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Case Number: W 0034/08 - 3.3.04

Application Number: PCT/DK 2006/000686

Publication Number: WO 2007/065433

IPC: C07K 16/08

Language of the proceedings: EN

Title of invention:
Anti-Orhopoxovirus recombinant polyclonal antibody

Applicant:
Symphogen A/S

Headword:
Polyclonal antibody/SYMPHOGEN

Relevant legal provisions:
PCT Art. 34(3)(a)
PCT R. 13.1, 13.2, 13.3, 40.2, 68.2, 68.3(c)

Keyword:
"Lack of unity a posteriori (inventions 1 and 2) - (no)"

Decisions cited:
G 0001/89, W 0013/87

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: W 0034/08 - 3.3.04

International Application No. PCT/DK 2006/000686

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 5 May 2009

Applicant: Symphogen A/S
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Decision under appeal: **Protest according to Rule 68.3(c) of the Patent Cooperation Treaty made by the applicants against the invitation of the European Patent Office (International Preliminary Examining Authority) to restrict the claims or pay additional fees dated 18 March 2008.**

Composition of the Board:

Chair: U. Kinkeldey
Members: M. Wieser
T. Bokor

Summary of Facts and Submissions

I. International patent application no. PCT/DK2006/000686 having the title "Anti-Orthopoxovirus recombinant polyclonal antibody" was filed on 4 December 2006 with thirty-three claims.

With letter dated 22 January 2008 the Applicant filed an amended set of claims 1 to 32 which should be the subject of the International Preliminary Examination according to the PCT.

Claims 1 and 22 read as follows:

"1. An anti-orthopoxovirus recombinant polyclonal antibody comprising distinct members which in union are capable of binding at least three orthopoxovirus related antigens wherein at least two distinct epitopes on the same orthopoxovirus related antigen are bound by said polyclonal antibody.

22. A screening procedure for selecting V_H and V_L sequence pairs capable of encoding a broad diversity of anti-orthopoxovirus antibodies comprising:

a. expressing an antibody or antibody fragment from a host cell transfected with a screening vector comprising a distinct member of the repertoire of V_H and V_L coding pairs,

b. contacting said antibody or antibody fragment with at least two different vaccinia virus strains and one or more of the following antigens A27L, A17L, D8L, H3L, L1R, A33R, B5R and VCP in parallel,

c. repeating step a) and b) for each V_H and V_L sequence pair in the repertoire of sequence pairs.

d. selecting the V_H and V_L sequence pairs encoding an antibody or antibody fragment which bind to at least one of the vaccinia virus strains and at least one of the antigens."

II. On 18 March 2008, the European Patent Office (EPO) acting as International Preliminary Examining Authority (IPEA) issued to the Applicant an invitation as set forth in Article 34(3)(a) and Rule 68.2 PCT to restrict the claims or to pay one additional examination fee because it considered that the subject-matter which had been searched did not comply with the requirement of unity of invention (Rule 13.1, 13.2 and 13.3 PCT). It indicated that this subject-matter related to two inventions claimed in the following two groups of claims:

Invention 1: claims 1-21, 25-32
anti-orthopoxovirus recombinant polyclonal antibody.

Invention 2: claims 22-24
screening procedure for selecting V_H and V_L sequence pairs capable of encoding a broad diversity of anti-orthopoxovirus antibodies.

III. The IPEA referred to the following prior art documents:

D1 Expert Opin. Biol. Ther., vol.4, no3, 2004, pages 387 to 396

D2 IDrugs, vol.5, no.8, 2005, pages pages 404 to 409

D3 WO 2005/042 774

D4 Journal of General Virology, vol.83, 2002, pages 1059 to 1067

D5 Journal of Virology, vol.77, no.15, 2003, pages 8256 to 8262

D6 Biochemistry and Biophysics, vol.382, 2002, pages 10 to 12

D7 Virology, vol.258, 1999, pages 189 to 200

IV. As regarded claim groups 1 and 2 listed above, the IPEA argued that the common inventive concept underlying the claims could be seen in the provision of a recombinant polyclonal anti-orthopoxovirus antibody. However, "[b]ased on the teaching of D1 and D2 it has to be concluded that the concept of the provision of a polyclonal and polyvalent anti-orthopoxovirus antibody which targets several antigens was already known and, thus, a general inventive concept is lacking in the present application." (see page 2 of the annex to the IPEA's invitation to restrict or to pay additional fees of 18 March 2008).

