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Datasheet for the decision of 7 March 2023

Case Number: T 2113/17 - 3.2.02

Application Number: 08841705.0

Publication Number: 2227268

IPC: A61M1/34

Language of the proceedings: EN

Title of invention:
OPTIMIZING CLEARANCE FOR PROTEIN BOUND MOLECULES USING CASCADE FILTRATION THERAPY

Patent Proprietor:
Nikkiso Co., Ltd.

Opponent:
Fresenius Medical Care AG & Co. KGaA

Headword:

Relevant legal provisions:
EPC Art. 54, 56, 84, 123(3)
RPBA 2020 Art. 12(2), 13(2), 25(2)
RPBA Art. 12(4), 12(2)

Keyword:

Primary object of appeal proceedings to review decision
Late-filed facts - submitted with the statement of grounds of appeal - admitted (no)
Amendment after summons - exceptional circumstances (no) - taken into account (no)
Amendments - broadening of claim (no)
Claims - clarity (yes)
Novelty - (yes)
Inventive step - (yes)

Decisions cited:

T 2117/18, G 0003/14

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 2113/17 - 3.2.02

D E C I S I O N
of Technical Board of Appeal 3.2.02
of 7 March 2023

Appellant: (Patent Proprietor)	Nikkiso Co., Ltd. Yebisu Garden Place Tower 20-3, Ebisu 4-chome Shibuya-ku Tokyo 150-6022 (JP)
Representative:	Grosse Schumacher Knauer von Hirschhausen Patent- und Rechtsanwälte Nymphenburger Strasse 14 80335 München (DE)
Respondent: (Opponent)	Fresenius Medical Care AG & Co. KGaA Else-Kröner-Strasse 1 61352 Bad Homburg (DE)
Representative:	Herrmann, Uwe Lorenz Seidler Gossel Rechtsanwälte Patentanwälte Partnerschaft mbB Widenmayerstraße 23 80538 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 25 July 2017 concerning the maintenance of European Patent No. 2227268 in amended form**

Composition of the Board:

Chairman	M. Alvazzi Delfrate
Members:	D. Ceccarelli
	N. Obrovski

Summary of Facts and Submissions

I. The patent proprietor and the opponent appealed against the Opposition Division's decision that account being taken of the amendments made by the patent proprietor during the opposition proceedings according to auxiliary request 1, the patent and the invention to which it relates met the requirements of the EPC. Subsequently, the patent proprietor withdrew its appeal.

II. Oral proceedings took place on 7 March 2023.

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 patent be maintained on the basis of one of auxiliary requests 1 to 5, filed by letter dated 9 November 2017.

III. The following documents are relevant to this decision:

D1: "Effectiveness of Combining Plasma Exchange and Continuous Hemodiafiltration in Patients With Postoperative Liver Failure"; Yonekawa et al.; Artificial Organs, 29(4): 324-328; Blackwell Publishing, Inc.; 2005

D2: "Usefulness of plasma exchange plus continuous hemodiafiltration to reduce adverse effects associated with plasma exchange in patients with acute liver failure"; Sadahiro et al.; Crit Care Med 2001, vol. 29, no. 7, 1386-1392

D3: DE 10 2004 054 747 A1

D4: WO 02/36247 A1

D5: US 2007/0066928 A1

IV. Claim 1 of auxiliary request 1 reads as follows:

"An extracorporeal blood filtration system (100) for removing unwanted molecules from a flow of blood from a patient, comprising:
a first hemofilter (13) for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood in a filtered blood flow;
a first substitution fluid (17) for supplementing the filtered blood flow to create a concentration differential in the combined fluid between the unwanted bound molecules and free unwanted molecules and to promote breakage of the protein bonds;
a second hemofilter (19) for filtering free unwanted molecules from the supplemented blood flow; and
a second substitution fluid (23) for supplementing outflow from the second hemofilter for return to the patient."

Claims 2 to 10 are dependent claims.

V. The appellant's arguments, where relevant to the decision, can be summarised as follows.

Admittance of objections

The features relating to the first hemofilter, to the first substitution fluid and to the second hemofilter, in claim 1 of auxiliary request 1, comprised added subject-matter. This objection had been raised at the earliest stage of the appeal proceedings, with the statement of grounds of appeal, and was highly relevant. Moreover, it would not delay the proceedings

as it only required it to be considered whether paragraph [0010] of the application as originally filed provided a basis for the features in question. For these reasons the objection was to be admitted into the appeal proceedings.

