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Datasheet for the decision of 27 November 2012

Case Number: T 0208/09 - 3.2.02

Application Number: 00948195.3

Publication Number: 1117449

IPC: A61M 1/16, A61M 1/34

Language of the proceedings: EN

Title of invention:
DIALYSIS MACHINE

Patent Proprietor:
GAMBRO HOSPAL (Schweiz) AG

Opponent:
Fresenius Medical Care Deutschland GmbH

Headword:
-

Relevant legal provisions:
EPC Art. 56, 114(2)

Keyword:
"Admissibility of evidence (yes)"
"Inventive step (yes)"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0208/09 - 3.2.02

D E C I S I O N
of the Technical Board of Appeal 3.2.02
of 27 November 2012

Appellant: (Opponent)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted on 25 November 2008 rejecting the opposition filed against European patent No. 1117449 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman: P. L. P. Weber
Members: C. Körber
I. Beckedorf

Summary of Facts and Submissions

I. On 25 November 2008 the Opposition Division posted its decision to reject the opposition against European patent No. 1 117 449.

II. An appeal was lodged against this decision by the opponent by notice received on 21 January 2009, with the appeal fee being paid on the same day. The statement setting out the grounds of appeal was received on 25 March 2009.

III. By communication of 22 August 2012, the Board forwarded its provisional opinion to the parties.

IV. Oral proceedings were held on 27 November 2012.

The final requests of the parties were as follows:

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

The respondent (patent proprietor) requested that the appeal be dismissed.

V. The following documents are of importance for the present decision:

D1: C.A. Baldamus: "Problems in Hemofiltration", Contr. Nephrol., Vol. 44, pp. 212-222 (1985);

D2: Drukker et al. (Eds.): "Replacement of Renal Function by Dialysis" 4th ed., Kluwer Academic

Publishers, Dordrecht/Boston/London (1996), pp. 134-140, 215-216, 226, 380-383, 390-412;

D3: D. Nussbaumer and H. Perl: "Einflussgrössen bei der Haemofiltration", Übersichtsreferat in "Wissenschaftliche Informationen" Fresenius, Nephrologie Heft 2/78;

D4: W.M. Deen et al.: "Dynamics of Glomerular Ultrafiltration in the Rat, IV. Determination of the Ultrafiltration Coefficient", Journal of Clinical Investigation, Vol. 52, pp. 1500-1508 (1973);

D5: A. Lauer et al.: "Continuous Arteriovenous Hemofiltration in the Critically Ill Patient", Annals of Internal Medicine, Vol. 99, pp. 455-460 (1983);

D6: J.P. Bosch et al.: "High Flux Hemofiltration", Artificial Organs, Vol. 2, pp. 339-342 (1978);

D7: US-A-5 401 238;

D8: DE-A-40 24 434;

D9: EP-A-0 089 003;

D10: EP-A-0 358 873.

VI. Claim 1 of the patent as granted reads as follows (with the feature denotation proposed by the appellant being inserted in square brackets):

"1. Dialysis machine (35) for treatment of a liquid to be filtered, comprising a liquid component, a cellular component and solutes, the machine comprising:
[1.1] - a filter (1) having a first and a second compartment (3, 4) separated by a semi-permeable membrane (2);
[1.2] - a first circuit (5, 6) for the liquid to be filtered, comprising a liquid inlet line (5) connected to an inlet of the first compartment (3) and a liquid outlet line (6) connected to an outlet of the first compartment (3);
[1.3] - a second circuit (10, 11) for a dialysis fluid comprising a dialysis liquid inlet line (10) connected to an inlet of the second compartment (4) and a dialysis liquid outlet line (11) connected to an outlet of the second compartment (4);
[1.4] - first pumping means (15) connected to the first circuit (5; 6) for circulating the liquid to be filtered through the first compartment (3);
[1.5] - second pumping means (17, 18, 19) connected to the second circuit (10, 11) for circulating a dialysis fluid in the second compartment (4) and for causing a flow of part of the liquid component and of the solutes through the membrane (2);
[1.6] - means for detecting (50) the value of a first parameter correlated with the controlled flow of the liquid, component through the membrane (2), the first parameter being a rate of ultrafiltration (UFR);
characterized by further comprising
[1.7] means for detecting the value of a second parameter correlated with the flow of the liquid component at the inlet of the filter (2), the second parameter being a plasma flow rate (Q_p);

