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Datasheet for the decision of 8 May 2018

Case Number: T 1608/13 - 3.2.02

Application Number: 03781225.2

Publication Number: 1572330

IPC: A61M1/16

Language of the proceedings: EN

Title of invention:
PERM SELECTIVE ASYMMETRIC HOLLOW FIBRE MEMBRANE FOR THE SEPARATION OF TOXIC MEDIATORS FROM BLOOD

Patent Proprietor:
Gambro Lundia AB

Opponent:
Fresenius Medical Care Deutschland GmbH

Headword:

Relevant legal provisions:
EPC Art. 83, 84, 100(b), 111(1)
EPC R. 42(1)(e)

Keyword:

Sufficiency of disclosure - relationship between Article 83 and Article 84
Grounds for opposition - lack of clarity no ground for opposition - insufficiency of disclosure (no)
Appeal decision - remittal to the department of first instance (yes)

Decisions cited:

T 0256/87, T 0585/92, T 0339/97, T 0083/01, T 0464/05, T 0608/07, T 0593/09, T 0967/09, T 2290/12

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1608/13 - 3.2.02

D E C I S I O N
of Technical Board of Appeal 3.2.02
of 8 May 2018

Appellant: (Patent Proprietor)	Gambro Lundia AB Box 10101 220 10 Lund (SE)
Representative:	Hornung, Veronika Margot c/o Gambro Dialysatoren GmbH Holger-Crafoord-Strasse 26 72379 Hechingen (DE)
Respondent: (Opponent)	Fresenius Medical Care Deutschland GmbH Else-Kröner-Strasse 1 61352 Bad Homburg (DE)
Representative:	Stolmár & Partner Patentanwälte PartG mbB Blumenstraße 17 80331 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 17 May 2013 revoking European patent No. 1572330 pursuant to Article 101(3)(b) EPC**

Composition of the Board:

Chairman	E. Dufrasne
Members:	D. Ceccarelli
	M. Stern

Summary of Facts and Submissions

I. The patent proprietor has appealed against the Opposition Division's decision, dispatched on 17 May 2013, to revoke European patent No. 1 572 330.

The patent was opposed on the grounds of lack of novelty and inventive step, insufficient disclosure and added subject-matter.

The Opposition Division held that the invention as defined in claim 1 of the patent as granted was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. Hence, the ground for opposition according to Article 100(b) EPC prejudiced the maintenance of the patent as granted. The Opposition Division did not decide on the other grounds on which the patent was opposed.

II. Notice of appeal was received on 10 July 2013. The appeal fee was paid on the same day. The statement setting out the grounds of appeal was received on 27 September 2013.

III. Oral proceedings took place on 8 May 2018.

The appellant requested that the decision under appeal be set aside and that the patent be maintained as granted or, in the alternative, on the basis of auxiliary request 1 filed with letter dated 26 September 2013.

A request for reimbursement of the appeal fee, made with the statement of grounds, was withdrawn during the oral proceedings.

The respondent requested that the appeal be dismissed.

IV. The following documents are mentioned in the present decision:

D7: European Standard EN 1283, 1996;
D9: "Analysis and Prediction of Sieving Curves for Ultrafiltration Membranes: A Universal Correlation?", A.S. Michaels, Separation Science and Technology, Vol. 15, No. 6, pp 1305-1322, 1980;
D17: "Replacement of Renal Function by Dialysis: A Textbook of Dialysis", Third Edition - Updated and Enlarged, edited by J.F. Maher, Kluwer Academic Publishers, pp 319-321, 1989;
E3: "Basic Principles of Membrane Technology", Second Edition, M. Mulder, Kluwer Academic Publishers, pp 182-189, 2003;
E4: EP-A-0 568 045.

V. Claim 1 of the patent as granted reads as follows:

"A permselective asymmetric hollow fibre membrane for the separation of toxic mediators from blood, comprised of at least one hydrophobic polymer and at least one hydrophilic polymer, wherein a separation layer is present in the innermost layer of the hollow fiber **characterized in that** said membrane allows passage of molecules having a molecular weight of up to 45 000 Daltons with a sieving coefficient of 0.1-1.0 in presence of whole blood,
and has a nominal cut-off of 200,000 Daltons, with a sieving coefficient of 0.1, in water."

VI. The appellant's arguments where relevant to the present decision may be summarised as follows:

In the impugned decision the Opposition Division had held that example 1 in the patent did not exemplify at least one way of carrying out the invention. However, that example provided clear and unambiguous instructions as to all manufacturing steps and parameters needed by the skilled person for manufacturing a membrane according to claim 1. Whether the nominal cut-off in water defined in claim 1 was explicitly disclosed in example 1 was irrelevant, as there was no reason to believe that the membrane of that example would not fulfil all the features of the claim. The respondent had not discharged its burden of proof in that respect.