The IPEA held that unity between the claims of inventions 1 and 2 was lacking as claim 22 merely described a method to find an antibody which binds at

least one vaccinia virus strain and at least one vaccinia virus antigen, but not a polyclonal antibody.

Moreover, the concept underlying invention 2 (claim 22), which was found to be the provision of a method for screening for single antibodies specific for vaccinia, was considered to be "reflected" in prior art document D7 (page 3 of the annex).

Finally, the IPEA defined the technical problem underlying the present application as being the provision of "... further antibodies to treat orthopoxovirus infections."

The solutions to this problem according to inventions 1 and 2 described in claims 1 to 32 were considered to be different from each other. In the absence of any further common technical feature which could be suitable to link the claimed subject-matter together as required by Rule 13.2 PCT the requirement for unity of invention referred to in Rule 13.1 PCT was not fulfilled (page 4 of the annex).

V. With response of 14 April 2008, the Applicant paid under protest one additional examination fee. He presented arguments that the inventions identified as 1 to 2 (see Section II supra) were unitary. As an auxiliary measure he requested, in case the IPEA should not agree that unity existed, that the examination of the invention as defined in claims 22 to 24, did not justify charging an additional examination fee, as it did not require any additional effort. As second auxiliary request he requested the Board of Appeal to

decide that the IPEA's invitation to restrict or to pay additional fees, to be insufficiently reasoned.

VI. With a communication dated 21 August 2008, a review board within the meaning of Rule 68.3(c) PCT confirmed the IPEA's opinion regarding lack of unity.

VII. On 19 September 2008 the Applicant paid the protest fee and presented further arguments. He requested reimbursement of the additional examination fee.

Reasons for the decision

1. The application was filed on 4 December 2006. Therefore, the protest is subject to the provisions of the PCT as in force from 1 April 2006. The Boards of Appeal are responsible for deciding on protests relating to PCT application pending at the time of entry into force of the EPC 2000 (13 December 2007). Details of the procedure are guided by the Decision of the President of the EPO dated 24 June 2007, Article 3 (OJ EPO 2007, Special edition No. 3, 140).

2. The protest fee has been paid in time and the protest contains a reasoned statement why the inventions for which the additional search fees have been paid should fulfil the requirement of unity. Accordingly, the protest was properly made and it is admissible (Rule 40.2 (c) and (e) PCT).

3. According to Rule 13.1 PCT, the international patent application shall relate to one invention only or to a group of inventions so linked as to form a single

inventive concept. If the IPEA considers that the claims lack this unity, it is empowered, under Article 34(3) and Rule 68.2 PCT, to invite the Applicant to pay additional fees.

4. Lack of unity may be directly evident *a priori*, i.e. before the examination of the merits of the claims in comparison with the state of the art revealed by the search (cf., for example, decision W 13/87 of 9 August 1988). Alternatively, having regard to decision G 1/89 of the Enlarged Board of Appeal (EBA), dated 2 May 1990 (OJ EPO 1991, 155), the ISA is also empowered to raise an objection *a posteriori*, i.e. after having taken the prior art revealed by the search into closer consideration. This practice is laid down in the PCT Search Guidelines, Chapter VII,9 (PCT Gazette 30/1992) which are the basis for a uniform practice of all International Searching Authorities. The Enlarged Board of Appeal indicated that such consideration represents only a provisional opinion on novelty and inventive step which is in no way binding upon the authorities subsequently responsible for the substantive examination of the application (point 8.1. of the Reasons for the decision). In point 8.2 of the Reasons, the EBA mentioned that such invitation to pay additional fees should always be made "with a view to giving the Applicant fair treatment" and should only be made in clear cases. This approach, developed by the EBA in view of objections to unity of the invention issued by the ISA is equally applicable to objections to unity by the IPEA.