The subject-matter of claim 1 of auxiliary request 1 was not inventive when starting from D3, in combination with D2 or D4. This objection had been anchored in compact form in the statement of grounds of appeal, by way of reference to submissions made in the first-instance proceedings, and was highly relevant. Hence, it was to be admitted into the appeal proceedings.

Extension of the scope of protection

The feature "a first hemofilter (13) for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood in a filtered blood flow", in claim 1 of auxiliary request 1, extended the scope of protection of the patent as granted. Systems were included in which the first hemofilter could filter out blood components, so that the hemoconcentration of the blood could be left unchanged or even decreased, in contrast to what was specified in claim 1 of the patent as granted.

Clarity

In claim 1 of auxiliary request 1, "unwanted molecules", "unwanted protein-bound molecules", "unwanted bound molecules" and "free unwanted molecules" were mentioned. For the person skilled in the art it was entirely unclear whether these

expressions, which had mainly been introduced into the claim by way of amendments after grant, meant the same or different molecules. Hence, the subject-matter of claim 1 of auxiliary request 1 lacked clarity.

Novelty

The subject-matter of claim 1 of auxiliary request 1 was not novel over D1 or D2.

Both D1 and D2 disclosed a system comprising, in particular, a first hemofilter for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood. This was in the form of a plasma separator, in view of the fact that plasma was composed mainly of water (90-91%). Since the plasma separator removed plasma, it followed that it removed water and other waste products from the blood while retaining the blood cells and the protein-bound molecules, which were too large to pass through the membrane of the plasma separator. Consequently, the concentration of the protein-bound unwanted molecules was increased. Moreover, according to the patent in suit a plasma separator and a hemofilter were equivalent (paragraphs [0004] and [0014]).

Inventive step

The subject-matter of claim 1 of auxiliary request 1 was not inventive when starting from D4, in combination with common general knowledge or D5.

The only distinguishing feature of the subject-matter of the claim over D4 was a second substitution fluid for supplementing outflow from the second hemofilter to

return to the patient. According to D4 substitution fluid was provided between two hemofilters.

The definition of the second substitution fluid in claim 1 was very general. It was merely required that the second substitution fluid could supplement the blood. Any solution that could be added to blood, and hence supplement it, would fall under this definition. This was confirmed by column 6, lines 1 to 3 and by paragraphs [0030], [0035] and [0046] of the patent as granted, which generally described the substitution fluid as any fluid having a desired concentration of electrolytes. The substitution fluid according to the claim did not have to completely replenish the fluid removed by the hemofilters.

The objective technical problem solved by the distinguishing feature could be regarded as that of avoiding blood coagulation in the extracorporeal blood filtration system. This was a universal problem in extracorporeal blood treatment systems.

The person skilled in the art knew that, for avoiding coagulation, it was routine to add an anticoagulant, e.g. citrate, upstream of the filters, and then to supplement the blood with calcium ions to balance the electrolytes in the blood returned to the patient. Moreover, D5 expressly taught adding citrate upstream of a hemofilter and supplementing the blood to be returned to the patient with an electrolyte source containing calcium ions (paragraph [0045]), contained in a substitution fluid added to blood (paragraphs [0048], [0078] and [0080] of D5). The patent itself acknowledged that according to D5 a substitution fluid was added to blood (paragraph [0009]). It followed that, in both a broad and a narrow interpretation of

the claim wording, the latter requiring that the second substitution fluid effectively compensated for the volume of fluid removed by the second hemofilter, the subject-matter of claim 1 of auxiliary request 1 was obvious in view of the combination of D4 with D5.

VI. The respondent's arguments, where relevant to the decision, can be summarised as follows.

Admittance of objections

The appellant had raised an objection of added subject-matter against claim 1 of auxiliary request 1, which corresponded to the request found allowable by the Opposition Division, for the first time on appeal. It was questionable against which part of the impugned decision this argument was made. Moreover, the objection was not relevant in substance. Hence, it was not to be admitted.

The objection of lack of inventive step against claim 1 of auxiliary request 1 starting from D3 was not to be admitted either, as grounds for it had been submitted late.

Extension of the scope of protection

As noted by the Opposition Division in the impugned decision, when a hemofilter filtered out water and other waste solutes from a blood flow and the concentration of the unwanted protein-bound molecules rose, the hemoconcentration of the blood then had to rise too, since it was harder for blood cells to pass through a hemofilter than proteins present in the blood.

