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Datasheet for the decision of 28 June 2022

Case Number: T 0719/18 - 3.2.02

Application Number: 11161916.9

Publication Number: 2510958

IPC: A61M1/36, A61B5/00

Language of the proceedings: EN

Title of invention:
Method and apparatus for monitoring a treatment of a patient, preferably for monitoring hemodialysis, hemodiafiltration and/or peritoneal dialysis

Patent Proprietor:
Fresenius Medical Care Deutschland GmbH

Opponent:
B. Braun Avitum AG

Headword:

Relevant legal provisions:
EPC Art. 54(3), 56
RPBA 2020 Art. 13(2)

Keyword:
Novelty - main request (no) - auxiliary request (yes)
Inventive step - auxiliary request (yes)
Late-filed objection - admitted (no)

Decisions cited:
G 0003/14, G 0009/91, T 0996/18

Catchword:

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 0719/18 - 3.2.02

D E C I S I O N
of Technical Board of Appeal 3.2.02
of 28 June 2022

Appellant: (Patent Proprietor)	Fresenius Medical Care Deutschland GmbH Else-Kröner-Strasse 1 61352 Bad Homburg (DE)
Representative:	Nordmeyer, Philipp Werner df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte PartG mbB Theatinerstraße 16 80333 München (DE)
Appellant: (Opponent)	B. Braun Avitum AG Schwarzenberger Weg 73-79 34212 Melsungen (DE)
Representative:	Winter, Brandl - Partnerschaft mbB Alois-Steinecker-Straße 22 85354 Freising (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 9 January 2018 concerning maintenance of the European Patent No. 2510958 in amended form.**

Composition of the Board:

Chairman	M. Alvazzi Delfrate
Members:	A. Martinez Möller
	C. Schmidt

Summary of Facts and Submissions

I. Appeals were filed by the patent proprietor and by the opponent against the opposition division's interlocutory decision, which found that, taking into account the amendments made by the patent proprietor according to the then auxiliary request 2, the patent and the invention to which it related met the requirements of the EPC.

II. Oral proceedings before the Board took place on 28 June 2022.

The appellant/proprietor ("the proprietor") requested that the decision under appeal be set aside and that the patent be maintained on the basis of the new main request (hereinafter "the main request", filed by letter of 18 May 2018 as auxiliary request I), on the basis of the new auxiliary request I (hereinafter "auxiliary request I", filed by letter of 18 May 2018 as auxiliary request III), or on the basis of one of auxiliary requests Ia, II or IV to X, filed on 30 May 2022 (auxiliary request Ia) and on 18 May 2018 (all other auxiliary requests).

The appellant/opponent ("the opponent") requested that the decision under appeal be set aside and that the patent be revoked.

III. Independent claims 1 and 11 of the **main request** read as follows:

1. "Method for monitoring a treatment of a patient, preferably for monitoring hemodialysis,

hemodiafiltration and/or peritoneal dialysis, the method comprising the steps of:

- irradiating a sample of a liquid used in the treatment with irradiation light of at least a first irradiation wavelength;
- detecting light emitted by the irradiated sample in at least a first detection wavelength wherein the detection wavelength is different from the first irradiation wavelength, and
- determining the presence and/or concentration of at least one analyte in the sample on the basis of the detected light,
characterized in that the liquid is a dialysis liquid and the detected light includes fluorescence light and the presence and/or concentration of the at least one analyte in the sample is determined on the basis of the detected fluorescence light, wherein the irradiation light is UV-light having a wavelength of between 180 nm and 400 nm, wherein the sample is irradiated with irradiation light of at least two separated, distinct wavelengths."

11. "Apparatus for monitoring a treatment of a patient, preferably for monitoring hemodialysis, hemodiafiltration and/or peritoneal dialysis, the apparatus comprising:

- a light source (7) for irradiating a sample of a liquid used in the treatment with irradiation light of at least a first irradiation wavelength;
- a detector (9) for detecting light emitted by the irradiated sample in at least a first detection wavelength wherein the detection wavelength is different from the first irradiation wavelength; and

- a control and analysis unit (11) for determining the presence and/or concentration of at least one analyte in the sample on the basis of the detected light, characterized in that the liquid is a dialysis liquid and the detector (9) is arranged to detect light including fluorescence light and the control and analysis unit (11) is arranged to determine the presence and/or concentration of the at least one analyte in the sample on the basis of the detected fluorescence light, wherein the light source emits irradiation light in the UV-range having a wavelength of between 180 nm and 400 nm, and wherein the light source is set to provide illumination light in at least two separated, distinct wavelengths."