In the impugned decision the Opposition Division had stated that the patent did not disclose sufficiently how the sieving coefficients in the presence of whole blood could be determined. However, the skilled person knew that D7 formed the basis for determining the sieving coefficients. The Opposition Division had noted that according to D7 both bovine and human plasma could be used to determine them and that the patent did not specify which type of plasma should be used. However, there was no reason to believe that there was a substantial difference between the plasma types cited in D7. Again, the respondent had provided no proof in that respect. The Opposition Division had also noted that D7 prescribed very specific cross-flow and filtration rates in relation to the maximum blood flow rate as defined by the manufacturer. Since the patent was silent on that maximum blood flow rate for the claimed membrane, the sieving coefficients could not be determined. However, the skilled person would always

choose maximum blood flow rates between practical operation limits, which were generally known for haemodialysers for medical use, and within those limits the influence of the flow rate on the outcome for a sieving coefficient measured in accordance with D7 was negligible, as also derivable from D17 (page 320, left column, first paragraph). The Opposition Division had also noted that D7 taught how to determine sieving coefficients for a hollow fibre module and not for a single hollow fibre as defined in claim 1. The mass transfer conditions strongly depended on the fibre density, length and flow distribution geometry of the module, which were not specified in the patent. However, the sieving coefficients were a function of the structure of the membrane and were not significantly influenced by the parameters mentioned by the Opposition Division within practical operation limits in the field of haemodialysis. The impugned decision also referred to the fact that the appellant had stated that variations of up to 20% among measurements of sieving coefficient values had to be expected. That was proof that the sieving coefficients as claimed could not be reliably determined. However, such variations could be expected between single measurements, whereas the skilled person knew that several measurements had to be performed in order to reduce standard deviation and improve the reliability of the final (average) measured value. According to the impugned decision, the patent did not disclose how the nominal cut-off in water had to be determined. However, it was common general knowledge (derivable from D9) that dextran would be used for determining the cut-off in a molecular range around 200,000 Dalton, as that was the commonly used tracer having a molecular weight distribution in that range.

In the impugned decision the Opposition Division had stated that the patent did not disclose sufficiently how the invention could be performed over the whole range defined in claim 1. However, the patent did not have to disclose all possible ways to obtain a membrane according to claim 1. A patent claim was intended to provide a generalisation of a specific disclosure, in a good balance between that disclosure and the contribution over the prior art. Rather, the skilled person, knowing standard haemodialysis membranes and starting from the manufacturing conditions and parameters used in example 1 of the patent, would be able to perform slight modifications of those parameters and, with some trial and error, using routine methods, obtain other membranes according to claim 1. Specifically, the given temperature range of 30° to 80° of the polymer solution from which the membrane was to be obtained, as mentioned in paragraph [0041] of the patent, had to be interpreted as a necessary but not sufficient condition in order for a membrane according to claim 1 to be obtained.

The present case was similar to that underlying decision T 339/97, in which a membrane with an exclusion limit for molecules between 30,000 and 40,000 Dalton was claimed. The board in that case had considered that the skilled person was in a position to readily determine the exclusion limit of a membrane, even if somewhat varying measured results were obtained. Such variations might possibly affect the clarity of the subject-matter claimed, but did not render the invention insufficiently disclosed since, in accordance with the findings in decision T 608/07, they would not deprive the skilled person of the promise of the invention. Clarity was not a ground for opposition.

It followed that the invention as defined in claim 1 of the patent as granted was sufficiently disclosed to the skilled person. The case had then to be remitted to the Opposition Division for further prosecution, in order for the remaining issues to be considered by two instances.

VII. The respondent's arguments where relevant to the present decision may be summarised as follows:

The Opposition Division had correctly decided that Article 83 EPC was not fulfilled for two main reasons, i.e. that the patent as granted did not provide any information how the features of claim 1 and example 1 could be determined and that the claimed invention could not be put into practice over its whole scope. According to decision T 585/92, in appeal proceedings it was the appellant who bore the burden of proving that the reasons for the impugned decision were not correct.