Clarity

The four formulations for unwanted molecules in claim 1 of auxiliary request 1 were clear in the context of the claim. In particular, the meaning of "free unwanted molecules" was clear in view of the definition of the breakage of the protein bonds.

Novelty

D1 and D2 did not disclose a first hemofilter suitable for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood.

A plasma separator as disclosed in D1 and D2 separated the blood plasma from the blood cells. Besides water and other waste solutes, the proteins and unwanted protein-bound molecules in the blood were also separated from the blood cells. Hence, only the relative amount of the blood cells was raised by the plasma separator. There was no disclosure in D1 or D2 according to which the concentration of proteins or unwanted protein-bound molecules could be affected.

Inventive step

The subject-matter of claim 1 of auxiliary request 1 was inventive when starting from D4, in combination with common general knowledge or D5.

D4 did not disclose a second substitution fluid for supplementing outflow from the second hemofilter to return to the patient.

The problem formulated by the appellant was not

correct, as it was not derivable from the teaching of the patent. Moreover, even if the person skilled in the art had wanted to solve a problem related to coagulation, they could have used anticoagulants other than citrate, which would not have required any supplement of electrolytes downstream of the second hemofilter.

In any case, the second substitution fluid as defined in claim 1 of auxiliary request 1 had to compensate (by complete replacement) for the volume of fluid removed by the second hemofilter, which, according to D4, was done upstream of the second hemofilter. An electrolyte solution comprising calcium ions as taught by D5 was not a substitution fluid as defined in the claim.

Reasons for the Decision

1. The invention

The invention relates to an extracorporeal blood filtration system for removing unwanted molecules from blood. Such molecules are typically inflammatory mediators produced by an excessive inflammatory response caused by diseases such as septic shock, systematic inflammatory response syndrome (SIRS), and multiple organ failure (MOF).

The system can be used for treating intensive-care patients suffering from inflammatory mediator-related diseases such as septic shock, systematic inflammatory response syndrome (SIRS), and multiple organ failure (MOF), which diseases can arise from the excessive release of inflammatory mediators into the bloodstream by overstimulation of the immune system.

An embodiment of the extracorporeal blood filtration system is depicted in Figure 2 of the patent, reproduced below.

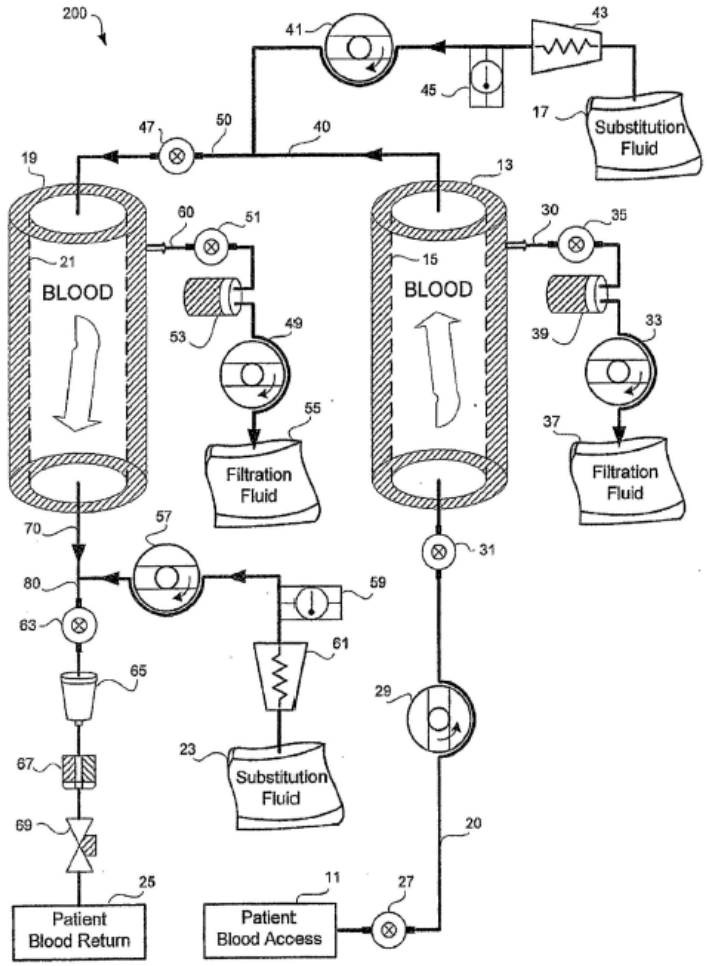


FIG. 2

The system as defined in claim 1 of auxiliary request 1 comprises a first hemofilter (13), a first substitution fluid (17) for supplementing the filtered blood flow, a second hemofilter (19) and a second substitution fluid (23) for supplementing outflow from the second hemofilter for return to the patient.

