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# Datasheet for the decision of 31 October 2012

**Case Number:** T 2003/08 - 3.3.04

**Application Number:** 96941378.0

**Publication Number:** 862444

**IPC:** A61K 35/14, A61P 9/00, C07K 1/22, A61M 1/36, C07K 14/72

**Language of the proceedings:** EN

**Title of invention:**
Treatment of dilated cardiomyopathy by removal of autoantibodies

**Patentees:**
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Felix, Stephan

**Opponent:**
Fresenius Medical Care Deutschland GmbH

**Headword:**
Dilated cardiomyopathy/EDWARDS

**Relevant legal provisions:**
EPC Art. 53(c), 54(1)(2)(4), 56, 83, 84, 112(1)(a), 117, 123(2)
EPC R. 117, 118(1)(2)(a)(c), 120(1)

**Relevant legal provisions (EPC 1973):**
EPC Art. 54(5)

**Keyword:**
"Request not to hear a witness due to failure to reply to the invitation in accordance with Rule 118(c) EPC (refused)";
"Request for referral of questions to the Enlarged Board of Appeal (refused)";
"Main request: added subject-matter (yes)"
"Auxiliary request: claims to be interpreted as relating to a second medical use (yes) - means used in the treatment to be considered as a substance or composition in the sense of decision G 5/83; oral disclosure at a lecture - evidence from the lecturer and a member of the audience may be sufficient to establish the oral disclosure - contrary to the application by the first instance of decision T 1212/97; oral disclosure and prior use - established beyond reasonable doubt (no); conformity of the claims with the requirements of the EPC (yes)"

**Decisions cited:**
G 0001/83, G 0005/83, G 0006/83, G 0001/04, G 0002/08, T 0017/81, T 0227/91, T 0329/94, T 0138/95, T 0789/96, T 0775/97, T 1212/97, T 0138/02, T 0144/04, T 0448/05, T 1314/05, T 1075/06, T 0213/07, T 1695/07, T 1099/09

**Catchword:**
see points 6 to 21 and 30 to 48

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Beschwerdekammern | Boards of Appeal | Chambres de recours

**Case Number:** T 2003/08 - 3.3.04

# D E C I S I O N
**of the Technical Board of Appeal 3.3.04**
**of 31 October 2012**

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**Decision under appeal:** **Interlocutory decision of the Opposition Division of the European Patent Office posted 12 August 2008 concerning maintenance of European patent No. 862444 in amended form.**

**Composition of the Board:**

**Chairman:** C. Rennie-Smith
**Members:** G. Alt
B. Claes

## Summary of Facts and Submissions

I. The appeals of the patent proprietor and the opponent lie from the interlocutory decision of the opposition division to maintain European patent 0 862 444 on the basis of a first auxiliary request. The title of the patent is *"Treatment of dilated cardiomyopathy by removal of autoantibodies"*. (The expression "dilated cardiomyopathy" is hereinafter abbreviated as "DCM").

II. The following documents are referred to in the present decision:

E1 "Eidesstattliche Versicherung" by Dr Wallukat dated 10 February 2005

E2 "Eidesstattliche Versicherung" by Dr Kunze dated 9 February 2005

E3 *"The role of immune mechanisms in cardiovascular disease"*, Eds. Schultheiss, H.-P. and Schwimmbeck, P., Springer Verlag 1997, pages 77-84: *"The possible pathogenic role of autoantibodies in myocarditis and dilated cardiomyopathy"*, Wallukat, G. *et al.*

E4 Circulation, vol. 89, June 1994, pages 2760-2767, Magnusson, Y. *et al.*

E5 European Heart Journal, vol. 12 (Supplement D), 1991, pages 178-181, Wallukat, G. *et al.*

E6 Annals of Medicine, vol. 27, April 1995, pages 169-173, Cetta, F. and Michels, V.V.

E7 The Lancet, vol. 344, September 1994, pages 773-777, Caforio, A.L. *et al.*

E8 EP 0 197 521 B1

E9 US 4,681,870

E10 Summary of Workshop 5 at the *"23. Congress of the International Society of Blood Transfusion"*, 3 to 8 July 1994, Amsterdam, Koll, R. et al.

E11 Letter of Dr Müller dated 16 February 1999

E12 European Heart Journal, vol. 12 (Supplement D), 1991, pages 76-80, Schwimmbeck, P.L. *et al.*

E23 "Eidesstattliche Versicherung" by Dr Müller dated 19 September 2007

E24 Letter of Prof. Schultheiss and Dr Schwimmbeck dated 30 October 1995

"Transcript of the hearing of the witnesses Dr Kunze and Dr Wallukat before the Technical Board of Appeal 3.3.04 on 20 September 2012", pages 1 to 83

III. The findings of the opposition division can be summarized as follows:

The **main request** in opposition proceedings was for the nine claims as granted, claims 1 and 9 being independent claims. The opposition division held that claim 9 infringed the requirements of Article 100(c)

EPC in combination with Article 123(2) EPC - a ground of opposition introduced by the opposition division *ex officio*.

Claim 9 read:

"9. A method for removing a significant portion of the immunoglobulin from plasma taken from a patient suffering from dilated cardiomyopathy, the method comprising:

(a) providing a column having coupled thereto a specific ligand for human immunoglobulin, which column is defined in any of Claims 1 to 7; and

(b) passing the plasma over the column under conditions which effect the binding of said specific ligand to immunoglobulin in the plasma."

In the opposition division's view this method was not disclosed in the application as filed because it lacked the feature of re-infusion of the plasma into the patient. Decision T 448/05 referred to by the patent proprietor was considered not to be applicable because the claims at stake in that decision related to a product and not to a method.

The **auxiliary request** in opposition proceedings comprised claims 1 to 8 of the main request, claim 1 being the only independent claim.

Claim 1 read:

"1. Use of a specific ligand for human immunoglobulin in the manufacture of a column having said ligand coupled thereto for the treatment of a patient suffering from dilated cardiomyopathy, said treatment comprising passing plasma of the patient over the column under conditions which effect the binding of said specific ligand to immunoglobulin in the patient's plasma, thereby removing a significant portion of the immunoglobulin from the patient's plasma, and reinfusing the plasma to the patient."

The opposition division held that claim 1 was to be interpreted as a claim to a second medical use because the means used in the claimed treatment was to be considered as a "medicament", in accordance with the criteria established by the case law, in particular decisions T 227/91, T 775/97 and T 138/02.

The contents of a lecture by Dr Wallukat at a symposium in Berlin in September 1995, could, in the absence of supporting evidence, not be established beyond reasonable doubt by the post-published document E3. Document E24, a document which the opponent had submitted during the oral proceedings in order to show that document E3 had been written shortly after the lecture, was not admitted into the proceedings because it was filed too late and not *prima facie* relevant. Nor did documents E1 and E2 prove beyond reasonable doubt that the subject-matter of claim 1 had been orally disclosed at the symposium. Document E1 was a declaration by Dr Wallukat, i.e. the lecturer himself and document E2 was a declaration by Dr Kunze, a member

of the audience. Neither of these declarations was supported by contemporary notes. According to decision T 1212/97 only information appearing in contemporary written notes made at the lecture by at least two members of the audience could usually be regarded as sufficient to establish orally disclosed information. Moreover, the recollection of the writer of document E2 could have been biased by additional knowledge stemming from collaboration with the lecturer. The opposition division considered it unnecessary to hear the witnesses Dr Wallukat and Dr Kunze, who had been offered by the opponent. In line with the reasoning in decision T 1212/97, the evidential situation was such that the testimonies of these witnesses could not make up for the deficiencies of the written evidence. Thus, Dr Wallukat's oral disclosure could not be considered to take away the novelty of the claimed subject-matter.

Moreover, the claimed subject-matter was also novel over an alleged public prior use which had not been proven up to the hilt by documents E11 and E23.

Finally, none of documents E4, E10 and E12 anticipated the claimed subject-matter. In particular, document E12 did not disclose a method of therapy for DCM involving all the features of claim 1 as the document neither disclosed immunoadsorption of the patients' plasma and the re-infusion of the treated plasma, nor any therapeutic effect by the removal of the autoantibodies. Furthermore, it was not even clear which of the results was obtained with serum from DCM and which with serum from myocarditis patients.

Document E12 represented the closest prior art document rather than documents E8 or E9. Since document E12 did not disclose a therapy for DCM, the problem to be solved, *vis-à-vis* the disclosure in this document, was to provide a therapy for DCM. Document E12 speculated as to the use of immunoadsorption of autoantibodies as a therapy for DCM, but this speculation was not supplemented by experimental data.

Documents E8 and E9 disclosed the process of immunoadsorption in the context of autoimmune diseases. However, it was neither established nor implied at the priority date of the patent, in particular not by documents E5 to E7, that DCM was in fact an autoimmune disease. Therefore, the skilled person would not combine the teachings of document E12 with those of documents E8 and E9. Accordingly, the opposition division considered that the subject-matter of all claims of the auxiliary request involved an inventive step.

The auxiliary request also fulfilled the requirement of sufficiency of disclosure.

IV. With its statement of the grounds of appeal the patent proprietor (hereinafter "appellant-patentee") filed a main request identical to the main request dealt with by the opposition division, i.e. the claims of the patent as granted and two auxiliary requests. Auxiliary request 2 was identical to the auxiliary request which the opposition division considered to comply with the patentability requirements of the EPC. The appellant-patentee subsequently filed auxiliary requests 3 to 9

with its reply of 17 April 2009 to the opponent's statement of the grounds of appeal.

V. In its statement of the grounds of appeal the opponent (hereinafter "appellant-opponent") repeated its offer of Dr Wallukat and Dr Kunze as witnesses and re-submitted document E24 which had not been admitted into the proceedings by the opposition division because it was late filed and not *prima facie* relevant.

VI. The board summoned the parties to oral proceedings to be held on 20 and 21 September 2012. In a communication accompanying the summons the board informed the parties *inter alia* that it considered that the criteria applied by the board in the case underlying decision T 1212/97 should not necessarily be followed exclusively, and that there may be circumstances in which the contents of an oral disclosure could be established solely on the basis of evidence from the lecturer and a member of the audience. The board therefore considered it appropriate to hear Dr Wallukat and Dr Kunze as witnesses.

VII. On 30 March 2012 the board issued an interlocutory decision pursuant to Article 117 EPC in combination with Rule 117 EPC to hear Dr Wallukat and Dr Kunze as witnesses.

VIII. Summonses to give evidence in accordance with Rule 118(1) EPC were sent to Dr Wallukat and Dr Kunze on 12 June 2012 by registered letters. The witnesses were *inter alia* informed that they should write to the registry of the board within two months after the receipt of the summonses confirming their attendance at

the date and time indicated in the summonses and stating the language in which they wished to give evidence. Both witnesses returned the acknowledgement of the receipt of the summons.

IX. With a letter of 20 August 2012 the appellant-patentee submitted replacement auxiliary requests 1 and 3 to 11. In a further letter dated 14 September 2012 the appellant-patentee observed that the time limit specified in the summonses to give evidence had expired and that neither Dr Wallukat nor Dr Kunze had responded confirming that they would be attending to give evidence.

