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Datasheet for the decision of 17 March 2023

Case Number: T 0468/20 - 3.3.08

Application Number: 16172486.9

Publication Number: 3085786

IPC: C12N15/115, A61K31/7088, A61M1/36, G01N33/564, G01N33/68

Language of the proceedings: EN

Title of invention:
USE OF APTAMERS IN THERAPY AND/OR DIAGNOSIS OF AUTOIMMUNE DISEASES

Applicant:
Charité - Universitätsmedizin Berlin
MAX-DELBRÜCK-CENTRUM FÜR MOLEKULARE MEDIZIN

Headword:
Aptamers for use in therapy of autoimmune diseases/CHARITÉ/MAX-DELBRÜCK-CENTRUM FÜR MOLEKULARE MEDIZIN

Relevant legal provisions:
EPC Art. 54(5), 84, 111(1)
RPBA 2020 Art. 13(2), 11

Keyword:
Main request and auxiliary requests 1 and 2 - lack of clarity (yes)
Auxiliary request 3 - lack of clarity (no)
Amendment after summons - exceptional circumstances (yes)
Remittal - (yes)

Decisions cited:
G 0005/83, G 0002/08, T 2003/08

Catchword:
No protection according to Article 54(5) EPC for a device

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Case Number: T 0468/20 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 17 March 2023

Appellant: (Applicant 1)	Charité - Universitätsmedizin Berlin Charitéplatz 1 10117 Berlin (DE)
Appellant: (Applicant 2)	MAX-DELBRÜCK-CENTRUM FÜR MOLEKULARE MEDIZIN Robert-Rössle-Strasse 10 13092 Berlin (DE)
Representative:	Klöckner, Christoph df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte PartG mbB Theatinerstraße 16 80333 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 4 October 2019 refusing European patent application No. 16172486.9 pursuant to Article 97(2) EPC**

Composition of the Board:

Chairwoman	T. Sommerfeld
Members:	D. Pilat
	A. Bacchin

Summary of Facts and Submissions

I. European patent application 16 172 486.9, published as EP 3 085 786, is a divisional application of the earlier European patent application No. 12 711 799.2 (EP 2 683 826) (hereinafter "the parent application") filed under the Patent Cooperation Treaty and published as WO 2012/119938.

II. The examining division decided that the subject matter of the claims according to the main request and to auxiliary requests 1 and 2 lacked clarity (Article 84 EPC) and that auxiliary requests 3 and 4 lacked unity of invention (Article 82 EPC). The application was refused.

III. The applicant (appellant) lodged an appeal and requested that the decision under appeal be set aside. It requested that a patent be granted on the basis of the claims of the main request or alternatively on the basis of the claims of any one of the first to seventh auxiliary requests filed with the statement of grounds of appeal and that the case be remitted to the examining division for further examination should the appealed decision be set aside.

IV. In a communication under Article 15(1) RPBA, the appellant was informed of the board's provisional opinion on the issues of the case.

V. In reply thereto, the appellant filed new claim requests, as eighth to sixteenth auxiliary requests.

VI. At the oral proceedings before the board, the appellant renamed the eighth auxiliary request as main request,

the ninth and twelfth auxiliary request as auxiliary requests 1 and 2, and filed a new request as sixteenth auxiliary request which was then renamed as auxiliary request 3. All other pending requests were withdrawn.

VII. Independent claims 1 and 8 of the main request read as follows:

"1. Aptamer comprising a nucleic acid sequence of SEQ ID No. 1, SEQ ID No. 2, SEQ ID No. 3 and/or a nucleic acid sequence being at least 80% identical to one of SEQ ID No. 1, 2 and 3 for use in therapy of autoimmune diseases by interfering with the interaction of autoantibodies specific for G-protein coupled receptors associated with autoimmune diseases, wherein the autoimmune disease is associated with the presence of autoantibodies specific for a G-protein coupled receptor.

8. Apheresis column comprising an aptamer according to one of claims 1 to 6 for use in therapy of an autoimmune disease, wherein the autoimmune disease is associated with the presence of autoantibodies specific for a G-protein coupled receptor, and wherein the autoantibodies are present in the serum of a patient suffering from said autoimmune disease, wherein the apheresis column is for use in apheresis as a medical technology in which the blood of a patient is passed through an apparatus that separates out one particular constituent and returns the remainder back to the circulation of the patient."