In essence, the patient's blood undergoes two cascaded hemofiltrations.

According to the patent (paragraph [0011]), this is done to better remove the unwanted molecules. It is assumed that some of the unwanted molecules are bound to larger proteins in the unfiltered blood. Because of their large size, the entities made up by the unwanted molecule and the protein are not removed by the first hemofiltration; however, the first hemofiltration is intended to raise the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood. The subsequent addition of the first substitution fluid is then intended to create a concentration differential in the combined fluid between the unwanted bound molecules and free unwanted molecules to promote breakage of the protein bonds, so that the unbound unwanted molecules are removed by the second hemofiltration.

2. Admittance of objections

2.1 The appellant's objections with regard to added subject-matter of claim 1 of auxiliary request 1 were raised for the first time on appeal.

Under Article 12(4) RPBA 2007, which applies by virtue of Article 25(2) RPBA 2020, the Board has discretion to hold inadmissible facts, evidence or requests which could have been presented in the first-instance proceedings.

Auxiliary request 1 corresponds to auxiliary request 1 held allowable by the Opposition Division after thorough discussion during the oral proceedings at first instance. There is no reason why the appellant could or should not have already raised the objections of added subject-matter in the first-instance

proceedings. By not doing so, the appellant did not enable the Opposition Division to decide on the issue, which would, if admitted on appeal, force the Board and the respondent to consider the objection from scratch. This is in contrast to the primary object of the appeal proceedings, which is to review the decision under appeal in a judicial manner (Article 12(2) RPBA 2020). Under these circumstances, the alleged high relevance of the objections, which is disputed by the respondent, and considerations of procedural economy are secondary aspects.

For these reasons the objection of added subject-matter was not admitted into the appeal proceedings under Article 12(4) RPBA 2007.

2.2 The appellant also submitted that the subject-matter of claim 1 of auxiliary request 1 was not inventive over the combination of D3 with D2 or D4.

In the statement of grounds of appeal, the appellant only referred to letters sent during the proceedings at first instance, before the impugned decision was notified to the parties. It did not provide any reasons why it requested that the decision under appeal be reversed in this respect.

As a rule, in appeal proceedings general references to submissions made in the proceedings before the departments of first instance are not taken into account due to a lack of substantiation. Otherwise, it would be left to the Board and the other party to determine which parts of such submissions are relevant to which parts of the decision under appeal or the other party's arguments (T 2117/18, point 2.2.13 of the Reasons). Hence, the appellant's references in the

statement of grounds do not meet the requirements of Article 12(2) and (4) RPBA 2007, which are applicable under Article 25(2) RPBA 2020 (see T 2117/18, point 2.2.1 of the Reasons), and are disregarded by the Board.

The appellant only substantiated the objection of lack of inventive step in view of the combination of D3 with D2 or D4 after notification of the summons to oral proceedings by the Board. For the reasons explained above, this amounts to an amendment to the appellant's appeal case.

Under Article 13(2) RPBA 2020 any amendment to a party's appeal case made after notification of a summons to oral proceedings must, in principle, not be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

The appellant did not outline any exceptional circumstances or provide cogent reasons for the amendment. The alleged *prima facie* relevance alone, disputed by the respondent, does not amount to exceptional circumstances.

Hence, the objection of lack of inventive step in view of the combination of D3 with D2 or D4 is not admitted into the appeal proceedings under Article 13(2) RPBA 2020.

3. Extension of the scope of protection

The appellant argued that since claim 1 of auxiliary request 1 did not state that the first hemofilter was for raising hemoconcentration of the blood in a

filtered blood flow, the scope of protection of the patent was extended by this request.

However, claim 1 of auxiliary request 1 defines the suitability of the first hemofilter for filtering out water and other waste solutes and for raising the concentration of the unwanted protein-bound molecules. This implies that the filter does not filter out the blood proteins bound to the unwanted molecules from the blood. In turn, contrary to the appellant's assertion, this excludes the fact that the filter can filter out blood components (i.e. white or red blood cells) which are larger in size than the blood proteins bound to the unwanted molecules. Hence, the first hemofilter as defined in the claim is inherently suitable for raising hemoconcentration in the filtered blood flow.

As a result, the scope of protection of claim 1 of auxiliary request 1 does not extend beyond that of the patent as granted, which means that the requirements of Article 123(3) EPC are fulfilled.