IV. Compared with the main request, claim 11 of **auxiliary request I** further includes the following feature added to the end of the claim:

1. "and the control and analysis unit (11) is arranged to compare the two different emission spectra induced by the two irradiation wavelengths to determine the presence and/or concentration of the analyte."

V. The following documents are relevant to this decision:

E6: EP 2397167 A1
E9: DE 69408976 T2
E10: DE 69916053 T2
E17: "Topics in Fluorescence Spectroscopy", Vol. 2, "Principles", Joseph R. Lakowicz, Kluwer Academic Publishers, 2002, ISBN 0-306-43875-5 (print) and ISBN 0-306-47058-6 (eBook)
E18: "Topics in Fluorescence Spectroscopy", Vol. 1, "Techniques", Joseph R. Lakowicz, Kluwer Academic

Publishers, 2002, ISBN 0-306-43874-7 (print) and ISBN 0-306-47057-8 (eBook)

VI. The opponent's arguments which are relevant to the present decision can be summarised as follows.

Main request - novelty over E6

The subject-matter of independent claims 1 and 11 was not novel over E6, which was an enabling disclosure of the subject-matter of these claims. Otherwise, the claimed invention would not be sufficiently disclosed either.

Independent claims 1 and 11 defined light of "at least" two separated, distinct wavelengths, thus encompassing any polychromatic or white light. This was anticipated by paragraph [0040] of E6, which disclosed a polychromatic light source. The last sentence of paragraph [0040] also disclosed irradiating the sample with more than one wavelength.

Moreover, the last feature of claim 11 merely required the light source to be able to provide at least two distinct wavelengths; this wording encompassed a source which could selectively emit with either of the two wavelengths.

Auxiliary request I - clarity

The feature added to claim 1 according to which the sample is irradiated with irradiation light of at least two separate, distinct wavelengths resulted in a lack of clarity because the claim did not specify the purpose of the further wavelength or its relationship to the other features of the claim.

Auxiliary request I - novelty over E6

The subject-matter of claim 1 was not novel over E6 for the same reasons as those submitted for the main request.

Auxiliary request I - inventive step over E10 and common general knowledge

Claim 1 was not inventive over E10 combined with common general knowledge as proven by E17 and E18, which were textbooks describing common general knowledge and should thus be admitted into the appeal proceedings.

Starting from E10 and in view of pages 349-350 of E17, the person skilled in the art would have considered using fluorescence measurements rather than absorbance measurements. The person skilled in the art would have also learned from E17 that it was beneficial to use two beams and would have used the two-beam geometry employing two lamps with different wavelengths disclosed on pages 392-293 of E18, thereby arriving at a method as defined by claim 1.

Auxiliary request I - inventive step over E9 and common general knowledge

Claim 1 was not inventive over E9 combined with common general knowledge. It would have been an obvious choice to use the method from E9 to measure glucose in the dialysis liquid rather than in the extracorporeal blood circuit of a dialysis system. For reasons similar to those explained when starting from E10, the person skilled in the art using common general knowledge as proven by E18 would have used two wavelengths.

Auxiliary request I - admittance of the new objections to claim 11 under Articles 84, 123(2) and 123(3) EPC

Claim 11 of auxiliary request I was unclear, comprised added subject-matter and resulted in an extension of the scope of protection as compared with claim 11 as granted.

These objections, filed at the oral proceedings before the Board, were to be admitted because they had been brought about by the Board's preliminary opinion and by the proprietor filing a further auxiliary request (auxiliary request Ia). Moreover, it should always be checked that amendments comply with Article 123 EPC.