X. Oral proceedings took place on 20 and 21 September 2012.

The testimonies of Dr Wallukat and Dr Kunze were heard. The board admitted all documentary evidence filed on appeal into the proceedings since both parties agreed. The appellant-patentee withdrew its auxiliary request 1 and did not renumber the subsequent auxiliary requests.

At the end of the oral proceedings the parties' requests were as follows:

The appellant-patentee requested that Dr Wallukat and Dr Kunze not be heard as witnesses. The appellant-patentee furthermore requested (1) as a main request that the decision under appeal be set aside and that the patent be maintained as granted; or alternatively (2) that the opponent's appeal be dismissed, i.e. that the patent be maintained on the basis of the claims allowed by the opposition division, i.e. the request named "Auxiliary Request 2"; or alternatively (3) that

the decision under appeal be set aside and that the patent be maintained on the basis of one of its further auxiliary requests 3 to 11 filed on 20 August 2012.

The appellant-opponent requested that Dr Wallukat and Dr Kunze be heard as witnesses. The appellant-opponent furthermore requested that the decision under appeal be set aside and that the patent be revoked.

Both the appellant-opponent and the appellant-patentee requested, in the event of an adverse decision in relation to novelty (Article 54 EPC), to refer to the Enlarged Board of Appeal respectively the question set out below and submitted by the appellant-opponent in its letter dated 20 August 2012 or the mirror-image question thereto.

"Ist eine medizintechnische Vorrichtung, wenn ja in welchem Umfang, der Anspruchsfassung der zweiten medizinischen Indikation zugänglich bzw. in welchem Sinne und wie weit sind die Begriffe "Medikament" und "Stoff und Stoffgemisch" gemäß dem Artikel 54(4),(5) und der Entscheidung G 01/83 auszulegen?"

XI. The board announced its decision in writing in a communication to the parties dated 31 October 2012.

XII. The appellant-opponent's arguments may be summarized as follows:

*Main request - Claim 9 - Amendments (Article 100(c) in combination with Article 123(2) EPC)*

All the passages indicated by the appellant-patentee as a basis for the subject-matter of claim 9 were taken out of their context. The passage on page 1 was a general statement regarding the state of the art and did not relate to the subject-matter of claim 9. The passage on page 2 was in the context of a treatment by therapy and concerned the use of ligands to manufacture the column and not a method for making modified plasma. Similarly, the passages on pages 7 and 9 related to a treatment by therapy. Decision T 448/05 was not applicable to the present subject-matter because the *in vivo* method did not implicitly disclose the *ex vivo* method. The attempt to circumvent exclusions from patentability by amendments could not justify the allowance of subject-matter contravening the requirements of Article 123(2) EPC.

*Auxiliary request 2 - Amendments (Article 123(2) EPC); sufficiency of disclosure (Article 83 EPC); clarity, support (Article 84 EPC)*

The appellant-opponent had no objections pursuant to Articles 83, 84 and 123(2) EPC.

*Request not to hear Dr Wallukat and Dr Kunze as witnesses*

The summonses had been sent to Dr Wallukat and Dr Kunze directly. They were scientists. The appellant-opponent's conduct clearly implied that the witnesses would be present. It explicitly offered the witnesses and made the deposit of the advance payment. If the witnesses were not to attend, the appellant-opponent's representative would have informed the other party and/or the board.

*Interpretation of claim 1 and novelty (Article 54 EPC)*

A mandatory characteristic of a "medicament" was that it was administered to a patients body, see decision T 138/02. Decision T 144/04 established that blood or plasma were not to be considered as part of a "complete" body. The claim underlying decision T 138/95 could not be interpreted as the use of a "device". Rather the device was the auxiliary means to achieve the administration of the medicament to the body. A further characteristic of a medicament was that it was consumed during the application in the sense that its original nature was changed so that it was irrevocably non-existent after administration and could not be put back into its original state by cleaning or regeneration, like for example a surgical instrument, see decision T 227/91, and moreover that it was a "finished product" in the sense it was alone responsible for the therapeutic effect, see decision T 775/97.

Decision T 1314/05 made it clear that a claim to a second medical use in the sense of decision G 5/83 was only amenable to products or compositions that were medicaments, but not to medical devices. In keeping with these principles the board in decision T 1099/09 did not interpret the use of a "*bandelette*" as the use of a "medicament".

The column which according to claim 1 was used for the therapeutic treatment did not have any of these required characteristics. It could therefore not be considered as a "medicament". Consequently, claim 1 did not relate to subject-matter for which the formulation of a claim to a second medical use was allowed by decision G 5/83 and therefore claim 1 could not be interpreted as a claim to a second medical use. Claim 1 was a claim to the use of a substance for the manufacture of a device which had to be suitable for the use in a therapeutic treatment.

The subject-matter of claim 1 was therefore not novel over the disclosure in each of documents E8 to E10.

Even if claim 1 was interpreted as a claim to a second medical use in accordance with decision G 5/83, the novelty of its subject-matter should not be acknowledged in view of (a) an oral disclosure during a lecture at a symposium in Berlin in September 1995 by Dr Wallukat - evidence for this disclosure came from documents E1 to E3, E24 and the testimony of Dr Wallukat and Dr Kunze, (b) a prior use by Dr Müller - evidence for the prior use came from documents E11 and E23 - and (c) the disclosure in document E12.

Both the declarations E1 and E2 and document E3 confirmed consistently the information which had been disclosed during the lecture, in particular that Figure 3 of document E3 was shown as a slide. Document E24 established that document E3 had been prepared in close temporal relationship to the lecture so that a deviation from the contents of the lecture for time reasons could be excluded. The opposition division was wrong to explain the consistency between the two declarations E1 and E2 by reference to research projects in which Dr Wallukat and Dr Kunze subsequently collaborated. It was also wrong to assume that for that reason the remaining audience understood less than Dr Kunze. Indeed members of the audience had general knowledge and skills in the field of myocarditis and DCM, so that the whole audience received the same information. Also the testimony given by Dr Wallukat and Dr Kunze during the oral proceedings before the board allowed only one conclusion, namely that the claimed subject-matter was made available at the lecture. Although decision T 1212/97 held that the declaration of two members of the audience was desirable in order to determine the accurate information that was conveyed to the audience of a lecture, it did not however hold that this was mandatory.

Documents E11 and E23 provided evidence that the claimed treatment had in fact taken place before the relevant date of the patent in suit.

Finally, document E12 explicitly disclosed on page 79, left column, second paragraph the elimination of pathogenic antibodies from the serum of patients as a

therapeutic treatment useful for patients suffering from DCM. The antibodies were removed from the sera by using a column having synthetic peptides bound to it as ligands. Although the document did not explicitly disclose the re-infusion of the treated serum, for the skilled person this was however an implicitly disclosed feature of the treatment.

*Inventive step (Article 56 EPC)*

The claimed subject-matter lacked an inventive step in view of either document E4 in combination with documents E8 or E9, or documents E8 or E9 in combination with documents E4, E6 or E7, or document E12 alone or in combination with common general knowledge.

Document E4 disclosed that the sera of patients with DCM contained autoantibodies increasing the heart beat rate of cultured rat cardiac myocytes, i.e. that the sera contained pathogenic antibodies. The document thus disclosed that DCM was an autoimmune disease. Although DCM was not explicitly mentioned, documents E8 and E9 disclosed methods of treatment involving the removal of pathogenic proteins such as immunoglobulins from body fluids. The documents disclosed in particular the removal of autoantibodies from the plasma of patients suffering from autoimmune diseases, by passing their plasma over a carrier-bound adsorbent. Thus, the combination of the teachings of these documents would motivate the skilled person to provide the subject-matter of claim 1.

Alternatively each of documents E8 or E9 could be considered as the closest prior art document. It was known to the skilled person that DCM was an autoimmune disease, see for example documents E4 to E7. Thus, the skilled person would have used the system disclosed in either of documents E8 or E9 in an obvious manner for the treatment of DCM. For this reason, the subject-matter of claim 1 lacked an inventive step.

If the re-infusion was not considered as a feature implicitly disclosed in document E12, it was at least a feature which lay within the common general knowledge of the skilled person. Moreover, the suggestion in document E12 that the removal of pathogenic antibodies would offer an approach to the therapy of DCM would in fact motivate the skilled person to use this approach. For these reasons also the subject-matter of claim 1 was obvious to the skilled person.

XIII. The appellant-patentee's arguments may be summarized as follows:

*Main request - Claim 9 - Amendments (Article 100(c) in combination with Article 123(2) EPC)*

It was derivable from the passages on page 1, final paragraph, page 2, second paragraph and page 7, lines 2 to 7 and page 9, lines 5 to 10 of the application as filed that the invention was the removal of immunoglobulins from the plasma of a patient suffering from DCM using a column as defined in the claim. The later re-infusion of the modified plasma was an application of the invention, not the invention itself. The re-infusion step was therefore not a mandatory

feature of the invention. In decision T 448/05 the board found that an intermediate product of an overall process that inevitably ended with a modified composition was disclosed as such. By the same logic the *ex vivo* method of making modified plasma was disclosed in the application as filed as a part of a method that subsequently infused the modified plasma into a patient and was therefore disclosed as such. Therefore, the logic of decision T 448/05 should also apply to the claimed method and not only to "chemical products".

European patent applications had to define the invention in a single document for consideration under a large number of different patent systems. Yet, the exclusion from patentability of medical methods varied between these jurisdictions. An applicant could not be required at the time of filing to take into account all these differences. Hence, the European Patent Office should not take and in fact does not take an overly formalistic approach to the assessment of those amendments intended solely to address the legal fiction established by the EPC of the exclusion from patentability of medical methods. For example, it was allowed to reformulate claims to a method of treatment into claims having the second medical use format, although there was no explicit basis for such wording. The requirements of Article 123(2) EPC were thus fulfilled.

*Auxiliary request 2*

*Request not to hear Dr Wallukat and Dr Kunze as witnesses*

Given that the witnesses Dr Wallukat and Dr Kunze had not responded to the summonses as requested by the board, the appellant-patentee had to assume that they would not be available. Their non-appearance would not be without precedent - they were absent from the oral proceedings before the opposition division. Yet, the appellant-patentee could not be sure that the witnesses would not attend. The appellant-opponent had played a procedural game because it alone knew whether the witnesses would attend. The uncertainty over the attendance of the witnesses was to the appellant-patentee's disadvantage, in particular in terms of the time invested for preparation in case the witnesses did not appear. If the board decided to hear the witnesses, that would mean that any party could deliberately leave another party and the board "in the dark".

*Interpretation of claim 1 and novelty (Article 54 EPC)*

Claim 1 was in a format for it to be considered as a second medical use claim. None of the decisions cited by the appellant-opponent helped its case.

The decision under appeal correctly recognized that, in contrast to the situation in decision T 144/04 where the blood was treated spatially and temporally separated from the operation of extraction, in the present case the blood was in a closed circuit

connected with the body and thus had to be considered as a part of the body.