4. Clarity

The opponent argued that the definition of "unwanted molecules", "unwanted protein-bound molecules", "unwanted bound molecules" and "free unwanted molecules" rendered claim 1 of auxiliary request 1 unclear.

Claim 1 of the patent as granted already defined "unwanted molecules". An objection of lack of clarity to this term cannot be considered in opposition (G 3/14, Order).

The other expressions do not introduce any clarity

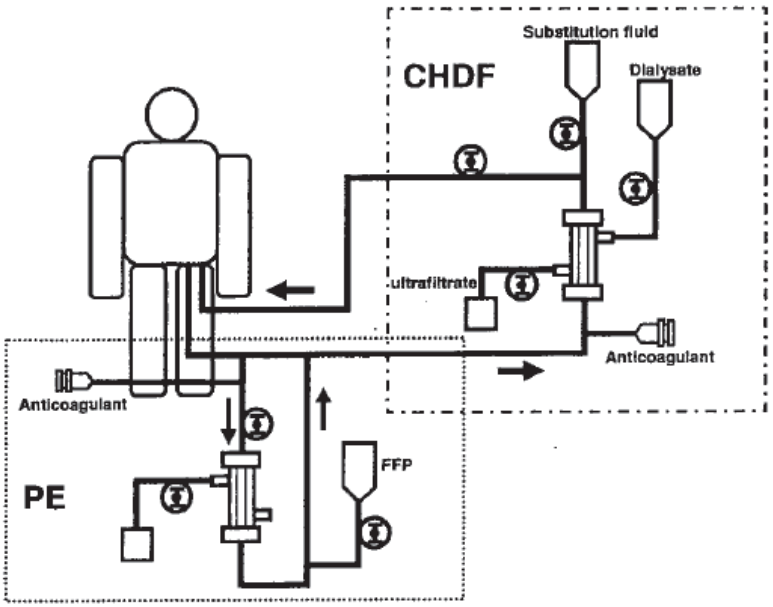
problems. "Unwanted protein-bound molecules" and "unwanted bound molecules" are simply the unwanted molecules which are bound to proteins. In contrast, "free unwanted molecules" are the molecules which are not bound to anything. The claim refers to "the unwanted bound molecules" after the introduction of "unwanted protein-bound molecules". The use of the definite article "the" in the first expression implies that the two expressions have the same meaning.

Hence, claim 1 of auxiliary request 1 fulfils the clarity requirements of Article 84 EPC.

5. Novelty

The appellant argued that the subject-matter of claim 1 of auxiliary request 1 lacked novelty over D1 or D2.

These documents disclose similar extracorporeal blood filtration systems (Figure 1 of each document). Figure 1 of D1 is reproduced below.



Each of these extracorporeal blood filtration systems comprises a first filter and a first fluid for supplementing the filtered blood flow (the plasma exchange (PE) part of the system in Figure 1 of D1), and a second hemofilter for filtering out unwanted molecules from the supplemented blood flow and a second substitution fluid for supplementing outflow from the second hemofilter for return to the patient (the continuous hemodiafiltration part (CHDF) of the system in Figure 1 of D1).

It is a matter of dispute whether the first filters according to D1 and D2 (plasma separators for plasma exchange) can be considered hemofilters for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood within the meaning of claim 1 of auxiliary request 1.

The Board noted the appellant's argument that, according to the patent in suit, a plasma separator and a hemofilter were equivalent (paragraphs [0004] and [0014]). In these paragraphs the patent explains that the invention could comprise a typical hemofiltration system such as that used in plasmapheresis. Still, the plasma separators according to D1 and D2 are not necessarily suitable for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood. Besides water and other waste solutes, these plasma separators may also filter out proteins, together with the molecules bound to them, which are smaller in size than the white and red blood cells. This depends on the non-disclosed pore size of the filters used in the plasma separators according to D1 and D2. If the plasma separators according to D1 and

D2 also filter out the unwanted protein-bound molecules, the concentration of these protein-bound molecules may decrease in the blood remaining downstream of the plasma separators.

It follows that neither D1 nor D2 directly and unambiguously discloses a first hemofilter suitable for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood in a filtered blood flow.

Hence, the subject-matter of claim 1 of auxiliary request 1 is novel over D1 and D2 (Article 54(1) and (2) EPC).

6. Inventive step

The appellant argued that the subject-matter of claim 1 of auxiliary request 1 lacked inventive step starting from D4, in combination with common general knowledge or D5.