VII. The proprietor's arguments which are relevant to the present decision can be summarised as follows.

Main request - novelty over E6

E6 did not teach how a particular analyte could be measured in a dialysis liquid having spectral overlap in the excitation and emission wavelengths as well as in the absorbance. Hence, E6 was not an enabling disclosure.

As regards claim 11, the terms "illumination light" and "irradiation light" had the same meaning and were used in the patent specification as equivalents. In view of the other features of claim 11, the last feature had to be construed as requiring the light source to be configured to irradiate the sample with two distinct wavelengths.

E6 only disclosed a polychromatic light source combined with a monochromator, as was also clear from claim 4. The last sentence of paragraph [0040] referred to the possibility of using another wavelength to see another molecule. The sample in E6 was thus irradiated with a single wavelength. Hence, the subject-matter of claims 1 and 11 was novel over E6.

Auxiliary request I - inventive step over E10 and common general knowledge

Claim 1 was inventive over E10 combined with common general knowledge.

E17 and E18 had been filed late in the opposition proceedings and the appealed decision was not based on them. They were thus not to be admitted. Moreover, the opponent's objection was based on a combination of E10, E17 and E18, rather than using E17 and E18 as proof of common general knowledge.

Even if the person skilled in the art starting from E10 had considered the teaching of E17 and E18, they would not have arrived at a method as defined in claim 1. Neither E17 nor E18 taught how to implement a fluorescence measurement for monitoring a treatment using two excitation wavelengths.

Auxiliary request I - inventive step over E9 and common general knowledge

Claim 1 was inventive over E9 combined with common general knowledge. E9 dealt with measuring glucose concentration in the blood. Hence, E9 would not have been used for dialysis liquid. Even if they had been considered by the person skilled in the art, E17 and

E18 did not prompt a person skilled in the art to irradiate a sample of dialysis liquid with two distinct excitation wavelengths.

Auxiliary request I - admittance of the new objections to claim 11 under Articles 84, 123(2) and 123(3) EPC

The objections had only been submitted at the oral proceedings before the Board and should not be admitted.

Reasons for the Decision

1. **Invention**

In extracorporeal blood treatment methods such as haemodialysis, haemodiafiltration and peritoneal dialysis, the patient's blood and dialysis liquid flow along respective sides of a porous dialysing membrane. The dialysis liquid is prepared such that a concentration gradient from the blood side to the dialysis-liquid side for certain substances is provided, thereby causing waste products to be removed from the patient's blood by diffusion through the membrane.

The use of membranes with large pore sizes is advantageous to allow middle-sized molecules to be removed; however, it increases the risk that vital blood components such as albumin are likewise removed from the blood. Moreover, the size of the pores in the membrane can also change with its use.

It is thus helpful to know during the extracorporeal blood treatment if or how much of one or more analytes, be it a waste product or a vital blood component such as albumin, is present in the dialysis liquid (see paragraphs [0010]-[0011] and [0018] of the patent specification).

The invention relates to a method and to an apparatus for monitoring a treatment of a patient, and in particular to detecting the presence and/or concentration of at least one analyte in a sample of dialysis liquid.

The sample is irradiated with light of at least a first irradiation wavelength and light emitted by the sample in at least a first detection wavelength different from the first irradiation wavelength is detected. The detected light includes fluorescence light. The presence and/or concentration of the at least one analyte is determined on the basis of the detected fluorescence light.

2. Main request - novelty over E6

2.1 Document E6 is prior art under Article 54(3) EPC. E6 deals with a method for determining waste products during dialysis, in particular for continually determining the concentration of middle-sized molecules in the used dialysis liquid (paragraph [0009]). Figure 3 and paragraph [0037] of E6 disclose that a light source 1 emits light towards the used dialysis liquid 3 at a predetermined intensity and wavelength, for example monochromatic light at 280 nm. The fluorescence light emitted by the sample is then measured by a photodetector 5. Based on the measured fluorescence

light, the concentration of components such as ß2-microglobulin is determined.

2.2 It is disputed whether the subject-matter of each of claims 1 and 11 of the main request is novel over E6, and in particular:

- whether E6 represents an enabling disclosure;
- whether the last feature of claim 1 is disclosed by E6; and
- whether the last feature of claim 11 is disclosed by E6.

These three points under dispute are addressed in the respective items below.