VIII. Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the amendment "... wherein the autoantibodies are specific for adrenergic alpha-1 receptor, adrenergic beta-1 receptor, adrenergic beta-2

receptor, endothelin 1 ETA receptor, muscarinic M2 receptor, angiotensin II AT1 receptor, and/or PAR receptors, and inhibiting the specific interaction of these autoantibodies with their target proteins, ..." was introduced between the clauses "associated with autoimmune diseases" and "wherein the autoimmune disease is associated with the presence of autoantibodies specific for a G-protein coupled receptor".

Claim 8 of auxiliary request 1 differs from claim 8 of the main request in that the amendment "... wherein the autoantibodies are specific for adrenergic alpha-1 receptor, adrenergic beta-1 receptor, adrenergic beta-2 receptor, endothelin 1 ETA receptor, muscarinic M2 receptor, angiotensin II AT1 receptor, and/or PAR receptors, ..." was introduced between the clauses "specific for a G-protein coupled receptor" and "and wherein the autoantibodies are present".

IX. In auxiliary request 2 claim 1 is identical to claim 1 of the main request, while claims 7 and 8 of the main request were deleted.

X. In auxiliary request 3 claim 1 is identical to claim 1 of auxiliary request 1, while claims 7 and 8 of the main request were deleted.

XI. The arguments of the appellant, insofar as relevant to the decision, may be summarised as follows:

Based on the common understanding conveyed by the excerpt from the Cambridge Dictionary, the skilled person, with a mind willing to understand, would have interpreted the term "by interfering with the interaction of autoantibodies specific for G-protein

coupled receptors" to mean disturbing, impairing, inhibiting and the like, the interaction of GPCR autoantibodies with their target GPCR.

Claim 8 could be interpreted either as second medical use claim or as product suitable for use claim, and both interpretations were clear. If claim 8 was considered to relate to a medical device, then decision T 2003/08, reasons 18 and 19, albeit referring to a Swiss type claim, were directly applicable to the purpose-limited formulation of present claim 8. If claim 8 was interpreted as being a product claim *per se* and not as a second medical use claim according to Article 54(5) EPC, then the product had to be construed as being at least suitable for the specific use of claim 8, i.e. medical apheresis.

XII. At the end of the oral proceedings, the appellant (applicant) requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request, filed as eighth auxiliary request with letter dated 16 February 2023; or alternatively on the basis of the claims of auxiliary requests 1 or 2, filed as ninth and twelfth auxiliary requests respectively, with letter dated 16 February 2023, or on the basis of the claims of auxiliary request 3, filed as sixteenth auxiliary request during the oral proceedings held on 17 March 2023. Further the appellant requested that the case be remitted to the examining division for further prosecution, if the board decided to set aside the appealed decision.

Reasons for the Decision

Admittance of the main request and auxiliary requests 1 to 3 (Article 13(2) RPBA)

1. The main request and auxiliary requests 1 to 3 were filed after the notification of the summons to oral proceedings and/or during the oral proceedings before the board and are thus in principle not to be taken into account unless there are exceptional circumstances, which have been justified by cogent reasons (Article 13(2) RPBA). The amendments introduced into the claims requests were made in reaction to issues concerning lack of clarity raised for the first time by the board in its communication under Article 15(1) RBPA. It is thus considered that there were exceptional circumstances justifying the admittance of amended claims at a late stage of the proceedings. The amendments to the claims *prima facie* overcome the objections made by the board and do not give rise to new objections. The board, exercising its discretion under Article 13(2) RPBA, thus decided to admit the main request and auxiliary requests 1 to 3 into the proceedings.

Main request - Article 84 EPC

Claim 1

2. In the decision under appeal, the examining division raised a clarity objection against the feature "wherein the autoimmune disease is associated with the presence of autoantibodies specific for a G-protein coupled receptor" of claim 1 because this group of functionally defined diseases could not be clearly identified.

3. The board disagrees with this finding. Claim 1 defines the group of diseases to be treated as being those autoimmune diseases wherein the autoantibodies are specific for a G-protein coupled receptor. While no specific autoimmune diseases are identified in claim 1, the skilled person would know how to determine whether a given disease belongs to the claimed group or not: in fact, the skilled person would only have to first determine whether the disease was autoimmune, i.e. if autoantibodies were present in the patient's serum and second, whether these autoantibodies were directed to a G-protein coupled receptor or not. Thus, the board considers that this feature is clear and that the group of diseases to be treated according to claim 1 is clearly defined.

4. The board however considers that the feature "by interfering with the interaction of autoantibodies..." is unclear because it is not apparent what "interfering with" should mean and which interaction is actually meant.