[1.8] - first means for calculating (60) a filtration factor FF as a function of the value of the first and second parameters;
[1.9] - first comparison means (65) for comparing the filtration factor (FF) with a limit value of admissibility; and
[1.10] - signaling means (70) for generating a signal (A) indicating the result of the comparison."

Claims 2 and 3 are dependent claims.

VII. The appellant's arguments are summarised as follows:

Documents D9 and D10 were submitted with the statement of grounds of appeal in reaction to the impugned decision and should therefore be admitted into the proceedings.

Document D7 disclosed a dialysis machine according to the preamble of claim 1. This was also the case for document D8, which implicitly disclosed means for detecting the ultrafiltration rate due to the fact that the machine of D8 comprised means for controlling this parameter. Both documents could therefore be regarded as closest prior art. The problem to be solved by the features of the characterising portion of claim 1 was to provide a dialysis machine allowing a safer and more efficient dialysis treatment. This corresponded to the problem stated in the patent in suit, for instance in paragraph [0017].

The solution according to claim 1 was obvious from D7 or D8 in view of D2. At page 390 of D2 it was mentioned that an overly aggressive fluid removal was to be

avoided and the middle molecular clearance to be increased, i.e. a safer and more efficient treatment was aimed at. D2 even addressed, at pages 134 to 135 and 216, the more specific problem of avoiding caking, also indicated in the patent in suit. D2 emphasised that the filtration factor, calculated as defined in feature [1.8] of claim 1 (page 392 of D2), was an important parameter which had to be kept in a certain range (page 380, Table 1), in particular below 0.5 (page 394, Figure 4), in order to avoid caking and to render the treatment safer and more efficient. With respect to feature [1.7] of claim 1, it was further indicated at page 391 of D2 that the hematocrit was to be measured. Features [1.9] and [1.10] were obvious in view of the fact that claim 1 of D7 already taught a comparison and the generation of a warning signal, or even in view of common technical knowledge.

Furthermore, the claimed invention was obvious in view of D1 or D5. At page 213 of D1 it was stated that the filtration factor, calculated with the same formula as in the patent in suit, was to be kept below 0.5 in order to achieve an adequate form of treatment. Even if means for detecting the plasma flow rate were not explicitly mentioned in D1, it was evident for the skilled person that the filtration factor was to be determined on that basis, particular in view of the fact that means for measuring were already disclosed in D7. The relevance of the filtration factor was also addressed in D5, and at page 459 it was stated that a range between 0.35 and 0.40 yielded maximal efficiency. Equation 4 at page 456 was identical to that used for the filtration factor according to the patent in suit. The calculation of the filtration factor required the determination of the

plasma flow rate. Equation 3 of D5 corresponded to the formula in paragraph [0024] of the patent in suit, and it was indicated at page 456 of D5 that the hematocrit was measured in order to obtain the plasma flow rate. The fact that the hematocrit was measured in samples collected from the blood lines was not relevant since the wording of claim 1 did not require a direct monitoring. Provided with this detailed teaching of D1 or D5, features [1.9] and [1.10] were trivial for the skilled person.

Claim 1 was also not inventive when taking into account D3. At pages 147 to 148 it was stated that the maximum removal of filtrate was 44.8%. As explained at page 146, this upper limit was due to the formation of a boundary layer in front of the membrane surface which limited the flow through the filter. Accordingly, the skilled person was made aware of the problem of caking, and that the filtration factor should not exceed a limit value (feature [1.9]). Provided with these pertinent hints, it was straightforward for the skilled person to carry out the remaining features of the characterising portion of claim 1.