2.3 The proprietor argued that E6 was not an enabling disclosure because it did not teach how to detect a specific analyte such as ß2-microglobulin in a dialysis liquid in which there were different molecules with overlapping spectra.

The principle of fluorescence measurement based on the Stokes shift is not only known to the person skilled in the art, but is also explained in paragraph [0036] of E6, which makes reference to Figure 2. The person skilled in the art either knows the excitation and emission wavelengths (referred to as the "fluorescence fingerprint" in paragraph [0067] of the patent specification) of a relevant fluorescent analyte such as ß2-microglobulin, or can look them up in the literature or determine them by measurement.

Indeed, as also explained in paragraphs [0021]-[0025] of the contested patent, fluorescence measurements are well suited to detection and quantification of specific

molecules in the dialysis liquid. In particular, paragraphs [0021] and [0024]-[0025] highlight that the detected light is proportional to the concentration of the analyte in the dialysis liquid, thereby excluding severe effects from spectral overlap or any effect by other non-fluorescent substances such as uric acid.

Hence, the proprietor's submissions regarding the alleged complexity of carrying out a fluorescence measurement of an analyte in a dialysis liquid are not convincing. While some issues may potentially reduce the accuracy of the method (see, for example, paragraph [0028] of the patent specification), what is relevant here is not how accurate the method in E6 is, but whether E6 constitutes an enabling disclosure.

The disclosure of E6, in particular the apparatus in Figure 3 and the corresponding explanations of the apparatus and method in paragraphs [0036]-[0040], thus enables the person skilled in the art to practise their teaching as regards the fluorescence measurement of an analyte in the dialysis fluid.

2.4 The last feature of claim 1 of the main request specifies that "the sample is irradiated with irradiation light of at least two separated, distinct wavelengths".

The wording "separated, distinct irradiation wavelengths" excludes a continuous spectrum such as that present in white light when read in a technically sensible manner.

E6 discloses, in claim 4 and paragraph [0040], lines 29-31, that the light source can be a polychromatic source. E6 likewise discloses using a monochromator in

order to obtain substantially monochromatic light from the polychromatic light source. In this regard, reference is made to claim 4 as well as to Figures 3 and 4, which show a light source 1 with a plurality of wavelengths λ_1, ..., λ_n, wherein the sample is irradiated with a single wavelength λ_i.

The last sentence of paragraph [0040] of E6 further discloses that by varying the light source (and a filter 4 located before the photodetector 5), molecules of different kinds can be detected. In view of the disclosure in Figures 3 and 4, this sentence hints at the possibility of choosing another irradiation wavelength λ_i from the plurality of wavelengths λ_1, ..., λ_n provided by the light source in the event that a different analyte is to be detected. While the ability of the light source to provide a further irradiation wavelength is necessary in order to carry out a method as defined by claim 1, E6 does not directly and unambiguously disclose a method for actually irradiating a sample with two distinct wavelengths, as required by the claim.

Hence, E6 does not disclose the last feature of claim 1. The subject-matter of claim 1 is thus novel over E6.

2.5 The last feature of apparatus claim 11 requires that "the light source is set to provide illumination light in at least two separated, distinct wavelengths".

The feature refers to "illumination light". It does not use the same term "irradiation light" previously used in claim 11 or a definite article to indicate an antecedence. Moreover, it is technically sensible to have a light source which can provide light in two distinct wavelengths and to use only one of the

wavelengths to irradiate the sample, for example depending on the excitation wavelength of the targeted analyte (as discussed for E6 above).

Therefore, the last feature of claim 11 is construed as requiring the light source to be able to provide light in at least two separated, distinct wavelengths. This is in contrast with the last feature of claim 1, which requires that the sample is actually irradiated with the two wavelengths.

E6 discloses, as discussed above with reference to Figures 3 and 4 and paragraph [0040], a light source which is able to provide light in at least two separated, distinct wavelengths, thereby anticipating the last feature of claim 11. Since this was the only disputed feature, the subject-matter of claim 11 is not novel over E6.