Decision T 138/02 did not require that the medicament be administered **into** a patient's body but just **to** a patient's body. The column and the ligand fulfilled this latter criterion, i.e. they were brought in contact with a part of the body, namely blood.

The opposition division was also correct to consider that the column with the bound ligand was "consumed" during use because the column eventually became saturated. Thus, the requirement for a "medicament" set out in decision T 227/91 was fulfilled.

That an adsorbent bound to a column was changed during the use was confirmed in decision T 138/02 where the board stated in point 2.6 of the Reasons that *"[i]t is thus for all practical purposes consumed during the treatment of the body fluid and differs, in this respect, from a surgical tool"*.

In decision T 1099/09 the board did not consider the "*bandelette*" as a "medicament" because the medical effect depended on geometry and positioning and did not result from the substance that was used for the manufacture of the "*bandelette*", i.e. it did not depend on a molecular interaction.

Claim 29 of the main request in the case underlying decision T 775/97 related to a surgical method. Claim 1 of the main request in the case underlying decision T 1314/05 related to the use of microelectrodes for the manufacture of an implant for the stimulation of

biological cells. The situations in both decisions did not apply to the present case because they clearly concerned the use of devices in surgical methods.

In contrast, the board in decision T 138/95 allowed a second medical use claim because the use related to the use of a device in a therapeutic method.

Accordingly, because claim 1 was to be interpreted as a second medical use claim, none of the disclosures in documents E8 to E10 was novelty-destroying.

The alleged oral disclosure of the claimed subject-matter by Dr Wallukat at a symposium in Berlin and the alleged prior use by Dr Müller, respectively, were not proven beyond reasonable doubt by documents E1 to E3, E24 and the oral testimony of Dr Wallukat and Dr Kunze and by documents E11 and E23, respectively. Documents E1 and E2 were declarations from the lecturer at the symposium, Dr Wallukat and a member of the audience, Dr Kunze. Both were written ten years after the lecture. Neither of them was accompanied by contemporary notes. It was therefore not plausible that the declarants could exactly remember what was said. Moreover, Dr Wallukat and Dr Kunze were clearly collaborating, so that Dr Kunze's mental landscape could be biased by information acquired on other occasions. Many of Dr Wallukat's and Dr Kunzes's statements during their testimony given during the oral proceedings before the board were inconsistent which increased the doubt on their ability to remember accurately. Nor could the oral testimony remove the doubt that Dr Wallukat and Dr Kunze may have supplemented their recollection by knowledge gained

later. Document E3 was not pretending to be a direct reproduction of the conference proceedings. Document E24 confirmed that Dr Wallukat gave a presentation, but it did not confirm - as far as document E3 allegedly disclosed the claimed subject-matter - that the claimed subject-matter had been disclosed at the lecture.

As for an oral disclosure also the level of proof for a prior use was high, i.e. it had to be proven beyond reasonable doubt or - as stated in decision T 472/92 - "up to the hilt". The contents of documents E11 and E23 did not reach this level, for example in the absence of any further support, one did not know whether the declarant said the truth.

The disclosure in document E12 differed from the claimed subject-matter by the removal of antibodies from serum and not plasma and it neither disclosed the re-infusion of the antibody-depleted serum nor any therapeutical effect for the removal of antibodies from the sera of patient with DCM.

*Inventive step (Article 56 EPC)*

Arguments based on a combination of documents E4 and E6 to E9 assumed that DCM was accepted to be an autoimmune disease that was caused by autoimmune antibodies and that the skilled person would expect that a method of removing these antibodies from the circulation of a patient with DCM by immunoapheresis would lead to a treatment of the disease. Documents E4, E6 and E7, all published shortly before the priority date of the disputed patent, and document E5 provided a strong indication that the aetiology of DCM was not seen as

established by a skilled person at the priority date of the patent. The skilled person would therefore not expect that merely reducing the level of autoantibodies in the blood - for example by using the techniques disclosed in documents E8 or E9 - would constitute a treatment of DCM. Even if the skilled person did expect that DCM was an autoimmune disease, document E4 taught that the autoantibodies were bound to their receptor and could not be removed by washing. Thus, the skilled person would not have combined the teaching of documents E4, E6 and E7 with the techniques disclosed in documents E8 and E9 which both suggested to apply the disclosed techniques to the treatment of autoimmune diseases.

Document E12 did not allow the conclusion that autoantibodies against adenine nucleotide translocator and myosin were present in the serum of patients with DCM at all. Indeed the data presented in document E12 mixed together results from patients with DCM and myocarditis. Moreover, the document disclosed *in vitro* assays, but not that the removal of the antibodies had a therapeutic effect on the disease. Therefore, the suggestion in document E12 that the removal of autoantibodies from the blood of patients suffering from DCM constituted a therapeutic approach to treat DCM was highly speculative. Moreover, it was not even established in the prior art that DCM was an autoimmune disease, in the sense that the disease was caused by the autoantibodies. Therefore, the skilled person would not have arrived at the subject-matter of claim 1 either by a combination of the teaching in document E12 with common general knowledge or by document E12 alone.

XIV. The arguments of both parties concerning their requests for referral of a question to the Enlarged Board of Appeal may be summarized as follows:

There was divergent case law on the patenting of claims to a second medical use of devices and there was also divergent case law on what a "medicament" was, see decisions T 138/95 and T 138/02. It should therefore be clarified whether or not the second medical use was allowable only for "medicaments" or also for "devices" used in medicine. If it was applicable only for "medicaments", it should be clarified what the definition of "medicament" was. If the present board should interpret claim 1 in a different way than the board in decision T 138/02, then there would be two contradicting decisions on the same issue which would generate considerable legal uncertainty.

## Reasons for the decision

*Applicable version of the European Patent Convention*

1. The mention of the grant of the present patent was published in the European Patent Bulletin on 12 May 2004. The version of the European Patent Convention revising that of the year 1973 ("EPC 1973") entered into force on 13 December 2007 ("EPC 2000"). Hence, Articles 53(c) and 54(4) EPC 2000 (corresponding to Articles 52(4) and 54(5) EPC 1973) apply and Article 54(5) EPC 2000 (for which no corresponding provision exists in the EPC 1973) does not apply, in accordance with Article 7(1), second sentence of the Act revising the EPC of 29 November 2000 and

Article Nos. 1 and 3 of the decision of the Administrative Council of 28 June 2001 on the transitional provisions under Article 7 of that Act (Special Edition No. 1, OJ EPO, 197).

*Main Request - Claim 9 - Amendments (Article 100(c) in combination with Article 123(2) EPC)*

2. The assessment of whether or not the requirements of Article 123(2) EPC are fulfilled includes determining the disclosure content of the application as filed which is - following established principles for the determination of disclosure contents of documents (Case Law of the Boards of Appeal, 6th edition 2010, I.C.2.1) - the information that the skilled person derives - explicitly or implicitly - directly and unambiguously from the document as a whole. Thus, it is for this purpose neither appropriate - as suggested by the appellant-patentee's arguments - to determine what the application as filed discloses specifically as the "invention", nor to consider only isolated parts of the application, nor even as also suggested by the appellant-patentee to apply different standards depending on the type of amendment and thus less strict because the amendment addresses the EPC's legal fiction of exclusion from patentability of medical methods.

3. The board agrees with the opposition division's finding that the method claimed in claim 9 (see section III above), a method which does not comprise as a third mandatory step the re-infusion of the plasma into the patient, is not derivable, either explicitly or implicitly, from the application as filed as a whole and in particular not from the passages referred to by

the appellant-patentee. Indeed, the passage on page 1 discloses the removal of auto-antibodies in the context of the treatment of patients with cardiomyopathy by immunoapheresis. The passage on page 7 discloses the extraction of antibodies in the course of immunoapheresis. The passage on page 9 discloses that the treatment system consists of plasmapheresis to obtain plasma and immunoapheresis. In these passages the references to the "treatment" and "immunoapheresis" directly and unambiguously imply that the method disclosed in these passages comprises as a mandatory step the re-infusion of the plasma to the patient. The passage on page 2 discloses a method for manufacturing a column.

4. This board considers that the crucial difference between the case underlying decision T 448/05 of 12 September 2006 and the present case is that in the former decision the board considered that the claimed intermediate product was disclosed ***per se*** by the combination of claims 19 and 25 (see first and second paragraph on page 6 of the Reasons). The circumstances are different in the present case because the method of claim 9 is not *per se* disclosed in the application as filed. Thus, decision T 448/05 (*supra*) does not help the appellant-patentee's case.

5. In view of the considerations above, the board concludes that claim 9 of the main request does not fulfil the requirements of Article 123(2) EPC. Therefore the main request is refused.

*Auxiliary request 2*

*Interpretation of claim 1*

6. In seven parallel decisions of 5 December 1984, all with corresponding texts in the different official languages of the European Patent Office and of which decisions G 1/83, G 5/83 and G 6/83 were published in the Official Journal of the European Patent Office (OJ EPO 1985, 60, 64, 67), the Enlarged Board decided that a claim in the form of a *"use of a substance or composition for the manufacture of a medicament for a specified new and inventive therapeutic application"* was the appropriate form of protection for inventions pertaining to a second or further new and inventive use in the medical domain (see point 23 of the Reasons). This type of claim is known as a "second medical use claim" or "Swiss-type claim". (Hereinafter reference will be made to decision G 5/83 (*supra*), published in English, the language of the present proceedings.)

7. It is not disputed by the parties, and the board agrees, that claim 1 of auxiliary request 2 (see section III above) has the format of a second medical use claim as envisaged by decision G 5/83 (*supra*). It is furthermore uncontested that the specific ligands for immunoglobulin referred to in claim 1 and a process for their generation were known in the art, as were the ligands when bound to a column and the manufacture of such a column. By way of example reference is made to the Therasorb-Ig column disclosed in document E10 which is in fact the column used in the examples of the present patent. Hence, the present invention is of the type considered in decision G 5/83 (*supra*), i.e. one

where the feature in claim 1 relating to the treatment of DCM patients is decisive for the patentability of the claimed invention.

8. The appellant-opponent has argued that claim 1 does not fulfil one prerequisite to qualify as a second medical use-claim in accordance with decision G 5/83 (*supra*), namely that a "medicament" is used in the treatment. Indeed the means used in the treatment were a "column", which is not a "medicament", but a "device". Therefore, despite it being drafted in the format of a second medical use claim, claim 1 should not be interpreted as such and therefore the treatment-feature should be neglected when assessing novelty.

9. Accordingly it needs to be decided whether or not claim 1 is to be construed as a second medical use claim. In the decision under appeal this question was answered in the affirmative (see section III above). The board comes to the same conclusion, although for different reasons which are set out below.

10. The board considers it helpful in this context to highlight the reasons that led the Enlarged Board of Appeal in decision G 5/83 (*supra*) to allow patent protection for further uses in the medical domain.