Furthermore, the claimed dialysis machine was obvious in view of D9 or D10. D9 disclosed a hematocrit-measuring device 24, and from the paragraphs bridging pages 10 and 11 and pages 15 and 16 it became clear that this measurement was used to change and control the ultrafiltration rate, and thus also the filtration factor, to avoid complications in the patient during the dialysis treatment. This teaching corresponded to what was defined in claim 2 of the patent in suit. Similar information could also be derived from D10 (reference

numerals 15 and 17 denoting the sensors for monitoring the hematocrit and 18 denoting the control system).

Document D4 taught that a filtration factor of 0.33 was reached and that this was an important parameter to be taken into account.

Document D6 disclosed that that high filtration factors in excess of 0.45 could be obtained throughout the course of treatment without adverse effects. Accordingly, the subject-matter of claim 1 was obvious from D7 or D8 in view of any one of documents D1 to D6, D9 or D10.

VIII. The respondent's arguments are summarised as follows:

Late-filed documents D9 and D10 should not be admitted into the appeal proceedings. This would result in a fresh case to be treated by the Board, which was not the purpose of appeal proceedings. Moreover, these documents were not prima facie relevant since they did not address the problem of caking and were silent with respect to the measurement of plasma flow rate.

Starting from D7 as closest prior art, the problem to be solved was how to control a dialysis machine, taking into account the variation of the haemoconcentration in the dialyser provoked by the ultrafiltration of the plasmatic water (plasma fluid), which could lead to clogging (by caking) of the dialyser.

The invention did not simply introduce the definition of a filtration factor FF, but more particularly the detected values of UFR and the plasma flow rate were

determined, so that the dialysis machine itself was rendered able to follow and compare the current value of the filtration factor in the course of the treatment, thus taking into account the patient's ability to refill blood with water during treatment as well as the effect of diluting infusions administered to the patient. The invention allowed the conditions of the blood filtration to be kept under control during treatment following any changes (for instance in the blood concentration and/or in the plasma flow rate) that might occur. The means for detecting the plasma flow rate were associated with the dialysis machine so as to determine in real time any variation in the plasma flow rate upstream of the filter during the treatment (i.e. the amount of water available for filtration), such variations, for example, being due to a change in the hematocrit of the patient or in the infusion flow rate of a liquid infused in the extracorporeal blood upstream of the filter.

There was no suggestion in D7 itself that the hematocrit or plasma flow rate could vary with time. On the contrary, it was explicitly stated that the hematocrit was set by the user to a fixed value. D7 therefore actually taught away from the invention.

Document D2, which was in fact not a single document but a collection of separate articles, did not mention the problem of caking and would thus not have been taken into account by the skilled person. Furthermore, there was no hint to continuously detect the actual value of the plasma flow rate.

D1 too said nothing about the problems of clogging or caking of the filter. Nor did it teach the detection of

the plasma flow rate. The same applied to document D5. A discontinuous sampling technique did not anticipate means for detecting as claimed.

D3 merely disclosed that there was the problem of getting as near as possible to the theoretical maximum filtrate removal with membrane surfaces as small as possible. D3 failed to give any teaching that a dialysis machine should be provided with means for detecting the plasma flow rate or means for calculating the actual filtration factor as a ratio of the detected plasma flow at the inlet of the dialyser. Moreover D3 did not teach comparing the filtration factor with a reference value and generating a signal from that comparison.

D9 dealt with controlling the transmembrane pressure, which was a concept entirely different from that underlying D7. Accordingly, the teachings of these two documents were not combinable. Moreover, even though D9 disclosed means for monitoring the hematocrit, this did not anticipate means for detecting the plasma flow rate as claimed, since there was no disclosure in D9 of the simultaneous determination of the blood flow rate.

D4 was not pertinent since it did not relate to a dialysis machine and merely taught that the value of the filtration factor of a single nephron of a rat was about 0.25 or 0.33.