3. Auxiliary request I

3.1 Clarity

In the written procedure the opponent argued that the addition of the feature "wherein the sample is irradiated with irradiation light of at least two separate, distinct wavelengths" to claim 1 resulted in a lack of clarity (see pages 8 and 9 of the opponent's submission dated 14 September 2018).

This feature, which is also found in claim 1 of the main request, comes from claim 3 as granted. This addition results in claim 1 of auxiliary request I corresponding to one of the alternatives defined by claim 3 as granted. Hence, any possible lack of clarity was already present in dependent claim 3 as granted. It

follows that claim 1 of auxiliary request I may not be examined for compliance with the requirements of Article 84 EPC (see Order of G 3/14). The objection of lack of clarity against claim 1 is thus dismissed.

3.2 Novelty over E6

Claim 1 of auxiliary request I is identical to claim 1 of the main request. For the same reasons as indicated under point 2.4 above, the subject-matter of claim 1 is novel over E6. Novelty of the subject-matter of claim 11 was not disputed and the Board does not see any disclosure in E6 for the feature according to which the control and analysis unit is arranged to compare the two different emission spectra induced by the two irradiation wavelengths to determine the presence and/or concentration of the analyte.

3.3 Inventive step over E10 and common general knowledge

3.3.1 In the written procedure the opponent argued that the claimed method lacked an inventive step starting from E10 in combination with common general knowledge as evidenced by E17 and E18.

3.3.2 E10 deals with determining the amount of urea or other waste products in dialysis liquid (paragraphs [0011]-[0014]). E10 teaches that this can be determined by measuring UV light absorption caused by these products (paragraphs [0032]-[0038]). E10 does not mention fluorescence.

It is undisputed that the following features distinguish the subject-matter of claim 1 from the disclosure of E10:

- detecting light emitted by the irradiated sample in at least a first detection wavelength, wherein the detection wavelength is different from the first irradiation wavelength;
- the detected light includes fluorescence light;
- the presence and/or concentration of the at least one analyte in the sample is determined on the basis of the detected fluorescence light; and
- the sample is irradiated with irradiation light of at least two separate, distinct wavelengths.

3.3.3 These features can be regarded as solving the problem of modifying the method from E10 to provide more sensitive and specific detection of an analyte.

3.3.4 Even if the disclosure on pages 349-350 of E17 were to be regarded as proving that it was common general knowledge that fluorescence is more sensitive than absorbance, it is questionable whether the person skilled in the art would have changed the measurement principle of E10, since determining waste products using absorbance is the core teaching of E10.

3.3.5 However, even if this change had been envisaged, a person skilled in the art still would not have been prompted to irradiate the sample with two distinct wavelengths.

The opponent's view that the reference to a "double-beam" arrangement on page 350 of E17 would directly lead to the paragraph bridging pages 392 and 393 of E18 and thereby to the use of two distinct wavelengths is not convincing. On one hand, as submitted by the proprietor in its reply to the appeal, such a sequential combination of documents goes far beyond the opponent's citation of E17 and E18 as proof of common

general knowledge. On the other hand, as indicated in point 7.2 of the Board's preliminary opinion, the cited passage of E18 is within a section dealing with fluorescence microscopy. The fluorescence microscopy illuminator system in E18 is unrelated to the double-beam arrangement for "monitoring scattered radiation", i.e. radiation diverted by the sample, mentioned on page 350 of E17. Hence, starting from the method in E10 and faced with the problem above, the person skilled in the art would not have considered, using common general knowledge, modifying the method to irradiate the sample with light of two distinct wavelengths, as required by claim 1.

3.3.6 It follows that the subject-matter of claim 1 is inventive over E10 and common general knowledge.

3.4 Inventive step over E9 and common general knowledge

3.4.1 E9 deals with glucose monitoring by measuring fluorescence light emitted by the glucose (page 1, lines 6-10). E9 discloses that the glucose measurement can be carried out in the extracorporeal blood circuit of a dialysis system (page 12, lines 6-13).

It is undisputed that at least the following features distinguish the subject-matter of claim 1 from the disclosure of E9:

- the liquid is a dialysis liquid;
- the sample is irradiated with irradiation light of at least two separate, distinct wavelengths.