10.1 At the time when decision G 5/83 (*supra*) was taken Article 54(5) EPC 1973 provided patent protection for inventions pertaining to the first use in the medical domain of a known substance or composition in the form of a purpose-limited product claim. Article 54(5) EPC 1973 stipulated: *"[...] shall not exclude the patentability of any substance or composition,*

*comprised in the state of the art, for use in a method referred to in Article 52, paragraph 4, provided that its use for any method referred to in that paragraph is not comprised in the state of the art*".

10.2 In point 22 of its decision G 5/83 (*supra*) the Enlarged Board of Appeal stated however that it "*does not deduce from the special provision of Article 54(5) EPC [*1973*] that there was any intention to exclude second (and further) medical indications from patent protection other than by a purpose-limited product claim*". Thus, the Enlarged Board considered that protection for further "medical" uses should be possible by analogy to the protection provided by Article 54(5) EPC 1973 for first "medical" uses.

10.3 The Enlarged Board of Appeal considered that the adequate form of protection for these inventions would be a claim to a "use" or a "method", but that this form of protection would be *"in direct conflict with the provisions of Article 52(4) EPC* [1973]*"* (points 12 and 13 of the Reasons).

Article 52(4) EPC 1973, to which the new Article 53(c) EPC 2000 in substance corresponds (see for example the decision of the Enlarged Board of Appeal G 1/04 published in the OJ EPO 2006, 334; point 10 of the Reasons), stipulates: *"Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application within the meaning of paragraph 1. This provision shall not apply*

*to products, in particular substances or compositions, for use in any of these methods."*

However, in point 23 of the Reasons for its decision the Enlarged Board in decision G 5/83 (*supra*) found it *"legitimate"* to allow claims which are directed to the *"use of a substance or composition for the manufacture of a medicament for a specified new and inventive therapeutic application"*.

11. Accordingly, this board judges that the expression "*for the manufacture of a medicament*" was considered by the Enlarged Board as a way to remove from the exclusion from patentability for lack of industrial applicability the sort of claim that the Enlarged Board **in substance** intended to allow, namely the use of a substance or composition for any of the methods recited in Article 52(4) EPC 1973.

12. It can be taken from the distinction made in the second sentence of Article 52(4) EPC 1973 (see point 10.3 above) that the meaning of the term "products" is not identical to the meaning of the terms "substances or compositions". Rather, according to the wording of Article 52(4) EPC 1973 "substances or compositions" are cited as a subgroup of the larger group of "products". Thus, (i) in view of the fact that Article 54(5) EPC 1973 relates to "substances and compositions" only, (ii) in view of the link made in Article 54(5) EPC 1973 to 52(4) EPC 1973 and (iii) in view of the connection established by the Enlarged Board to Article 54(5) EPC 1973 (see point 10.2 above), this board concludes that the Enlarged Board intended to allow the special form of protection **only** for those

uses in the medical domain which concern products which qualify as "substances or compositions".

13. Moreover, again in view of the link made by the Enlarged Board to Article 54(5) EPC 1973 (see point 10.2 above), the present board is convinced that the term "therapeutic application" in the wording of the claim allowed by the Enlarged Board is to be interpreted as referring to any of the methods referred to in Article 52(4) EPC 1973. In fact, the Enlarged Board states in point 21 of the Reasons: *"It is clearly understood that the application of this special approach to the derivation of novelty can only be applied to claims to the use of substances or compositions intended for use in a method referred to in Article 52(4) EPC* [1973]".

14. It follows from the observations and considerations in points 10 to 12 above, that in the light of decision G 5/83 (*supra*) it is therefore of pivotal importance to establish whether or not the means used in the treatment of DCM according to the present claims constitute a "substance or composition", rather than to establish whether or not it constitutes a "medicament".

15. In its decision G 5/83 (*supra*) the Enlarged Board does not give an explicit definition of what is encompassed by the terms "substance" or "composition". Yet, in view of the claims at stake in the referring decision T 17/81 of 30 May 1983 - they were essentially directed to the use of 1,4-dihydro-2,6-dimethyl-4-(3'-nitrophenyl)-pyridin-3-ß-methoxyethylester-5-isopropylester to treat pathologically decreased cerebral functions - this board deduces from the gist

of decision G 5/83 (*supra*) as a whole, and in particular from the specific reference to *"chemical substance or composition"* in point 10 of the Reasons for the decision and in the light of the observations in point 12 above, that in the context of decision G 5/83 (*supra*) "substance" or "composition" refers at least to products which qualify as "chemical" entities or compositions of "chemical" entities.

16. A "device", as for example a stent or a catheter, would not normally be denoted as a chemical entity. Therefore, decision G 5/83 (*supra;* and Article 54(5) EPC 2000, which according to the Enlarged Board in decision G 2/08, OJ EPO 2010, point 5.9 ff. is considered to fill the lacuna in the EPC 1973 which had been filled in a praetorian way by the Enlarged Board of Appeal with decision G 5/83 (*supra*) and the case law based on that decision) has consistently been interpreted by the boards as not providing for the patentability of uses in any of the methods recited in Article 52(4) EPC 1973 (or Article 53(c) EPC 2000) involving means that are a "device" (see for example decision T 1314/05 of 15 April 2008, point 3.2 of the Reasons; decision T 213/07 of 19 March 2009, point 3 of the Reasons; decision T 1099/09 of 12 January 2012, points 3.2, 3.3 and 7.2 of the Reasons, where the relevant claims related to the use of a "device" in a treatment by therapy; or decision T 775/97 of 3 April 2001, point 2.6, second paragraph of the Reasons, where the relevant claim related to the use of a "device" in a treatment by surgery).

17. In the present board's view, it also emerges from the whole reasoning of decision G 5/83 (*supra*) that it is

the "substance" or "composition" which is responsible for the "medical" - in the case of a treatment by therapy the "therapeutic" - effect, i.e. that the "substance" or "composition" is the active agent in the medical use. Reference is made in particular to the statement in point 23 of the Reasons of decision G 5/83 (*supra*): *"For these reasons, the Enlarged Board considers that it is legitimate in principle to allow claims ... even in a case in which the process of manufacture as such does not differ from known processes using the same* ***active*** *ingredient."* (emphasis added). A similar view on the interpretation of decision G 5/83 (*supra*) as regards this aspect was expressed in decision T 1099/09 (*supra;* point 4.3 of the Reasons).

18. Consequently, in accordance with the reasoning in decision G 5/83 (*supra*) and in view of the claim at issue here which relates to the treatment of patients by therapy, the board considers that it is decisive for determining whether or not a "substance" or "composition" is used in a treatment to establish (a) the means by which the therapeutic effect is achieved and (b) whether that which achieves the therapeutic effect is a chemical entity or composition of chemical entities.

19. In the present case the therapeutic effect on which the treatment according to claim 1 is based is the removal of immunoglobulin from the plasma of patients suffering from DCM. This effect is achieved by the "specific ligand for human immunoglobulin" which is undisputedly a chemical entity. The "column" serves as a carrier for the ligand and is not instrumental in achieving the

therapeutic effect. In fact, the ligand could also bind immunoglobulin, if it was not bound to the column, i.e. if it was free in solution. Accordingly, the board judges that the means used for the treatment in accordance with claim 1 is to be considered as a "substance" or "composition" in the sense of decision G 5/83 (*supra*).

20. Several decisions were considered in the context of the issue raised by the appellant-opponent's argument.

20.1 In decision T 138/95 of 12 October 1999 a claim to the *"Use of a **polypeptide** selected from growth factors and cytokines **for the manufacture of a device** for delivering to the blood stream of a patient a **therapeutic dose of the peptide** by systemic delivery by pulmonary adsorption [...]"* was considered by the board without any observations or comments as a second medical use claim within the meaning of decision G 5/83 (*supra*; sections VI and VII of the Facts and Submissions and points 2 and 4 of the Reasons of decision T 138/95 (*supra*); emphasis added).

In decision T 138/02 of 27 June 2006 the claim under consideration was to the *"Use of a material comprising a **porous water insoluble carrier** and **a compound covalently immobilized onto said carrier**, [...] for **the manufacture of an adsorbent** for the **treatment of a disease** selected from the group consisting of [...] by removing at least one cytokine selected from the group [...] from body fluid [...]."* (emphasis added). The board concluded that this claim was not directed to a second medical use in line with decision G 5/83 (*supra*), because the means actually used in the treatment after

the manufacture were not a "medicament". The board defined "medicament" as characterized by *"it be administered to a patient's body in order to treat a disease"* (see points 2.5 to 2.7 of the Reasons).

Thus, in both those decisions the relevant claims related to the use of "means" for a treatment by therapy and it was decisive for the interpretation of the claim - as for example in decisions T 213/07 (*supra*) and T 1099/09 (*supra*) - whether or not the "means" were to be considered as a "substance" or "composition". The board notes that in none of decisions T 138/95, T 138/02 and T 213/07 (all *supra*) was it decided whether or not the means used in the claimed treatment were "substances or compositions" **within the meaning of decision G 5/83**. Therefore, the board considers that these decisions do not help to elucidate the issue at stake here. In this board's view, decision T 1099/09 (*supra*) supports its view on the present issue (see in particular point 3.4 and point 4.3 of the Reasons).

20.2 Decisions T 227/91 of 15 December 1992 and T 775/97 (*supra*) were cited by the appellant-opponent because they give a definition of the term "medicament" with which the subject matter of claim 1 would - in the appellant-opponent's view - not comply. In the first of those decisions, T 227/91 (*supra*), the board dealt with the following claim:

*"1. [...] Use,* ***in the manufacture of a laser surgical instrument*** *for intercepting an incident laser beam having a particular wavelength after the laser beam has energised a desired surgical target site but before the laser beam energises material adjacent to the surgical*

*target site, of:* ***substrate means*** *(16) adapted to transmit energy received from said laser beam away from said surgical target site, said substrate means having a high thermal conductivity and an exterior surface; and* ***coating means*** *(18) adapted to absorb laser energy at said wavelength, said coating means covering substantially the entirety of the exterior surface of the substrate means, having a high absorptivity for energy at that wavelength and having a thickness in excess of one quarter of the wavelength of the laser beam; characterized by said coating means having a thickness substantially equal to 0.1 (a.t)0.5, where a = thermal diffusivity of the coating means t = effective pulse time of the laser beam."* (emphasis added).

In decision T 775/97 (*supra*) the following claim was at issue:

*"29. Use of a mutually connected* ***first tube*** *(160A)* ***and first tubular member*** *(166A) and a mutually connected* ***second tube*** *(160B) and* ***second tubular member*** *(166B), as defined in any one of claims 1 to 26,* ***for the manufacture of a device for use in a surgical method*** *in which the tubular members and tubes are intraluminally delivered in the first diameter condition of the tubular members into a body passageway (152) to be repaired, to be disposed therein substantially even and on the same level as each other, and the tubular members are subsequently expanded and deformed, by the application from the interior of the tubular members of a radially outwardly extending force, from the first diameter to the second, expanded and deformed, diameter with portions of the first and second tubular members*

*being in a substantially flat adjacent relationship, whereby the adjacent portions are substantially flattened towards each other to substantially close off and substantially remove any gaps that may otherwise be present within the body passageway between the tubular members;* ***to form a bilateral passageway in the body passageway to repair the body passageway."*** (emphasis added).