5. The appellant considered that this term was clear based on the definition provided in the excerpt from the Cambridge Dictionary. The first part of the clause "interfering with" meant disturbing, impairing, inhibiting and the like, but could not mean enhancing. The second part of the clause referred to an "interaction of autoantibodies specific for G-protein coupled receptors associated with autoimmune diseases", which would be interpreted by the skilled person as referring to the interaction of GPCR autoantibodies with their GPCR target.

6. The board considers that even if, based on the definition provided by the Cambridge Dictionary, the

first part of the clause "interfering with" means disturbing, impairing, inhibiting and the like, it remains a relative term. The skilled person cannot clearly decide at which point an interaction is disturbed, impaired, or inhibited and at which point it is not yet the case. Neither the patent nor the general knowledge indicate which experimental conditions must be used to test this activity. As many different equally valid interpretations can be attributed to the term "interfering with", the skilled person cannot clearly establish what falls under this definition and determine whether an aptamer falls within the scope of protection of claim 1 or not. The subject-matter of claim 1 lacks clarity.

Claim 8

7. The board considers that the apheresis column of claim 8 cannot be considered as a "substance or composition" within the meaning of Article 54(5) EPC. According to this provision the patentability of any *substance or composition*, comprised in the state of the art, for any specific use in a medical method referred to in Article 53(c) EPC is not excluded, provided that such use is not comprised in the state of the art. This special form of protection is thus limited to certain products, i.e. medical substances and compositions, for specified new (and inventive) therapeutic or other medical applications. A therapeutic effect must be achieved by the substance or composition. The wording used in claim 8 however casts doubt on the claim's category and thus on its scope of protection. In fact, as agreed by the appellant, claim 8 can be interpreted as either relating to a product claim suitable for use in therapy or to a purpose-limited product claim whose therapeutic effect must be taken into account under Article 54(5)

EPC. Thus, claim 8 is ambiguous and open to interpretation.

8. Appellant contended that claim 8 was a purpose-limited product claim in line with Article 54(5) EPC. The aptamer referred to in claim 8 was clearly the substance by which the therapeutic effect within the meaning of decision G 5/83 was achieved, whereas the "apharesis column" was not instrumental in achieving the therapeutic effect but was only the carrier for the ligand. Thus, reasons 18 and 19 of decision T 2003/08 were applicable to the wording of claim 8, which related to an apheresis column comprising an aptamer, even if this decision was based on a so-called Swiss-type claim (Case Law of the Boards of Appeal of the European Patent Office 10th edition 2022, Chapter I.C. 7.2.4 g)).

9. Claim 1 underlying decision T 2003/08 was directed to the "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...". Thus, this claim clearly related to the use of a substance or composition (the specific ligand for human immunoglobulin) for the manufacture of a medicament (in the form of a column having said ligand coupled thereto) for a specified new and inventive therapeutic application, a so-called Swiss-type claim according to Article 54(5) EPC 1973 (Decision G 5/83, point 23 of the reasons). The therapeutic effect on which the treatment of claim 1 was based, i.e. the removal of immunoglobulin from the plasma of patients suffering from DCM, was achieved by the specific ligand, for which the column merely served as a carrier.

10. Present claim 8 is directed to an "Apheresis column comprising an aptamer according to one of claims 1 to 6 for use in therapy of ...". In order to determine whether claim 8 is a second medical use type claim formulated in accordance to Article 54(5) EPC and G 2/08, OJ 2010, 456, or not, it is pivotal to establish whether or not (i) the means used in the treatment of the disease constitutes a "substance or composition" i.e. "chemical" substances or compositions and whether (ii) the means achieving the therapeutic effect is a "chemical" substance or composition within the meaning of decision G 5/83 (G 5/83 point 10 of the reasons and decision T 2003/08, points 14, 18, 19).

11. An apheresis column is clearly a device and neither a substance nor a composition. It is a carrier for the aptamer through which the therapeutic effect is actually achieved. The indication in claim 8 that the apheresis column comprises an aptamer according to claim 1 cannot alter the nature of the product - a device - for which protection is sought. Since the apheresis column is neither a substance nor a composition by which the therapeutic effect is achieved, the exception to the general novelty requirement which enables the applicant to obtain patent protection for a new therapeutic application of a known medicament under Article 54(5) EPC is not applicable. Nor does claim 8 conform with the wording used in decision T 2003/08 directed at the use of a substance in a so-called Swiss-type claim. Although claim 8 is drafted in a so-called purpose-related use formulation wherein the purpose is a medical use, since the product for which protection is sought is a device instead of a substance or composition, the scope of protection conferred by the purpose-related use formulation must be regarded as descriptive instead of

restrictive. As the category of claim 8 is ambiguous, the scope of protection cannot be determined with certainty. Therefore, claim 8 infringes the requirements of Article 84 EPC.