According to decisions T 593/09 and T 83/01, if a parameter defining the invention was described in such an ambiguous way as to make its determination or measurement impossible for the skilled person, that resulted in the invention being insufficiently disclosed. The patent did not describe how to measure the claimed nominal cut-off of 200,000 Dalton or the sieving coefficient as defined in the characterising portion of claim 1. It was doubtful that the skilled person would implement the measuring method described in D7. D7 concerned the determination of sieving coefficients of filter modules and not hollow fibre membranes, and used a different definition of the sieving coefficient, according to the equation under point 5.4.2.2. Moreover, E4 disclosed a different

measuring method. For any measuring method to be possibly performed it was not disclosed which molecule had to be used, how the membrane had to be arranged in a filter module, and which kind of plasma and which flow conditions had to be used. All of these parameters had an influence on the measurement of the sieving coefficient, as explained in E3, pages 183 and 184. Regarding the dependence of the sieving coefficient on the flow rate, the appellant's arguments based on D17 were to be disregarded, since D17 was not concerned with determining the sieving coefficient in blood or water, but in plasma, which had a different protein content. According to D17 (page 320, last paragraph), the presence of proteins had a strong influence on the sieving coefficient. The appellant's statement that the skilled person would know that dextran had to be used to determine the nominal cut-off as defined in claim 1 was also not credible. The patent did not mention dextran at all, and there were different methods for determining sieving coefficients. Contrary to the appellant's assertions, the sieving coefficient also depended on the geometry of the fibres within a module, as derivable from D17, figure 17 and page 320, first paragraph. The appellant itself, in a letter dated 15 November 2012, had admitted that in the measurement of a sieving coefficient variations of up to 20% had to be expected. Hence, the skilled person could not measure the sieving coefficients defined in claim 1 of the patent as granted with a precision necessary to establish whether a given membrane solved the problem of the invention or, at least, to establish whether the membrane fell within the scope of the claim. This last uncertainty alone, according to the jurisprudence of the boards of appeal (for example T 464/05 or T 256/87), resulted in an insufficient disclosure.

The appellant had not proved that a membrane with the combination of sieving coefficients defined in claim 1 of the patent as granted could be manufactured. In the letter dated 15 November 2012 it had shown that a membrane manufactured according to example 1 of the patent had a sieving coefficient of 0.1 in water already for molecules of 66,000 Dalton. That implied that for molecules of 200,000 Dalton the sieving coefficient would be much smaller, contrary to the requirements of claim 1 of the patent as granted. The patent as granted was also contradictory, in particular concerning the sieving coefficient for molecules of up to 45,000 Dalton. In particular, figure 3b showed that for those molecules the sieving coefficient was 0.8 to 1, contrary to the requirement of claim 1, according to which it had to be 0.1 to 1. Moreover, according to the patent, paragraphs [0043] to [0056], the manufacturing of a membrane depended on so many parameters that it was not feasible, without undue burden, for the skilled person to try to modify the specific manufacturing method proposed in example 1 and work out the invention over the whole scope defined in claim 1. That could also be derived from the membranes obtained according to examples 2 and 3 of the patent, which constituted comparative examples even if they were obtained under almost the same manufacturing conditions as in example 1. In particular it was hardly conceivable that a membrane according to claim 1 of the patent as granted could be obtained in the whole temperature range of 30° to 80° of the polymer solution mentioned in paragraph [0041] of the patent.

Decision T 339/97 was not relevant, in particular because in the present case the membrane was defined by two retention parameters which influenced each other. Moreover, one of these parameters was a single value of

the cut-off of 200,000 Dalton, and not a range.

The case should not be remitted to the Opposition Division for further prosecution, but the patent had to be revoked also on the grounds of added subject-matter, lack of novelty and lack of inventive step.

Reasons for the Decision

1. The appeal is admissible.

2. The invention relates to a permselective asymmetric hollow fibre membrane for the separation of toxic mediators from blood.

According to the patent, the membrane is useful for treating systemic inflammatory response syndrome (SIRS) and multiorgan system failure (MOSF) (paragraph [0012]), which are dangerous secondary complications deriving for example from a serious illness, trauma or major surgery (paragraph [0002]). The success of the treatment, which is performed by haemofiltration and may be carried out as continuous renal replacement therapy (paragraph [0062]), depends on the ability to effectively remove from the blood the various host-derived inflammatory toxic mediators (TM) responsible for organ dysfunction. Haemofiltration membranes used in conventional intermittent haemodialysis for treating renal failures remain deficient in the treatment of MOSF because they are not effective in removing toxic mediators in the upper molecular weight range (paragraph [0004]).

The membrane according to the invention is characterised by parameters expressing its permeability

for molecules of a certain molecular weight, in the presence of whole blood and water respectively.