The board notes that in neither of these decisions did the board express any doubt that the means used in the treatment were a "device" and did not decide on the issue of whether what was used was a "substance" or "composition" within the meaning of decision G 5/83 (*supra*).

Furthermore, as already observed in point 14 above, the board considers that in order to decide whether or not a claim complies with the requirements set out in decision G 5/83 (*supra*) an assessment of whether or not a "medicament" is used is not in fact needed. Instead it is necessary to decide whether or not a "substance" or "composition" within the meaning of G 5/83 (supra) is used. However, even if it was necessary to decide whether or not a "medicament" was used, the board notes that in decisions T 227/91, T 775/97 and also in decision T 138/02 (all *supra*) different boards even had different views on the essential characteristics of a "medicament" which demonstrates in this board's view that it would be undesirable to take any one of those definitions as being generally applicable.

20.3 The appellant-opponent has furthermore relied on decision T 144/04 of 18 February 2005 where the claim

at issue was directed to *"**A method** for the extracorporal removal of lipids selected from cholesterol, triglycerides and other lipids from animal plasma, serum or other suitable blood fractions, said method comprising: providing plasma, serum or other suitable blood fractions, mixing with an extraction solvent (mixture) which extracts the said lipids from the fraction, wherein the extraction solvent is removed from the delipidated fraction by mixing the delipidated fraction with an adsorbent specific for the extraction solvent."* (emphasis added).

The appellant-opponent has argued that this claim related to a treatment-method very similar to that of present claim 1, i.e. the **extracorporal** removal of unwanted blood components, and that the board held that the claimed method was not a method of treatment by therapy in the sense of Article 52(4) EPC [1973] because it was carried out **extracorporally**, i.e. not "on" the body. By analogy, it was argued that the column used extracorporally according to the present claim 1 could not be considered as a "medicament".

The board notes first, that the claim at issue in decision T 144/04 (*supra*) was not a second medical use claim, but a claim to a method and that the relevant issue was whether or not the claimed method of treatment by therapy fell within the ambit of subject-matter excluded under Article 52(4) EPC 1973, i.e. whether or not the treatment by therapy was to be considered as such a treatment in the sense of Article 52(4) EPC 1973 (see also decisions T 329/94 of 11 June 1997 and T 789/96 of 23 August 2001 where the same issue was considered). Therefore, decision

T 144/04 (*supra*) is *prima facie* not relevant for the specific issue arising here in relation to a second medical use claim, namely if the used "means" are a "substance" or "composition" in the sense of decision G 5/83 (*supra*). Moreover, the board in decision T 144/04 (*supra*) gave no opinion - explicit or implicit - on what is considered to be a "medicament", whether in a general sense or in the sense of decision G 5/83 (*supra*).

20.4 For the present board a question which could rather arise from decision T 144/04 or decisions T 329/94 and T 789/96 (all *supra;* see point 20.3 above) and in the light of decision G 5/83 (*supra;* see point 13 above) is whether or not the feature in present claim 1 relating to the treatment *"said treatment comprising passing plasma of the patient over the column under conditions which effect the binding of said specific ligand to immunoglobulin in the patient's plasma, thereby removing a significant portion of the immunoglobulin from the patient's plasma, and reinfusing the plasma to the patient"* is to be considered as a "*method referred to in Article 52(4) EPC [1973]*".

Decision T 144/04 (*supra*) held that the claimed method was not a method according to Article 52(4) EPC 1973 because the removal of the lipids took place "**extracorporally**", i.e. the blood when it was treated was "unlinked" to the patient's body, see (i) the steps in claim 1 of decision T 144/04 (*supra*) of mixing plasma, serum or other suitable blood fractions with an extraction solvent and of mixing the delipidated fraction with an adsorbant, and see (ii) in point 2 of the Reasons (a) the originally present feature that the

removal of lipids happens in a **discontinuous** flow system and (b) the disclosure in the application that it was an object to provide a method whereby a patient's plasma or serum can be treated **remote** from a patient.

In the present case the treatment referred to in claim 1 is a so-called immunoapheresis which achieves the therapeutic effect extracorporally, i.e. the unwanted components in the plasma, immunoglobulins, are removed spatially separated from the patient's body. Yet here the patient's plasma, the patient's body and the means achieving the therapeutic effect, i.e. the ligand bound to the column are linked in a continuous circuit. Therefore, the treatment in the present case is different from the treatment dealt with in decision T 144/04 (*supra*). Hence, the board sees no reason based on decision T 144/04 (*supra*) not to consider the treatment defined in claim 1 as a treatment by therapy in accordance with Article 53(c) EPC (or Article 52(4) EPC 1973). The treatment-feature therefore does not preclude the interpretation of claim 1 as a second medical use claim.

Other decisions also support the board's view in this respect. In decision T 1075/06 of 17 May 2011 the board decided that the claimed blood processing method for the removal of certain blood components which that board qualified as *"blood component therapy"* or *"therapeutic plasma exchange"* was a method of treatment of the human body by therapy and thus refused the claim pursuant to Article 53(c) EPC. In decision T 1695/07 of 28 September 2011 the board considered a blood manipulation process involving the continuous removal

of blood from a patient, its subsequent flowing through a circulating line of an extracorporal circuit and its re-delivery to the patient as a method of treatment of the human body by surgery. The claim was therefore excepted from patentability pursuant to Article 53(c) EPC.

21. In view of the considerations above, the board judges that claim 1 and its dependent claims 2 to 8 are to be interpreted as claims to a second medical use in the sense of decision G 5/83 (*supra*). Accordingly, the indication of the purpose *"for the treatment of a patient suffering from dilated cardiomyopathy [...]"* is not merely descriptive and needs consideration when assessing the patentability (here in particular the novelty and inventive step) of the claimed subject-matter.

*Request for referral of questions to the Enlarged Board of Appeal*

22. Regarding the interpretation of claim 1 both parties have requested that a question be referred to the Enlarged Board of Appeal. The question was formulated in German (see section X above) and concerns, put simply, two issues. First, whether the special approach to novelty allowed by the Enlarged Board of Appeal in decision G 5/83 (*supra*) also applies to uses of "medical devices" and second, what the meaning of the terms "substance", "composition" and "medicament" in the light of Articles 54(4) EPC 1973 and decision G 5/83 (*supra*) are.

23. Pursuant to Article 112(1)(a) EPC, in order to ensure uniform application of the law or if a point of law of fundamental importance arises, a Board of Appeal shall, during proceedings on a case and either of its own motion or following a request from a party to the appeal, refer any question to the Enlarged Board of Appeal if it considers that a decision is required for the above purposes.

24. The first part of the question is not relevant to the present decision since the means used is not a "medical device" (see point 19 above).

25. As to the second part of the question, the board does not recognize in its interpretation of the meaning of "substance", "composition" and "medicament" true circumstances of a deviation from any earlier case law, essentially because it is not aware of any case law that dealt specifically with the issue of whether means used in a therapeutic treatment qualify as a "substance" or "composition" within the meaning of G 5/83 (*supra*; see points 20.1 to 20.3 above).

26. Moreover, a referral is also not necessary for a decision in the present case because the board could decide the issue itself on the basis of the EPC [1973] and decision G 5/83 (see points 6 to 19, 20.4, 21 above). The board notes furthermore that the question is formulated so broadly that it encompasses many aspects which are not relevant for deciding the issue at stake here.

27. Therefore, the parties' request for a referral of a question to the Enlarged Board of Appeal is refused.

*Amendments - Article 123(2) EPC; sufficiency of disclosure - Article 83 EPC; clarity, support - Article 84 EPC*

28. The appellant-opponent had no objections pursuant to Articles 123(2), 84 and 83 EPC and also the board has no objections.

*Novelty - Article 54 EPC*

29. The appellant-opponent argues that the subject-matter of claim 1, even when it is interpreted as a claim to a second medical use, is not novel in view of any of the following disclosures: an oral disclosure during a lecture in Berlin on 15 September 1995 by Dr Wallukat at the symposium "The Role of Immune Mechanisms in Cardiovascular Disease", a prior use by Dr Müller in the period of 3 July to 7 July 1995 at the "Deutsches Herzzentrum" hospital in Berlin, and the written disclosure in document E12.

*Oral disclosure*

*Request not to hear the witnesses Dr Wallukat and Dr Kunze*

30. By an interlocutory decision in accordance with Article 117 and Rule 117 EPC the board decided that it was necessary to hear Dr Wallukat and Dr Kunze as witnesses.

31. The witnesses were summoned in accordance with Rule 118 EPC. In accordance with the second half-sentence of Rule 118(2)(c) EPC Dr Wallukat and Dr Kunze were invited to confirm within two months of receipt of the summons that they were prepared to appear before the

board. Neither of the two witnesses replied, either within the given time limit or at all. Yet, both witnesses were present on the day for which they were summoned. The appellant-patentee requested the board to refrain from hearing them.

32. The failure to react to the invitation in the summonses does not have any influence on the board's view that the witness-evidence of Dr Wallukat and Dr Kunze was necessary in the present case and therefore is no reason for the board to change its interlocutory decision.

33. Rule 120(1) EPC indicates as the consequence of a failure to reply to the summons that "if no reply is received within the period specified in the summons, the European Patent Office may, in accordance with Article 131(2), request the competent court to hear the person concerned." However, in the event Dr Wallukat and Dr Kunze were present on the date indicated in the summonses and the board could hear them as witnesses so that it was not necessary to take any other such step.

34. The appellant-patentee submitted that the missing replies had put it in a disadvantageous situation because it was uncertain whether or not the witnesses would attend and because, if they did not attend, it nevertheless had to be prepared for them to attend. The board has therefore considered whether the appellant-patentee's right to be heard was violated by the fact that, despite the missing replies, the witnesses would be heard on the date for which they were summoned.

When asked by the chairman of the board at the oral proceedings whether or not the appellant-patentee's representative was prepared for both eventualities, i.e. for both the presence and absence of the witnesses, the appellant-patentee's representative confirmed that he was. Also the appellant-patentee had not asked for a break for preparation or even for an adjournment of the hearing. Thus, the appellant-patentee was prepared to hear the witnesses and therefore its right to be heard would not be violated, if the witnesses were in fact heard.

35. The appellant-patentee also submitted that the appellant-opponent had played a procedural game by withholding the information that the witnesses would attend. However, although it is often a party - here the appellant-opponent - who offers a witness, the witness is not the party itself. This is illustrated, for example, by the fact that the summons for the witness hearing can be sent to the witness directly (as in the present case) and not necessarily to the representative of the party in question. Thus, the appellant-opponent is not responsible for the actions of a witness. It is of course desirable that a party, or its representative, who wishes a witness to be heard, takes all practical steps to ensure the attendance of that witness. That does not mean however, that, if a witness does not itself comply with a request directed to it, the party or representative is indulging in "procedural games".