Auxiliary request 1 - Article 84 EPC

12. The amendments introduced into claim 8 of auxiliary request 1 do not overcome the ambiguity described above for claim 8 of the main request. The skilled person would not know whether the wording of claim 8 is a purpose-limited product claim in line with Article 54(5) EPC or a product defined by an intended use. Thus, the scope of protection of claim 8 is unclear, which is contrary to the requirements of Article 84 EPC.

Auxiliary request 2 - Article 84 EPC

13. Given that claim 1 of the main request and auxiliary request 2 are identical, auxiliary request 2 also infringes the requirements of Article 84 EPC for the reasons given above (points 4. to 6.).

Auxiliary request 3

14. Claim 1 of auxiliary request 3 is identical to claim 1 of auxiliary request 1, whereas claims 2 to 6 are identical to claims 2 to 6 of the main request. Claims 7 to 9 of the main request were deleted.

Clarity

15. The amendment in claim 1 clarifying that "interfering with the interaction of autoantibodies..." means "inhibiting the specific interaction of these

autoantibodies with their target proteins" overcomes the clarity objection raised against claim 1 of the main request (see above, points 2. and 3.). A further amendment to claim 1 in relation to claim 1 present in the requests decided upon by the examining division is the deletion of the feature "wherein the aptamer binds specifically and with high affinity to said autoantibodies". This amendment successfully overcomes a clarity objection raised by the board in its communication pursuant to Article 15(1) RPBA (point 7., second paragraph on page 4 to first paragraph on page 5).

16. The amendment in claim 2 clarifying that "the selective ingredient is responsible for specifically separating out the autoantibodies present in blood which are specifically targeted by the aptamer" overcomes the clarity objection raised by the board in its communication pursuant to Article 15(1) RPBA, point 7., fourth paragraph on page5.

17. The amendment "according to any one of claims ... for use according to..." in dependent claims 3 to 6 overcomes a further clarity objection raised by the board in its communication pursuant to Article 15(1) RPBA, point 7., last paragraph on page 5.

18. Finally, claims 7 to 9 have been deleted and therefore the clarity objection raised against claim 8 of the main request has been overcome (see above, point 7.).

19. Auxiliary request 3 thus meets the requirements of Article 84 EPC.

Further remarks

20. Deletion of claims 7 to 9 also overcomes the objection for lack of unity of invention raised by the examining division, since it was claim 9 of the then auxiliary requests 3 and 4 (claim 8 of present main request) which, by not being restricted to a medical use but rather directed to the product as such, was considered to relate to an invention that was not unitary with the invention as defined in the other claims.

21. The amendments made to claims 1 and 2 of auxiliary request 3 have a basis, respectively, in paragraphs [0010] and [0056], of the patent application and in the corresponding passages of the parent application (page 3, second paragraph and page 13, third paragraph, respectively). The requirements of Article 123(2) EPC and Article 76(1) EPC are thus also fulfilled.

Remittal to the examining division for further prosecution (Article 111(1) EPC and Article 11 RPBA)

22. Under Article 111(1), second sentence, EPC the board may either decide on the appeal or remit the case to the department which was responsible for the decision appealed. The appropriateness of remittal to the department of first instance is a matter for decision by the board, which assesses each case on its merits. Even if there is no absolute right to have every issue decided upon by two instances (cf. Article 11, first sentence, RPBA, which requires special reasons for remitting a case), it has to be emphasized that it is the primary object of the appeal proceedings to review the decision under appeal in a judicial manner (Article 12(2) RPBA).

23. In point 7.1. of the board's communication under Article 15(1) RPBA, the appellant was informed that the

board intended to grant the request for remittal if it decided to set aside the appealed decision.

24. In view of the fact that the appealed decision was only based on Articles 84 and 82 EPC, and that the findings of the examining division on those issues have been reversed in the present proceedings, special reasons present themselves for remitting the case to the first instance for further examination (Article 11 RPBA).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division for further prosecution.

The Registrar: The Chairwoman:

L. Malécot-Grob T. Sommerfeld

Decision electronically authenticated