There was no suggestion in D6 to provide a dialysis machine with any means corresponding to those as claimed. D6 also relied on samples to determine the hematocrit and concentration values necessary for determining the

instant value of the filtration factor. D6 failed to disclose any means for detecting the plasma flow rate.

D8 was simply a conventional dialysis system having a control for the fluid balance. It could not be regarded as closest prior art since nothing in D8 prompted the reader in any direction. The purpose and effect were different from the invention, and there were no teachings or suggestions in relation to the objective technical problem to be solved. Accordingly, D7 represented the closest prior art.

Reasons for the Decision

1. The appeal is admissible.

2. Admissibility of D9 and D10

Documents D9 and D10 were filed with the statement setting out the grounds of appeal, in response to the finding of the Opposition Division that the detection of the plasma flow rate related to a dynamic process requiring a timely indication (2nd paragraph of point 11.5 of the Reasons of the impugned decision). D9 and D10 both disclose means for continuously monitoring the hematocrit (see reference numerals 24 and 15, respectively) in order to control the ultrafiltration rate and water removal (see pages 10 to 11 of D9) or the blood pump (reference numeral 14 in D10). Accordingly, in that respect they go beyond the disclosure of the prior-art documents considered in the first-instance opposition proceedings, in particular beyond D2 and D5 which fail to disclose a continuous monitoring of the

hematocrit (see points 3.1.5 and 3.1.7 below). Under these circumstances, the submission of D9 and D10 cannot be considered as constituting a fresh case as alleged by the respondent. It is rather to be seen as a bona fide reaction to the impugned decision by the losing party. In addition, the documents were filed with the statement setting out the grounds of appeal, i.e. at the very beginning of the appeal proceedings. The Board therefore does not find it appropriate to disregard these documents under Article 114(2) EPC and hence admits D9 and D10 into the proceedings.

3. Inventive step

3.1 Document D7 as starting point

3.1.1 Document D7 as closest prior art undisputedly discloses a dialysis machine comprising the features of the preamble of claim 1. Its subject-matter is distinguished over D7 by the features of the characterising portion. The dialysis machine of D7 does not include any means for detecting critical conditions at the filter membrane potentially diminishing the efficiency of the treatment.

3.1.2 Therefore the technical effect achieved by the distinguishing features can be seen in a timely indication of dangerous and critical conditions due to partial blocking or "caking" of the filter or membrane (cf. paragraphs [0008], [0018] and [0040] of the patent in suit), based on the recognition that these conditions do not depend on the absolute values of the parameters under control, but on the relationship between the ultrafiltration rate and the plasma flow rate, which may change during the course of the treatment (see paragraph

[0023]), for instance due to variation of the patient's hematocrit over time.

3.1.3 Accordingly, the objective technical problem solved by the invention is to provide a dialysis machine that informs the operator of the dialysis machine about the occurrence of critical conditions due to caking during a dialysis treatment. The Board does not accept the more general definition of the problem suggested by the appellant, namely to improve the safety and efficiency of the dialysis machine, which, of course, is a constant endeavour for the person skilled in the field of dialysis but in the present case not the specific technical problem directly solved by the distinguishing features.

3.1.4 Document D7 teaches the generation of an alarm signal for the operator if prescription variations, i.e. deviations of the set values of certain treatment parameters from desired values previously stored, are detected (column 1, lines 46 to 56 and claim 1 of D7). This, however, does not constitute a hint towards making the operator aware of the specific and time-dependent conditions mentioned above. On the contrary, it is explicitly stated that the patient's hematocrit value is either a standard value or set by the operator (column 2, lines 57 to 66). There is no indication that this value may change during the treatment. The skilled person does not have any reason to contemplate temporal variations of this value and possible problems associated therewith, and there is no motivation for detecting plasma flow rate. In fact, D7 does not recognise the danger of variations of the patient's hematocrit in relation to the caking of the filter.