36. Therefore, the board decided to refuse the appellant-patentee's request not to hear the witnesses. This decision was taken in the particular circumstances of

the present case and should not be taken to mean that in other cases the failure to meet the time limit of Rule 118(c) EPC will always remain without consequences.

*Evaluation of evidence: documents E1, E2, E3 and E24; oral testimony of Dr Wallukat and Dr Kunze*

*Documents E1, E2 and E3*

37. In the context of the alleged oral disclosure of the subject-matter of claim 1 by Dr Wallukat the board observes that, in contrast to a written document the contents of which are fixed and can be read again and again, an oral presentation is ephemeral. Therefore, the standard of proof for ascertaining the contents of an oral disclosure is high. What has been said, or to use the terms of Article 54(2) EPC, what has been "made available to the public" has to be put beyond reasonable doubt. In the often-cited decision in case T 1212/97 of 14 May 2001 the board expressed the view that *"written notes made at the lecture by at least two members of the audience can usually be regarded as sufficient"* for that purpose (see point 4 of the Reasons).

38. However, a fact also alluded to by the board in case T 1212/97 (*supra*) in point 4 is that the amount of evidence necessary to establish the content of an oral presentation beyond reasonable doubt is to be judged on a case to case basis, i.e. it depends on the quality of the evidence in each case. In the present board's view decision T 1212/97 (*supra*) cannot therefore be interpreted as setting an absolute standard for the

amount of evidence necessary to prove the contents of an oral disclosure.

39. In the present case the opposition division found that the evidence available to it - documents E1, E2, E3 - did not prove beyond reasonable doubt that the subject-matter of claim 1 was made available during Dr Wallukat's lecture.

39.1 Document E3, an article published in a book (according to the bibliographic data on page 3 of document E3: *Proceedings of the International Symposium on "The Role of Immune Mechanisms in Cardiovascular Disease")*, disclosed all the features of claim 1, but was published after the priority date. There was no supplementary evidence to establish that the relevant contents of document E3 had in fact been made available to the public at the lecture. Document E24, aimed at proving that document E3 had been written shortly after the conference, was not admitted by the opposition division into the proceedings due to its late filing and lack of *prima facie* relevance. This document was re-filed in appeal proceedings and the board has - by agreement between the parties - admitted it into the proceedings (see sections V and X above; see also point 47 below).

39.2 Documents E1 and E2 are each a so-called "Eidesstattliche Versicherung" (i.e. a declaration made in lieu of an oath, hereinafter "declaration"), declaration E1 being that of the lecturer himself, Dr Wallukat, and declaration E2 that of a member of the audience, Dr Kunze. Neither of the two declarations was supported by contemporary notes. The opposition

division therefore concluded that these declarations did not satisfy the criteria in decision T 1212/97 (*supra*) for establishing the contents of an oral disclosure beyond reasonable doubt. Further, the objectivity of the contents of declaration E2 could be questioned in view of a later professional cooperation of Dr Kunze and Dr Wallukat. Moreover, in view of the nature of the written evidence E1 and E2 the opposition division declined in the light of decision T 1212/97 (*supra*) to hear Dr Wallukat and Dr Kunze as witnesses because their oral testimony would not make good the "deficiencies" of their declarations.

40. The board shares the opposition division's view on the evidential quality of document E3. It cannot automatically be assumed that a written publication, although it appears in a book referred to as "proceedings" of a conference, identically reproduces the lectures.

41. As the opposition division, but for different reasons, the board comes to the conclusion that documents E1 and E2 *per se* are not of a quality to put the contents of an oral disclosure beyond reasonable doubt. First, the long lapse of time between the event to be recalled and the writing of the declarations - around 10 years - together with the absence of contemporary notes sheds *prima facie* doubt on the correctness of the recollection of Dr Wallukat and Dr Kunze, as does the possibility that their recollection was tainted by the contents of document E3, later publications or information gained from their subsequent professional relationship. Second, relations with the appellant-

opponent's company could possibly have influenced Dr Wallukat's and Dr Kunze's objectivity.

42. As noted above in point 38 and as also already pointed out in its preliminary opinion (see section VI above), the board is not convinced that decision T 1212/97 (*supra*) is the last word on the *quantum* of proof for prior disclosures during lectures. The board considers that there may be circumstances where evidence from the lecturer and only one member of the audience is convincing enough to reach the standard of proof - i.e. beyond reasonable doubt.

*Oral testimony of Dr Wallukat and Dr Kunze*

43. The board felt that its reservations concerning declarations E1 and E2 and document E3 could possibly be dispelled by hearing the authors of declarations E1 and E2 themselves. In contrast to the opposition division the board therefore considered it appropriate to hear Dr Wallukat and Dr Kunze as witnesses because their testimony could affect the outcome of the proceedings.

44. The following is a selection of statements made by Dr Wallukat and Dr Kunze during their testimonies. The page numbers indicated are those of the "Transcript" of the witness hearing.

44.1 General details about the conference

Dr Wallukat remembered who the organizer was, that he had been invited by him, the venue and date of the conference, that many American colleagues participated,

that he had seen Dr Kunze in the auditorium during his lecture and that he had not presented a poster (pages 54, 55 and 61). Also Dr Kunze recalled who the organizer was, the venue and date, that the conference "came quickly" - it took place six weeks after the announcement, that he had heard about it, but that he had additionally received an invitation, and that he went there for two days as evidenced from parking tickets (pages 6, 8 and 9).

Both Dr Wallukat and Dr Kunze could not remember whether poster sessions took place during the conference (pages 9, 55 and 56), whether Dr Wallukat's lecture was held in the morning or in the afternoon (pages 11 and 59) and who introduced the speakers (pages 13, 14 and 59).

44.2 The lecture

44.2.1 Circumstances

Whereas Dr Kunze remembered that the lecture room was the great ballroom of the hotel in which the conference was held, Dr Wallukat only remembered that it was one of the bigger lecture rooms of this hotel (pages 31 and 74). Dr Kunze remembered Dr Wallukat's presentation, but could not remember any other presentation without recourse to document E3 (page 20).

Both Dr Wallukat and Dr Kunze agree in their recollection that during Dr Wallukat's presentation the room was not really full (pages 31, 32 and 60).

44.2.2 Slides

Dr Wallukat said that he had shown slides of all the figures disclosed in document E3 plus those in an envelope which he brought with him to the witness hearing plus possibly two or three more (pages 74 and 75).

Dr Kunze said that Dr Wallukat had shown 8 to 10 slides which were all in Dr Wallukat's envelope (page 32).

44.2.3 Contents of the lecture

Dr Wallukat said that the data presented at the lecture were "brand new". Dr Kunze said that he did not need to make notes because he knew what was said.

Dr Wallukat stated that the gist of his lecture was that he and Dr Müller had noticed that the relevant antibodies decreased in the course of the healing process in a patient with myocarditis and that at the same time the patient's heart function improved (pages 53, 71 and 79).

Dr Kunze said that during the lecture Dr Wallukat reported on a patient with myocarditis, by whom in the course of the healing process, the antibodies disappeared (page 16) and that this had given him the idea to reduce antibodies in patients suffering from DCM - for which there was no cure (pages 17 and 18) and that the take-home message was: if you reduce the antibodies, then this improves the function of the heart and its anatomy (page 49).

44.2.4 Patient identification

Dr Kunze stated that Dr Wallukat had identified the myocarditis-patient by initials (page 16), whereas Dr Wallukat said that he had not identified the patient by any means (page 59).

44.2.5 Extent of the reduction of immunoglobulin

Dr Wallukat stated that he had not disclosed during the lecture any details of the extent to which the immunglobulin portion in the patient's blood was reduced.

Dr Kunze said that Dr Wallukat had disclosed that the level of immunoglobulins was decreased to the extent of 80%. That this was a good value had not been known at the time (page 21).

44.2.6 Discussion after the lecture

Dr Wallukat was not sure about the intensity of the discussion immediately after his lecture and whether the "bridge-to-transplant" issue had been discussed (pages 60 and 70). He recalled that in later personal conversations at the symposium other participants, in particular Prof. Maisch, had expressed appreciation of the new method presented by him (page 64).

Dr Kunze appeared not to be sure that there had been a discussion immediately after Dr Wallukat's presentation (page 19: "Frage: Aber nach den Vorträgen gibt es eine Fragerunde. Antwort: Ja, das ist dann **normalerweise** die Podiumsrunde ..."), but he remembered that he

participated as listener at the "Podiumsrunde" where the participants expressed surprise about the new treatment (page 19). Dr Kunze also said that the "bridge-to-tranplant" issue had been mentioned at the "Podiumsrunde" (war "auf dem Podium") (page 45).

44.3 Collaboration between Dr Wallukat and Dr Kunze before the lecture

Dr Wallukat said that he had not worked directly with Dr Kunze on aspects of DCM in the days, weeks or months preceding the presentation and that Dr Kunze had not been involved in the studies that led to the data presented at the presentation (page 76). They only cooperated later in the context of the firm "Affina" where they tried to develop new adsorbers, also with the aim of using them for the treatment of DCM (pages 76 and 77).

Dr Kunze said that he had often had discussions with Dr Wallukat about DCM or immunoaphereses before his presentation (page 34) and that he himself, Dr Wallukat and Dr Müller had together determined the regimen to reduce the level of immunoglobulins by 80% (pages 23 and 35). Dr Kunze said that after the presentation the collaboration was intensified. He said that he and Dr Wallukat developed new adsorbers in the context of the firm "Affina" which had been founded in 1999 (pages 35 and 36).

44.4 Declarations E1 and E2

Dr Wallukat and Dr Kunze both stated that they had written the declarations themselves (pages 37 and 83),

but neither of them spontaneously recalled when exactly this happened (pages 37 and 77).

Dr Wallukat said that he had not used anything to refresh his memory when he wrote the declaration. Dr Kunze said that he had used document E3 and his memory; moreover, he knew the publications of Dr Wallukat and Dr Borda and he could of course not at the time of his oral testimony distinguish precisely between what he knew in 1995 and the knowledge he had acquired later (pages 39 and 40).

44.5 Conformity of the contents of document E3 with those of the lecture

Dr Wallukat and Dr Kunze both remembered that Figure 3 of document E3 had been shown as a slide at the lecture.

Dr Wallukat could not remember whether he had shown a slide with the data of Table 1 of document E3 (page 80) whereas Dr Kunze said that such a slide had been presented (page 46).

Dr Wallukat remembered that he had said more during the lecture than what was disclosed in document E3, in particular that he had shown slides with data of patients treated at the "Charité" hospital (pages 73, 80 and 83). Dr Kunze said that the contents of document E3 were an accurate reproduction of what Dr Wallukat had said (page 23) and that the only point that was additionally mentioned in the lecture was how to measure the antibodies (page 44).

44.6 Relationship to the appellant-opponent

Dr Kunze said that he had been working for the last five years as medical advisor for the appellant-opponent's company (page 4) and Dr Wallukat said that he never had any relations with this company (pages 53 and 78).