3. In the impugned decision, the Opposition Division held that the invention as defined in claim 1 of the patent as granted was not sufficiently disclosed, mainly for two reasons (point 3 of the reasons): the patent did not provide sufficient information to enable the skilled person to determine the parameters defined in claim 1 and example 1, and the invention could not "be worked over the whole range claimed". The respondent endorsed the Opposition Division's view and provided supporting arguments.

3.1 Referring to T 585/92 the respondent argued that in appeal, after the Opposition Division had revoked the patent, the burden of proof was shifted to the appellant to prove that the decision was wrong. However, the primary aim of appeal proceedings is to review the decision under appeal on the basis of the submissions and requests of the parties. This clearly encompasses the review of the Opposition Division's reasoning, in particular the assessment of the respondent's objections considered in the decision. If the reasoning as such is found to be wrong, there cannot be any shift of the burden of proof on the substance. As regards the latter, it is established jurisprudence that a successful objection of lack of sufficiency presupposes that there are serious doubts substantiated by verifiable facts (T 967/09 and other cases cited in Case Law of the Boards of Appeal of the European Patent Office, 8th edition 2016, III.G.5.5.2.2). It is primarily the respondent's duty to provide such facts in support of its objections.

3.2 As far as determining the parameters is concerned, the respondent's arguments relate to the defined sieving coefficients, in the presence of whole blood and water respectively. The nominal cut-off has been explicitly defined in terms of a sieving coefficient of 0.1.

The description of the patent (paragraph [0027]) provides a definition of a sieving coefficient of a membrane, i.e. the ratio of the concentration of a specific molecule in the filtrate to the concentration in the feed. The higher the sieving coefficient, the higher the membrane's permeability to a given molecule. In view of the definition in the patent, the claimed membrane should be relatively permeable to small (or light) molecules with a molecular weight up to 45,000 Dalton in the presence of whole blood and almost impermeable to large (or heavy) molecules with a molecular weight exceeding 200,000 Dalton in the presence of water.

3.3 The Board notes that a patent document is directed to the skilled person, who interprets it in the light of the common general knowledge in the technical field concerned. Consequently, it is not necessary for all the details of the invention to be specifically described in order for a disclosure to be sufficient. In the present case, in the absence of a description in the patent of a specific measuring method for determining the sieving coefficient of a membrane for the separation of toxic mediators from blood by haemofiltration, the skilled person would first look for applicable standards in the field, if present. D7 is a European standard for haemodialysers, haemodiafilters, haemofilters, haemoconcentrators and their extracorporeal circuits. In point 5.4.2 the standard teaches how to measure the sieving

coefficient, by using bovine or human plasma as test fluids under certain flow conditions, for haemodiafilters, haemofilters and haemoconcentrators. This is precisely the field of the invention. Hence, the skilled person would turn to D7 and apply its teaching. Whether other methods for carrying out the measurements are available, as argued by the respondent with reference to E4, is not decisive as long as there is no evidence that the results in the specific field of the invention would be contradictory depending on the chosen method. The respondent has not provided any such evidence.

The Board sees no contradiction between the definition of the sieving coefficient in the patent and the one provided in point 5.4.2.2 of D7. The latter definition, according to which the sieving coefficient is provided by twice the concentration of the molecule in the filtrate divided by the sum of the concentrations at the inlet and at the outlet, both at the blood side - or feed, within the meaning of the patent - of a device containing the membrane to be tested, simply takes into account the variations in concentration at the inlet and outlet of the blood side of the device.

The argument that D7 concerns the determination of sieving coefficients of complete filter modules and not hollow fibre membranes - and that for that reason its teaching is not applicable to the membrane according to claim 1 - is not convincing. It has to be noted that the claimed membrane is for the specific use in known blood purification procedures with known filter modules. Hence, the skilled person would provide the filter module with the membrane to be tested as is generally known in the art. The respondent has not provided any evidence that this would not be the case.

The respondent further argued that the molecules to be filtered, the specific way the membrane was arranged in the filter module, and the specific kind of plasma and flow conditions used in accordance with the teaching of D7 would all influence the measurements. Since the patent did not specify any of these variables, the measurements would not be reproducible. The Board notes that the blood purification procedure in which the claimed membrane is to be used is designed to filter out known blood proteins and to take place under known limited ranges of operation in terms of transmembrane pressure, cross-flow rate and temperature. Certainly, as derivable in particular from E3 and D17 referred to by the respondent, within those ranges of operation a certain variability of the sieving coefficient is to be expected. This variability, which is not the one that may be present between any two measurements, but the one resulting from a statistically relevant series of measurements in the known ranges of operation, can result, at most, in a lack of clarity of the subject-matter claimed as far as concerns the end points of the sieving coefficient range in the presence of whole blood and the molecules with the defined molecular weight.