3.1.5 Document D2

D2 teaches that a filtration factor FF can be calculated as a function of the rate of ultrafiltration and the plasma flow rate as defined in feature [1.8] of claim 1 (page 392, bottom of left-hand column). Table 1 at page 380 indicates a range of 0.35 to 0.50 of the FF for conventional hemofilters. In the first paragraph of the left-hand column of page 216 it is further stated that at low blood flow rates the FF may exceed 30%, leading to a rise in plasma protein concentration and the deposit of proteins on the membrane, thereby influencing its permeability. To reduce this effect it is suggested to use high blood flow rates. In the following two paragraphs, the fact that hematocrit and hemoconcentration may influence the filtration rate is generally addressed. However, even if this is regarded as a hint towards the possible occurrence of caking of the filter, this information does not render obvious the solution according to claim 1. There is no indication in D2 that the patient's hematocrit may vary during the treatment, and that it could thus be advantageous to detect the resulting temporal variation of the plasma flow rate. Accordingly, even if D7 motivated the skilled person to consider detecting the plasma flow rate, there would be no reason to take into account the teaching given in D2. Means for detecting the plasma flow rate cannot be derived from the disclosure at page 391, 2nd paragraph of the right-hand column, since it is stated that the hematocrit is measured in a "timed collection" of the filtrate. Contrary to the appellant's view, such a discontinuous measurement technique involving sampling cannot be equated with "means for detecting the value of

a second parameter ..." as defined in feature [1.7] of claim 1. From the patent in suit it is clear that "detecting" is to be understood in a dynamic sense (see, for instance, paragraphs [0026], [0027] and [0040]), in contrast to a discontinuous sampling technique, usually involving centrifugation (cf. D5, page 456, bottom of left-hand column), where the measurement results are not being available for at least several minutes. Such a delay would clearly counteract the aim of the invention. Accordingly, the subject-matter of claim 1 is not obvious from D7 in view of D2.

3.1.6 Document D1

D1 deals with hemofiltration. It also teaches that the filtration factor is a relevant parameter, to be calculated as indicated in feature [1.8] of claim 1, and that it should be kept below about 0.5 (page 213, 2nd and 3rd paragraphs). It is further indicated that the plasma flow rate is dependent on the hematocrit. However, there is no indication in D1 that the hematocrit or plasma flow rate may vary during the treatment, possibly resulting in caking of the filter, and that it could be advantageous to detect the plasma flow rate in order to inform the operator of the dialysis machine about the occurrence of critical conditions due to caking. The mere fact that it is known from D1 that the filtration factor is a relevant parameter to be kept below an upper limit value does not point towards the objective technical problem indicated above (point 3.1.3) and does not render obvious its solution as defined by the characterising portion of claim 1, in particular its feature [1.7].

3.1.7 Document D5

D5 also relates to hemofiltration. It teaches that the filtration factor can be calculated as indicated in feature [1.8] of claim 1, with the plasma flow rate being determined on the basis of hematocrit measurements performed on blood samples collected from sampling sleeves and subsequently subjected to centrifugation (page 456, section "Operational characteristics and determinants of ultrafiltration rate"). However, as already mentioned above (point 3.1.5), such a discontinuous measurement technique involving sampling cannot be equated with "means for detecting the value of a second parameter ..." as defined in feature [1.7] of claim 1. There is no indication in D5 that the temporal change of hematocrit or plasma flow rate is to be determined. At page 459 (last paragraph of left-hand column) it is stated that the filtration factor should be kept between 0.35 and 0.40 in order to achieve maximal efficiency during hemofiltration. However, there is nothing in D5 pointing towards the objective technical problem indicated above (point 3.1.3).

3.1.8 Document D3

D3 deals with hemofiltration as well and addresses the problem of getting as close as possible to a theoretical maximum of filtrate removal to be achieved with membrane surfaces as small as possible (pages 147 to 149). In the introductory portion (bottom paragraph of page 146) there is a general statement that the filtration rate is limited due to a continuous increase in protein concentration and hematocrit. However, even if this information is regarded as a general hint towards the

possible occurrence of caking of the filter, it does not render obvious the solution according to claim 1. There is no indication in D3 that the plasma flow rate or the hematocrit is to be detected and the filtration factor to be calculated as defined in features [1.7] and [1.8], to make the operator of a dialysis machine aware of the occurrence of critical conditions due to caking during a dialysis treatment.