45. The board appreciates that both witnesses were honest and open in their testimony and appeared genuinely to be trying to assist the board. The board draws the following conclusions after hearing the oral testimony:

- It appears that any relation of Dr Wallukat and Dr Kunze to the appellant-opponent at the time of writing the declarations, i.e. the party in whose support the declarations were made, can be excluded, so that any influence on their evidence for that reason can be eliminated.

- It is accepted that attention plays a key role in storing information in the human brain. This is why, for example, emotionally charged events are better and longer remembered. The board did however not gain the impression that the lecture was perceived by Dr Wallukat as an outstanding and therefore easily memorisable event. For example, Dr Wallukat could not remember the lecture room, or the time of the day when he gave the lecture.

- Both Dr Wallukat and Dr Kunze do not have a recollection of all details of the conference and the lecture. It would in fact be surprising if they had - human memory fades with the passage of

time. In many aspects the witnesses have recollections, but they are diverging - the extent of their collaboration in the period before and shortly after the lecture, the information that was disclosed (or not) during the lecture and the identity of the contents of the lecture and document E3 are particularly noteworthy. The board cannot exclude that the divergence in recollection is due to mixing up knowledge from the lecture and knowledge gained from later collaboration and joint publications. In other aspects Dr Wallukat's and Dr Kunze's recollection is uniform, in particular about Dr Wallukat's disclosure at the lecture that patients with DCM had been treated by immunoapheresis. The board is not sure whether the recollection of details falling in this category is spontaneous, i.e. whether it has been made independently of written information, such as for example the declarations or document E3.

46. *In toto*, the oral testimony of Dr Wallukat and Dr Kunze could not dispel the board's doubts that, during Dr Wallukat's presentation, what is stated in declarations E1 and E2 as having been said was in fact actually said, that a slide with the contents of Figure 3 of document E3 was actually shown, or even that the complete contents of document E3 were actually disclosed.

*Document E24*

47. As to the post-published document E3 as evidence of what was said during Dr Wallukat's lecture, document E24 does not add anything to prove how much of the

contents of document E3 was made available at the lecture. Document E24 appears to be a standard letter sent to all speakers at the conference (otherwise the writers would not have expressed the hope that Dr Wallukat, who lives in Berlin as they must have known, had "einen angenehmen Aufenthalt in Berlin"). Document E24 does not contain anything from which it could be concluded that the document had to be an accurate reproduction of the lecture. The indication of the maximum amount of pages and figures suggests that shortening may be necessary, but it does not indicate that nothing of relevance can be added.

48. Taking together all the evidence before it, the board is not in a position to conclude that it has been established beyond reasonable doubt that Dr Wallukat disclosed during his lecture subject-matter falling within claim 1. Hence, the novelty-objection based on the oral disclosure fails for this reason.

*Prior use - documents E11 and E23*

49. Document E11 is a letter to Dr Wallukat dated 16 February 1999 signed by Dr Müller. Under the heading "Sehr geehrter Herr Dr. Wallukat" it is stated that at the "Deutsches Herzzentrum" hospital in Berlin in the period from 3 July 1995 to 7 July 1995 one patient with DCM was treated with an IgG immunoadsorption for the elimination of ß1-autoantibodies. It is further stated that the necessary instruments, IgG-columns and accessories were provided by the firm Baxter.

Document E23 is a "Eidesstattliche Versicherung" from Dr Müller dated 19 September 2007. It is stated that he

had treated a patient with DCM for the first time during the period from 3 July 1995 to 7 July 1995 at the hospital "Deutsches Herzzentrum" in Berlin by IgG-immunadsorption or "immunoapheresis" for the elimination of ß-antibodies, that the necessary equipment was provided by the firm Baxter and that this patient, all later treated patients and also the staff involved at the "Herzzentrum" were not under any obligation of secrecy.

50. As with oral disclosures, alleged prior uses have to be established beyond reasonable doubt. Thus, the board has to be convinced that the use was "made available to the public" - as required by Article 54(2) EPC.

Documents E11 and E23 are from the person who has conducted the alleged prior use. Assuming that the treated patient and staff involved in the treatment represent the "public", documents E11 and E23 demonstrate that the person carrying out the treatment knew what he was doing, but they do not demonstrate what was actually made available to the public. Thus, like the opposition division, the board cannot come to the conclusion that the prior use has been established beyond reasonable doubt. Therefore, the novelty objection based on the prior use is not successful.

*Document E12*

51. The appellant-opponent submitted that document E12 disclosed a process for the removal of auto-antibodies from sera of DCM patients by passing their sera over a column to which specific ligands are bound, that this process was described in document E12 as a new

therapeutic approach for the treatment of DCM and that, although the step of re-introducing the serum into the patient was not explicitly mentioned in the document, the skilled person would consider that as implicitly disclosed because it was evident that, once serum is removed from a patient, it has to be re-infused. Consequently, the subject-matter of claim 1 was not novel in view of document E12.

52. The disclosure content of a document is the information that a skilled person directly and unambiguously derives from it when he or she reads the document as a whole with his or her common general knowledge (Case law of the Boards of appeal, 6th edition 2010, I.C.2 and 2.1, second and third paragraph).

53. There are passages in document E12 which disclose the removal of autoantibodies from the serum of DCM and myocarditis (MC) patients and in which it is stated that this could be considered as a therapeutic approach, see for example page 76, second column: *"In a second step, we investigated the possible use of synthetic peptides as absorbants* ***for the specific removal of autoantibodies*** *from the serum of patients with MC and DCM. This would mean* ***a new approach to the therapy*** *of MC and DCM by the elimination of possibly pathogenic autoantibodies."*; page 78, first column, last paragraph: *"Using synthetic peptides derived from ANT or myosin it was possible to isolate and thus* ***eliminate more than 95% of the autoantibodies*** *from the sera of patients with MC and DCM (Fig. 2)."*; page 78, second column:*"By specific immunoabsorption to synthetic peptides, the* ***autoantibodies can specifically be removed*** *from the serum of patients with MC and DCM, thus* ***offering a new***

***approach to the therapy*** *in MC and DCM.";* page 79, first column: *"The identification of major antigenic determinants on a molecular level using synthetic peptides* ***could also offer a new approach to therapy*** *of MC and DCM.";* the last paragraph of the document: *"In conclusion, the synthetic peptides have been shown to be suitable as antigens in antibody screening tests and* ***provide a new approach to the therapy*** *of MC and DCM."* (emphasis added).

54. The actual process of removing autoantibodies from the sera of DCM and MC patients mentioned in the passages cited above is described on page 77 of document E12 (see the paragraphs "Affinity Chromatography" and "Patients") and may be summarized as follows: Sera from 72 patients with DCM or MC - which are known according to document E12 to contain autoantibodies to adenine nucleotide translocator (ANT) or cardiac myosin (see page 76, first column, second paragraph) - were used for the study together with sera from control groups. The immunoglobulins from the sera were initially concentrated by ammonium sulphate precipitation. These pre-treated sera were applied to a column which had been loaded with thiopropylsepharose 6B to which synthetic peptides derived from these proteins (ANT - 2 different peptides and cardiac myosin - 3 different peptides, see Table 1) were coupled. Non-specific antibodies were then removed by washing with a buffer. Specific antibodies, i.e. those having bound to the peptides on the column, were then eluted. Figure 2 shows the elution profile.

55. The board is convinced that the skilled person would directly and unambiguously derive from the disclosure

in document E12 as a whole and in particular from the passages as summarized in point 54 above that the removal of antibodies has not been made in the context of the treatment of a patient, but in the context of *in vitro* laboratory experiments. The board considers its view to be supported by the last paragraph of the introduction: *"Here we report the identification of main antigenic determinants of the ANT and myosin, their usefulness as antigens in antibody screening tests and the affinity chromatographic* ***isolation*** *of autoantibodies."* (emphasis added) and by the use of the conditional tense or terms pointing into the future when the removal of antibodies is mentioned in relation to therapy, see in the citations above: *"would mean a new approach"*, *"thus offering a new approach"*, *"could also offer"*. Finally, there is no sign of any disclosure of a therapeutic effect in document E12.

56. The last sentence of the document E12 seems rather assertive. However, remarks in the last paragraphs of scientific publications are often so. Either the results presented in the publication are evaluated in an extremely careful or in an extremely optimistic manner and, in either case, they are often speculative. In the board's view, the skilled person would not change his or her interpretation of the tangible disclosure in document E12 in view of such a remark.

57. Since document E12 discloses an *in vitro* assay for the removal of antibodies from sera and not a treatment, the skilled person would not conclude that document E12 implicitly discloses a step of re-infusion of the serum into the patient. Thus, like the opposition division,

the board comes to the conclusion that document E12 does not anticipate the subject-matter of claim 1.

58. If follows from points 37 to 57 above that the subject-matter of claim 1 and its dependent claims 2 to 8 fulfils the requirements of Article 54 EPC.

*Inventive step - Article 56 EPC*

59. Since it could not be established with sufficient certainty that Dr Wallukat's oral disclosure or Dr Müller's prior use had made available to the public subject-matter falling under the terms of claim 1, and since it has not been argued that any other subject-matter had been made available by the oral disclosure or the prior use, the appellant-opponent's argumentation of lack of inventive step submitted at the oral proceedings before the board based on these disclosures is not dealt with in this decision.

60. At these oral proceedings the appellant-opponent essentially reiterated its arguments from the opposition proceedings as to why the subject-matter of claim 1 lacked an inventive step, namely in view of document E12, in view of any of documents E8 or E9 in combination with any of documents E4, E6 or E7 or in view of a combination of document E4 with documents E8 or E9.

61. It is established practice in proceedings before the EPO that inventive step is assessed according to the problem-solution-approach which involves the determination of the closest prior art document, the formulation of the problem to be solved in view of the

closest prior art document and its solution. According to established case law the closest prior art document is a disclosure providing the most promising springboard towards the claimed invention. As established by the case law this is normally a document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention (Case Law of the Boards of Appeal, 6th edition 2010, I.D.3.1).

62. The purpose of the invention as claimed in the present auxiliary request 2 is the treatment of patients suffering from DCM.

*Closest prior art*

63. The main result of the experiments disclosed in document E4 is that sera of DCM patients contain autoantibodies against the ß1-adrenergic receptor which have a positive chronotropic effect on the heart-beat rate of cultured rat cardiac myocytes. It is however mentioned in the section "Background" on page 2760, second sentence and on page 2766, first column, first full paragraph, first and second sentence and last three sentences that the treatment with ß1-receptor selective beta-blockers has beneficial therapeutic effects in some DCM patients. It transpired from Dr Wallukat's and Dr Kunze's explanations during their oral testimony that, in fact, in the priority year of the disputed patent, 1995, transplantation was considered as the only "real" treatment" for DCM (see in particular the sentence bridging pages 16 and 17 of the "Transcript"). Thus, although it may not be satisfactory, document E4 discloses a treatment for DCM.

The board therefore considers that document E4 represents the closest prior art document.