Clarity (Article 84 EPC) and sufficiency of disclosure (Article 83 EPC) are two distinct requirements of the EPC, as reaffirmed in recent case law (T 2290/12, Reasons 3.1, citing T 608/07, Reasons 2.5.2). In the present case, the technical problem which the invention aims to solve is how to improve the effectiveness of a blood treatment by providing a membrane that permits a better separation of toxic mediators in the upper molecular weight range (up to 45,000 Dalton), while better retaining albumin, which has a molecular weight

of 68,000 Dalton (paragraph [0013] of the patent). The Board does not see how - and the respondent has not explained why - a potential lack of clarity deriving from the claim definition of the sieving coefficient in the presence of whole blood could have a major impact on implementing a membrane which solves that specific problem. Hence, using the wording of T 608/07, with which the Board concurs, such a potential lack of clarity would not deprive the skilled person of the promise of the invention, and would not result in insufficiency of disclosure. As far as lack of clarity is concerned, it is not a ground for opposition.

3.4 As regards determination of the cut-off of 200,000 Dalton in the presence of water, similar considerations apply. The respondent's arguments focus on the uncertainty arising from the variety of possible test molecules that could be used to determine the cut-off. The appellant referred to D9, a review article concerning the determination of sieving curves for ultrafiltration membranes, which stated that the most commonly employed test molecules were exemplified by dextrans and certain derivatives, particularly because of their availability in widely differing molecular weight ranges (page 1306, second paragraph). The respondent provided no evidence quantifying the alleged influence of the specific test molecules in the determination of the cut-off. In the absence of such evidence there is no reason to believe that the resulting uncertainty could go beyond the domain of clarity and extend to insufficiency of disclosure.

3.5 In conclusion, as far as determination of the sieving coefficients is concerned, the Board concurs with the findings in T 339/97 (Reasons 3.1), in which a membrane with an exclusion limit for molecules between 30,000

and 40,000 Dalton was claimed. In the present case, too, the skilled person is in a position to readily determine the claimed sieving coefficient and cut-off, even if its determination is affected by some variability.

3.6 As regards the question whether the invention could "be worked over the whole range claimed", the respondent first argued that it was not proven that a membrane with the combination of sieving coefficients defined in claim 1 of the patent as granted could be manufactured. The appellant pointed to example 1 of the patent, which constituted an embodiment of the invention and provided clear and unambiguous instructions as to all manufacturing steps and parameters needed by the skilled person to manufacture a membrane according to claim 1. The Board notes that the respondent's arguments do not go beyond mere assertions, since no supporting evidence has been presented. For example, no test results have been provided to show that, following the steps described in example 1, the membrane obtained does not possess the features defined in claim 1. Since no serious doubts substantiated by verifiable facts have been raised by the respondent, the Board concludes that example 1 is a sufficient disclosure of at least one way of carrying out the invention, in compliance with Rule 42(1)(e) EPC. Whether other examples or figures of the patent disclose membranes outside the scope of claim 1 is irrelevant in that respect.

3.7 The respondent further argued that the manufacturing of a membrane depended on so many parameters that it was not feasible, without undue burden, to work out the invention over the whole scope defined in claim 1. The Board notes that for the disclosure to be sufficient the patent is not required to describe every possible

membrane falling within the claimed subject-matter. Rather, a certain level of generalisation is the very purpose of the claims. More specifically, there is clearly no need for the patent to disclose methods for manufacturing all possible membranes with all possible combinations of sieving coefficients falling within the scope of claim 1. In the absence of specific evidence in support of the contrary, the Board is convinced that, on the basis of the manufacturing method of example 1, the skilled person would need only routine trial and error to slightly modify some of the parameters of the method and obtain other membranes according to claim 1.

3.8 In conclusion, since none of the respondent's arguments as to insufficiency of disclosure are convincing, the Board considers that the ground for opposition under Article 100(b) EPC does not prejudice the maintenance of the patent as granted. Hence, the impugned decision is to be set aside.

4. Under Article 111(1) EPC, following the examination as to the allowability of the appeal, the Board retains the discretion to remit the case to the department which was responsible for the decision appealed for further prosecution.

Since the impugned decision did not deal with the other grounds for opposition invoked by the respondent, the Board decides to remit the case to the Opposition Division for further prosecution, in order for the parties to have those grounds too possibly considered by two instances.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution.

The Registrar: The Chairman:

D. Hampe E. Dufrasne

Decision electronically authenticated