It is common ground that D4 discloses a hemodiafiltration system comprising two cascaded hemofilters (page 4, lines 15 to 18). The first hemofilter is suitable for raising the concentration of the unwanted protein-bound molecules by filtering out water and other waste solutes from the blood in a filtered blood flow (the filter essentially filters out plasma water; page 5, lines 7 to 9). The system also comprises a first substitution fluid for supplementing the filtered blood flow to create a concentration differential in the combined fluid between the unwanted bound molecules and free unwanted molecules and to promote breakage of the protein bonds (page 5, lines 9 to 11). The second hemofilter is suitable for filtering

out free unwanted molecules from the supplemented blood flow.

D4 does not disclose a second substitution fluid for supplementing outflow from the second hemofilter for return to the patient. In the system according to D4 the first substitution fluid compensates for the loss both at the first and at the second hemofilters (page 5, lines 9 to 18). Moreover, D4 explains the advantages of having a single substitution fluid downstream of the first filter (page 5, line 18 to page 6, line 2).

For the formulation of the objective technical problem and the assessment of inventive step it is crucial to establish the technical meaning of the distinguishing feature, i.e. a second substitution fluid for supplementing outflow from the second hemofilter for return to the patient.

While the appellant argued that any solution that could be added to blood, in any quantity, would fall under the meaning of the distinguishing feature, the respondent argued that the second substitution fluid had to compensate (by complete replacement) for the volume of fluid removed by the second hemofilter.

The Board shares the respondent's view. The term "substitution fluid", which is a known term in the art, implies that the fluid should be suitable for substituting, i.e. taking the place of, another fluid. The claim inherently prescribes which fluid is to be substituted, namely the fluid removed by the second hemofilter, as it specifies that the second substitution fluid is for supplementing outflow from the second hemofilter. Moreover, it is clear from the

claim that essentially all the fluid removed by the second hemofilter has to be substituted, as the resulting fluid after the substitution is to be returned to the patient, inherently without harming them. This interpretation does not contradict the teaching of the patent, in particular column 6, lines 1 to 3 and paragraphs [0030], [0035] and [0046] mentioned by the appellant, which merely disclose the general composition of a suitable substitution fluid.

In view of this interpretation, the Board doubts that the problem formulated by the appellant, i.e. that of avoiding blood coagulation in the extracorporeal blood filtration system, can be regarded as the objective technical problem solved by the distinguishing feature.

In any case, even if it were to be assumed that the person skilled in the art wanted to provide anticoagulation by adding citrate in the system in D4, as argued by the appellant, the provision of calcium ions (known as such when citrate anticoagulation is performed) administered downstream of the second hemofilter would not amount to the provision of a second substitution fluid within the meaning of claim 1 of auxiliary request 1. Calcium ions are not intended to compensate (by complete replacement) for the volume of fluid removed by the second hemofilter.

It follows that the combination of D4 with the common general knowledge does not render the subject-matter of claim 1 of auxiliary request 1 obvious.

D5, cited in the patent in paragraph [0009], concerns the automation and optimisation of citrate anticoagulation. It teaches an electrolyte source "to replenish blood flow [...] with electrolytes such as

[...] calcium [...] that may have been depleted through filtration" (paragraph [0045]). According to paragraph [0048] the electrolytes may be included in a substitution fluid or provided from a separate source. Hence, the Board accepts the appellant's argument that D5 discloses a substitution fluid; however, when considering the teaching of D5 for providing citrate anticoagulation in the system in D4, the person skilled in the art would have provided the electrolytes downstream of the second hemofilter from a separate source. This is because D4 teaches that it is advantageous to provide a single substitution fluid downstream of the first hemofilter for compensating for the loss both at the first and at the second hemofilters (page 5, lines 9 to page 6, line 2). The electrolyte solution alone would not be a second substitution fluid within the meaning of claim 1 of auxiliary request 1.

Hence, the combination of D4 with D5 does not render the subject-matter of claim 1 of auxiliary request 1 obvious either.

It follows that the subject-matter of claim 1 of auxiliary request 1 is inventive (Article 56 EPC) when starting from D4, in combination with common general knowledge or D5.

7. In conclusion, none of the appellant's objections prejudices the maintenance of the patent on the basis of auxiliary request 1.

Since auxiliary request 1 corresponds to the request held allowable by the Opposition Division in the impugned decision, the appeal has to be dismissed.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Chavinier-Tomsic M. Alvazzi Delfrate

Decision electronically authenticated