64. In agreement with the opposition division the board considers that neither of documents E8 and E9 represents the closest prior art document. These documents disclose the use of immunoglobulin adsorbents for the treatment of various diseases, including autoimmune diseases. Neither of the two documents explicitly mentions DCM. The appellant-opponent argues however that the treatment of DCM was implicitly disclosed in documents E8 and E9 because, as could be seen from documents E5, E6 and E7, at the priority date of the disputed patent DCM was considered to be an autoimmune disease.

65. DCM is a chronic heart muscle disease which is characterized by a poorly contracting and dilated left and/or right ventricle. The decreased heart function can affect the lungs, liver, and other body systems so that symptoms of the disease are variable.

At the priority date of the disputed patent a disease was normally characterized as an "autoimmune disease", if autoantibodies were the **cause** of the disease, i.e. its aetiologic agent (see for example document E8, page 29, line 19 to 21 or document E10, page 2, first half-sentence of the paragraph "Autoimmune Diseases - Ig-Therasorb").

65.1 In its introduction summarizing prior art knowledge, document E5, a scientific publication issued around four years before the priority date of the disputed patent, mentions on the one hand that *"autoimmune*

*mechanisms* ***have been proposed*** *to play a significant part in the pathogenesis of myocarditis and DCM"* and on the other hand that at the same time DCM *"is believed to develop in many cases* ***secondary to an acute viral myocarditis"***. Document E5 reports that sera of patients with DCM contain anti-ß1-receptor autoantibodies which accelerate the heart-beat rate of cultured rat cardiomyocytes. The authors allude to the discriminatory power of these autoantibodies and thus to their possible role as markers because, while having been found in the sera of DCM patients, these antibodies were absent from the sera of a large majority of patients with ischemic heart disease, from the sera of healthy subjects and from the sera of patients with acute myocardial infarction, allergic asthma and hypertension without cardiac dysfunction and Crohn's disease (see page 179, "Results", first paragraph) (emphasis added).

65.2 Document E7 is a scientific publication published around fourteen months before the priority date of the patent in suit. According to the last sentence of the introduction the study disclosed in the document "*assessed cardiological status and screened for antibodies in relatives of DCM patients.*" The results are summarized in the first sentence of the discussion as follows: "*Organ-specific antibodies were found in 41% of DCM patients and in 20% of their symptom-free relatives, but were absent or uncommon in normal subjects and in genetically unrelated symptom-free individuals from the same household, in particular the patient's spouses. This* ***lends strong evidence*** *for genetic predisposition and involvement of organ-specific autoimmunity in DCM.*" It is then further

stated in the discussion-section on pages 776 and 777 that "*the features seen in DCM resemble those found in insulin-dependent diabetes mellitus (IDDM)*", IDDM being known as an organ-specific autoimmune disease, but that the frequency of antibody positive patients is "*markedly different in DCM and IDDM*". Whereas autoantibodies to each of the cardiac antigens so far reported are found in only 30-40% of DCM patients, 80 to 90% of IDDM patients are positive. The authors conclude on the one hand that "*[t]he absence of cardiac antibodies in the majority of DCM patients could also indicate that* ***they are early markers*** *that are no longer detectable with disease progression*" and on the other hand that "*DCM might be heterogeneous with a proportion of the antibody-negative cases having a* ***non-autoimmune pathogenesis.***" In the following paragraph it is stated that "*[o]ur study examines the issue of disease heterogeneity and* ***indicates that autoimmunity is involved*** *in most pedigrees with familial and non-familial DCM.*" Yet, the subsequent paragraph starts with the question *"Will the cardiac antibody be a* ***marker*** *of disease predisposition in first-degree relatives of patients with DCM?"* The first three sentences of the last paragraph of the discussion section read: *"Organ-specific cardiac antibodies present in relatives of patients with and without familial DCM* ***provides evidence for autoimmunity in approximately 60%*** *of both familial and non-familial forms of the disease.* ***However, whether these antibodies have a direct pathogenic role remains to be established"***. In the first paragraph of the "Summary" it is stated that "*[o]rgan-specific cardiac antibodies can be found in patients with dilated cardiomyopathy (DCM and their relatives which* ***supports the idea*** *that*

*DCM is an autoimmune disease*". The "Summary" ends with the sentence: "*These antibodies are associated with mid left ventricular systolic dysfunction on echocardiography and* ***may be early markers*** *for relatives at risk of DCM.*" (emphasis added).

65.3 Document E6 is a review article summarizing *"recent investigations of the autoimmune basis of DCM" (*see last sentence of the "Introduction"*)*. It was published in April 1995, i.e. seven months before the priority date of the patent in suit and can thus be considered to provide an overview of the knowledge at the priority date of the patent in suit. The following is stated on page 172 in the last paragraph of the publication: *"In conclusion,* ***the role of immune factors in the pathogenesis of DCM remains uncertain****. The reasons for some of the* ***conflicting results*** *regarding the various aspects of immune function as they relate to DCM patients are unclear. [...] Immune factors* ***may*** *be important in the pathogenesis of DCM; however,* ***nonimmune genetically determined factors are also likely*** *to have a role in most patients with familial DCM. A post-viral infection autoimmune process* ***may*** *be a causative factor in DCM; however, auto-antibodies* ***may be markers of disease rather than the definitive aetiology****. Furthermore,* ***a 'virus-immune-theory' would explain less than half of the cases of DCM*** *(46, 47). Despite these confounding factors, evaluation of DCM patients should be vigorously pursued* ***to establish*** *the role, if any, of immune factors in the pathogenesis and progression of the disease."* (emphasis added).

65.4 The board observes that it is not stated expressly in any of documents E5 to E7 that autoantibodies are the

aetiologic agent of DCM and that DCM is therefore an autoimmune disease. This is understandable in view of the definition set out in point 65.1 above from which, in the board's view, it follows that the mere presence of autoantibodies in a patient suffering from a particular disease does not automatically imply that this disease is an autoimmune disease. It moreover seems that the authors of documents E5 to E7 avoid being too assertive as to the autoimmune aetiology of DCM because they use for example terms and expressions such as "*have been proposed*", "*lends strong evidence*", "*supports the idea*", "*may*" or "*indicates*". The authors on the other hand clearly state for example that a direct pathogenic role of the antibodies "*remains to be established*", that the role of immune factors in the pathogenesis of DCM "*remains uncertain*" and that there are "*conflicting results*". Moreover, the authors allude to the possibility that DCM has no autoimmune aetiology at all when they suggest that a post-viral infection autoimmune process may be a causative factor in DCM or that the auto-antibodies may be markers of the disease.

66. In the light of the observations in point 65.4 above the board cannot come to the conclusion that documents E5 to E7, either alone or in combination, establish that at the priority date of the disputed patent DCM was considered to be an autoimmune disease. Consequently, the skilled person would not have considered that the treatment of DCM was implicitly disclosed in any of documents E8 and E9 and therefore these documents cannot be considered to be related to the purpose of the present invention, the treatment of patients suffering from DCM.

67. The same is true of document E12, considered by the opposition division to represent the closest prior art because, as observed above in points 51 to 57, document E12 does not disclose the "treatment" of DCM, but the *in vitro* removal of autoantibodies from sera.

*Problem to be solved and its solution*

68. Starting from the disclosure in document E4 as representing the closest prior art document the problem to be solved by the claimed subject-matter is the provision of a further treatment for DCM.

69. According to claim 1 the solution to this problem is the use of a specific ligand for human immunoglobulin coupled to a column for removing "a significant portion of the immunoglobulin" from a patient's plasma which is thereafter re-infused.

The removal of "a significant portion of the immunoglobulin" has the effect of also removing autoantibodies against cardiac tissue: *"It is postulated that the removal of these autoantibodies is the basis of the efficacy of the IA* [immunoapheresis] *treatment of patients with* [dilated] *cardiomyophathy."* (paragraph [0003] of the patent).

Depending on the nature of the specific ligand the intended removal of the autoantibodies is more or less specific. According to claim 2 the use as a ligand of, for example, "polyclonal anti-human immunoglobulin antibodies" or "protein A" implies the removal of antibodies of all classes or specific classes of antibodies, respectively, *inter alia* autoantibodies of

these classes. The use according to claims 5 and 6 of a ligand which is defined as a peptide mimicking the structure of the ß1-adrenergic receptor, implies the specific removal of autoantibodies directed to the ß1-adrenergic receptor.

70. In view of the results disclosed on pages 9 to 11 of the description of the disputed patent the board is satisfied that the problem can be considered as being solved by the claimed subject-matter.

*Obviousness*

71. It needs to be determined whether or not the skilled person, when starting from the closest prior art, would have been motivated to provide the claimed subject-matter as a solution to the problem to be solved. A skilled person is considered to be motivated to provide claimed subject-matter if tangible reasons exist on the basis of which he or she would expect that the claimed subject-matter solves the problem, i.e. if the skilled person has a reasonable expectation of success. In contrast, a mere hope to succeed would not be sufficiently motivating (Case Law of the Boards of Appeal, 6th edition 2010, I.D.6, in particular paragraphs 1 to 3).

72. Document E4 - and also document E5 (see point 65.2 above), both published in 1994 - disclose *in vitro* experiments showing that the sera of DCM patients contain autoantibodies to the ß1-adrenergic receptor which have a positive chronotrophic effect on cultured rat cardiomyocytes. It is not explained, nor would it seem evident to the skilled person on the basis of his

or her common general knowledge, how this effect could be the cause of DCM (see points 63, 65.1 and 65.4 above). Therefore, the disclosure in these documents would not give the skilled person any reason to expect that the removal of these antibodies would constitute a successful "treatment" of DCM.

73. Documents E6 and E7 do not establish that DCM is an autoimmune disease (see points 65.2 to 65.4 above) nor do they provide the skilled person with any other suggestion how the removal of cardiac autoantibodies would influence the pathogenesis of DCM.

74. For the reasons given in points 64 to 66 above documents E8 and E9 are not relevant for the assessment of the obviousness of the claimed subject-matter and nor is document E10 because it also only refers to autoimmune diseases in general without mentioning DCM.

75. The board concludes on the basis of its observations in points 53 to 57 above that the disclosure in document E12 as regards the treatment DCM-affected patients by the removal of immunoglobulin from their blood is speculative disclosure and would therefore at best give the skilled person a hope to succeed when following the suggestion in that document.

76. Hence, the board cannot come the conclusion that the disclosure in any of the documents referred to by the appellant-opponent would have given the skilled person the perception to succeed in achieving a therapeutic effect when treating a patient suffering from DCM by the removal of a significant portion of immunoglobulin and thereby of *inter alia* relevant autoantibodies. Thus,

the skilled person would not have been motivated to provide the claimed subject-matter as a solution to the underlying problem. Hence, as the opposition division, the board considers that the claimed subject-matter is not obvious.

77. The subject-matter of claim 1 and its dependent claims 2 to 8 therefore involves an inventive step and thus complies with the requirements of Article 56 EPC.

**Order**

**For these reasons it is decided that:**

The appeals of both appellants are dismissed.

The Registrar: The Chairman:

P. Cremona C. Rennie-Smith