not contain any luminophor.

Document D4 relates to the *in vivo* measuring of the concentration of gases in blood using fluorescent-type indicators. A measuring cell comprising a light-transmissive surface forms a flow-through chamber connected to a patient's blood circulation. The chamber comprises a luminophor for a continuous monitoring of the concentration of the gases in the blood flow (see column 5, lines 43 to 57 and column 8, lines 62 to 69).

Thus, document D4 does not disclose an "essentially sealed container" within the meaning of claim 3, for the taking of a blood sample and its measuring at a location remote from the patient.

Document D6 discloses a device for both sampling and analysing a fluid, such as blood. The measuring chamber has a transparent wall part and, apart from its inlet opening, it forms an essentially sealed container (see claim 1 and Figure 6a). The measuring chamber contains at least one reagent for reacting with the sample to be measured, but the document does not specify that it constitutes a luminophor, for the monitoring of oxygen by luminescence quenching.

Document D11 discloses a sampling service similar to that of document D6, which contains a reagent specifically adapted for the determination of hemoglobin concentration in whole blood by optical absorption measurements.

The remaining documents on the file do not come closer to the subject-matter of independent claim 3 which, accordingly, is novel within the meaning of Article 54 EPC.

3.2 Inventive step

3.2.1 The closest prior art in the Board's opinion is constituted by the sampling device of document D6, from which the subject-matter of independent claim 3 is distinguished in that it contains a luminophor, the luminescence of which is quenched in the presence of oxygen.

The sampling device of document D6 comprises a semi-permeable membrane 11 which permits electrochemical measurements by means of electrodes 18, 19 externally contacted with the membrane, as is shown in Figure 3. This sampling device also allows for optical transmission measurements as is shown in Figure 4.

Thus, the sampling device of document D6 already allows for the measurement of oxygen concentration in blood either by the electrochemical method or by the optical transmission method.

The technical problem solved by the sampling device set out in independent claim 3, as objectively defined in view of the closest prior art, thus consists in providing the sampling device of document D6 with the capacity of allowing for the measurement of oxygen in blood via a still further method.

3.2.2 There is no evidence on the file that the skilled person actually would have had any obvious reason to

contemplate supplementing the known sampling device with a still further capability of measuring oxygen in blood.

The less so could he have had any obvious reason to envisage precisely the oxygen determination technique involving flourescence quenching. Other alternative oxygen determination techniques were indeed available to him at the priority date of the patent, like the chemiluminescence or the use of immobilized hemoglobin, as disclosed e.g. in the following documents submitted by the respondent in the opposition procedure:

D14: T. M. Freeman et al., "Oxygen Probe Based on Tetrakis(alkylamino)ethylene Chemiluminescence", Anal.Chem.,1981, volume 53, pages 98 to 102; and

D15: Z. Zhujun et al., "Optical Sensor for Oxygen Based on Immobilized Hemoglobin", Anal. Chem., 1986, volume 58, pages 220 to 222.

Neither is there any evidence on the file that at the priority date of the patent luminescence quenching was a standard method of measuring oxygen in blood, which the skilled person would immediately have considered in his search for a further oxygen determination technique to be implemented via the sampling device of document D6.

For the above reasons, the skilled person would not in the Board's opinion have had any obvious reason to provide the sampling device of document D2 with a luminophor, the luminescence of which is quenched in the presence of oxygen, if not with the benefit of hindsight.

3.2.3 The Board cannot either conceive any logical sequence of obvious steps which could have led the skilled person to the claimed sampling device, starting from the teaching of document D4, as was further alleged by the appellant.

As a matter of fact, document D4 is dedicated to the **continuous** monitoring of oxygen in a patient's blood, and it consistently emphasises the extremely fast response of the measuring technique disclosed there, measuring times of over 30 seconds being considered undesirably long (see column 1, lines 59 to 61, column 2, lines 9 to 12, or column 4, lines 4 to 6).

The use of the claimed sampling device does not however preserve this essential capability of the technique of document D4 to allow continuous and fast monitoring of a patient, and it cannot therefore be considered to follow from an obvious development of the teaching of document D4, accordingly.

3.2.4 For the above reasons, the subject-matter of independent claim 3 involves and inventive step within the meaning of Article 56 EPC.

4. The same conclusion applies to the subject-matter of independent claims 1 and 11, both of which imply substantially the same limitations as independent claim 3, in terms of a method of and of a system for the photometric *in vitro* determination of the content of oxygen in a blood sample, respectively, and to the subject-matter of the dependent claims, by virtue of their appendence to independent claims 1 and 3, respectively.

5. Since the grounds for opposition invoked by the appellant do not prejudice the maintenance of the patent unamended, the appealed decision to reject the opposition by virtue of Article 102(2) EPC was justified.

## Order

## For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

P. Martorana E. Turrini