3.4.2 E9 discloses that the method could be used for monitoring different liquids or organs (see last paragraph of page 12). However, E9 does not prompt a

person skilled in the art to specifically measure the dialysis liquid. The opponent's argument that this was an obvious alternative to monitoring blood in an extracorporeal blood circuit is not convincing; the information obtained by quantifying glucose in the dialysis liquid (i.e. the glucose lost by the patient during dialysis) and by quantifying the actual glucose level in the patient's blood is different. Hence, the person skilled in the art would not have considered monitoring glucose in the dialysis liquid without being prompted by the prior art.

3.4.3 As regards the second distinguishing feature, the opponent did not mention which problem it solved, but instead referred to the paragraph bridging pages 392 and 393 of E18 as proof that it was common general knowledge in the art to use two distinct wavelengths.

For reasons similar to those explained for the objection starting from E10 above, there is no reason why the person skilled in the art starting from E9 would have considered using an illuminator system from an imaging technique such as fluorescence microscopy.

3.4.4 It follows that the subject-matter of claim 1 is inventive over E9 and common general knowledge.

3.5 The opponent's objections of lack of inventive step were directed to claim 1. With regard to claim 11 of auxiliary request I, a technically sensible reading of the claim and in particular of its last two features reveals that the "two irradiation wavelengths" are provided by the light source. Hence, in view of the conclusion for claim 1, the Board has no reason to doubt that the subject-matter of claim 11 is also inventive when starting from either of E10 or E9.

3.6 Admittance of the new objections to claim 11 under Articles 84, 123(2) and 123(3) EPC

3.6.1 At the oral proceedings before the Board, the opponent raised new objections under Articles 84, 123(2) and 123(3) EPC to claim 11 of auxiliary request I. These objections constitute an amendment to the opponent's appeal case. Their admittance is thus subject to Article 13(2) RPBA 2020.

3.6.2 The opponent argued that these objections had been brought about by the Board's preliminary opinion on the feature of providing "illumination light" and by a new auxiliary request (Ia) being subsequently filed by the proprietor, which, according to the opponent, was an acknowledgement by the proprietor that "illumination light" and "irradiation light" were not the same.

This justification for the late filing of the objections disregards the fact that the interpretation of the feature "wherein the light source is set to provide illumination light ...", and in particular whether the feature required the sample to be irradiated with this light, was already addressed in point 15.4 of the appealed decision and was discussed by both parties in their written submissions in the appeal. Hence, the Board did not raise any new issues in its preliminary opinion. While it is correct that the proprietor filed a new auxiliary request Ia, the opponent's objections are not directed to this new request Ia, a request which is not even under discussion.

The Board thus concludes that the reasons put forward by the opponent do not define exceptional circumstances within the meaning of Article 13(2) RPBA 2020.

3.6.3 The opponent further argued that it must always be checked that amendments comply with Article 123 EPC. It is true that according to G 9/91 (point 19 of the Reasons), "in case of amendments of the claims in the course of opposition or appeal proceedings, such amendments are to be fully examined as to their compatibility with the requirements of the EPC (e.g. with regard to the provisions of Article 123(2) and (3) EPC)". Indeed, it is possible for the Board to raise an objection ex officio on the basis of said examination (see T 996/18, point 5.1.1). This does not mean, however, that any amendment to an opponent's case raising an objection to the amendments should always be considered, as this would take away the Board's discretion under Article 114(2) EPC and run contrary to the provisions of Article 13(2) RPBA 2020. Hence, the opponent's argument is not convincing.

3.6.4 The Board thus decided not to admit these new objections into the appeal proceedings (Article 13(2) RBPA 2020).

3.7 The opponent had no further objections to auxiliary request I, and nor did it object to the proprietor's request that page 6 of the patent specification be replaced with page 6 as filed during the oral proceedings before the Board.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent in the following version:
   - claims 1 to 15 of the new auxiliary request I, filed as auxiliary request III by letter dated 18 May 2018,
   - description: pages 2 to 5 and 7 to 12 of the patent specification and page 6 as filed during the oral proceedings before the Board, and
   - drawings of the patent specification.

The Registrar: The Chairman:

D. Hampe M. Alvazzi Delfrate

Decision electronically authenticated