3.1.9 Document D9

D9 discloses a dialysis machine comprising a hematocrit measurement device 24 for continuously measuring hematocrit during hemodialyis. The measured value is compared to a set value, and when it is larger or smaller than the set value the driving power supplied to decompression pump 28 is decreased or increased respectively (paragraph bridging pages 15 and 16). Due to the resulting change in transmembrane pressure, the ultrafiltration rate is thus controlled on the basis of the measured hematocrit in order to optimise water removal without causing complications in the patient (paragraph bridging pages 10 and 11). This concept of adjusting transmembrane pressure is quite different from that used in D7, and already for this reason it is questionable whether the skilled person would consult D9, which moreover does not give any hint towards the objective problem indicated above (point 3.1.3). Furthermore, even though hematocrit is being monitored in the machine of D9, there is no indication that the blood flow rate is determined. Accordingly, it cannot be said that D9 discloses means for detecting the plasma flow rate (which is dependent on both the blood flow rate and hematocrit), let alone the calculation of the

filtration factor as a function thereof (feature [1.8]). The fact that claim 2 of the patent in suit also deals with means for controlling the pumps is of no relevance, since claim 2 refers back to claim 1, its features being additional to those of claim 1.

3.1.10 Documents D4, D6 and D10

The teaching of document D10 does not go beyond that of D9. D4 and D6 were only cursorily referred to by the appellant (in the written proceedings). D4 deals with glomerular ultrafiltration in rats and states that a filtration factor of 0.25 or 0.33 was reached in a single nephron. D6 relates to hemofiltration and discloses the calculation of the filtration factor as defined in feature [1.8]. It is further stated that no "adverse effects" were detected even if the filtration factor was beyond 0.45. These documents are more remote from the invention and in no way suited to render it obvious when starting from D7.

3.1.11 From the above it follows that the subject-matter of claim 1 is not obvious from D7 in combination with any of the above-mentioned documents.

3.2 Document D8 as starting point

In the written proceedings, the appellant has further challenged inventive step with the skilled person starting from D8 and aiming to achieve a safer and more efficient treatment (column 1, lines 16 to 29 of D8). D8 is not closer to the subject-matter of claim 1 than D7. The distinguishing features over D8 are - at least - those of the characterising portion of claim 1. It

follows that the objective technical problem when starting from D8 is again as indicated above under point 3.1.3, which is more specific than that of the cited statement in D8 on which the appellant relies. D8 gives no hint towards this objective technical problem. Accordingly, for reasons analogous to those given above with respect to D7 as closest prior art, the subject-matter of claim 1 is not rendered obvious from D8 in view of any of the prior-art documents discussed above. The fact that D8 states that the ultrafiltration rate is controlled such that the difference between desired and measured reduction of blood volume is minimised (column 11, lines 46 to 54) and that it is mentioned in the patent in suit that the ultrafiltration rate may be altered if the filtration factor does not have an acceptable value (paragraph [0034]) does not imply that D8 is to be regarded as closest prior art. Controlling the rate of ultrafiltration does not even necessarily imply detecting it (feature [1.5]).

Moreover, in column 2, line 45 to 48, and column 2, line 64, to column 3, line 2, of D8 it is stated that a continuous measurement of the hematocrit is problematic, and that a different approach based on pressure measurements is therefore pursued (page 3, lines 3 et seq.). Accordingly, D8 is not only more remote than D7 from the invention, but even seems to teach away from the invention.

3.3 From the above it follows that the subject-matter of claim 1 is based on an inventive step within the meaning of Article 56 EPC in view of the cited prior-art documents.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

D. Hampe P. L. P. Weber