5. The IPEA has based its finding of lack of unity upon an *a posteriori* consideration. They found that the common

inventive concept underlying the claims could be seen in the provision of a recombinant polyclonal anti-orthopoxovirus antibody. However, "[b]ased on the teaching of D1 and D2 it has to be concluded that the concept of the provision of a polyclonal and polyvalent anti-orthopoxovirus antibody which targets several antigens was already known and, thus, a general inventive concept is lacking in the present application."

6. However, in the Board's judgement, the disclosure in documents D1 and D2 of recombinant polyclonal anti-orthopoxovirus antibodies, which is not disputed by the Applicant, has no effect upon the novelty of the subject-matter of claim 1 which refers to a recombinant polyclonal anti-orthopoxovirus antibody comprising distinct members which in union are capable of binding a least three orthopoxovirus related antigens wherein at least two distinct epitopes on the same orthopoxovirus related antigen are bound by said polyclonal antibody. Such antibody is not disclosed in document D1 or in document D2.

7. Therefore, the Board disagrees with the IPEA that the technical problem underlying the claimed subject-matter lies in the provision of "further antibodies to treat orthopoxovirus infections".

8. In the light of the disclosure in document D1 or D2, which likewise are considered to represent the closest state of the art for the subject-matter of the claims that have been defined by the IPEA as invention 1 (see section II above), the problem to be solved is seen in the provision of recombinant polyclonal anti-

orthopoxovirus antibodies with higher complexity and improved potency.

This problem has been solved according to claim 1 by providing a recombinant polyclonal antibody targeting at least three antigens and at least two epitopes on the same antigen.

Whether or not the IPEA considered this solution according to claim 1 as involving an inventive step cannot be derived from the invitation to restrict or pay additional fees.

9. With regard to claims 22-24 (defined by the IPEA as invention 2), the IPEA argued that they merely referred to a method for finding an antibody which binds at least one vaccinia virus strain and at least one vaccinia virus antigen, wherein epitope found on the virus and on the antigen may be identical, but not to a method for finding a polyclonal antibody.

The concept of the method of claim 22 was moreover "reflected" by the disclosure in document D7.

10. Claim 22 refers to a screening procedure for selecting V_H and V_L sequence pairs capable of encoding a broad diversity of anti-orthopoxovirus antibodies. After the expression of an antibody or antibody fragment from a host cell transfected with a vector comprising the coding sequence for a distinct V_H and V_L pair (claim 22, step a), the antibody or antibody fragment is contacted with at least two different vaccinia virus strains and with one or more of eight distinct vaccinia virus antigens (claim 22, step b). Steps a and b are repeated

for different V_H and V_L sequence pairs (step c) and sequence pairs encoding an antibody or antibody fragment which binds to at last one of the vaccinia virus strains and at least one of the antigens are selected.

11. The Board notes that the "concept underlying invention 2" (claims 22 to 24) is not "reflected" by the disclosure in document D7, as stated by the IPEA on page 3 of the annex to the invitation to restrict or pay additional fees. Document D7, which is concerned with the production and characterization of human mAb Fab fragments to Vaccinia virus from a phage-display combinatorial library, clearly states that the Fab fragments have not been tested for binding against known Vaccinia virus antigens (see D7, page 195, left column, second paragraph).

12. The IPEA argues that the screening procedure of claim 22 describes a method which merely allows to find a single antibody binding to at least one vaccinia virus strain and at least one vaccinia virus antigen, wherein the antibody may recognize the identical epitope on the virus and on the antigen. According to the IPEA, the method of claim 22 (invention 2) does not allow to find an anti-orthopoxovirus recombinant polyclonal antibody according to claim 1 (invention 1).

13. The Board agrees that the method of claim 22 will result in the identification of single antibodies having specific, but different binding characteristics. However, this will result in the selection of different antibodies with a broad spectrum of reactivity. Such

antibodies can be combined to design a recombinant polyclonal antibody according to claim 1.

14. The decisive question for the purpose of the present invention, namely, is there a **special technical feature** that defines a contribution which each of the claimed inventions makes over the prior art (Rule 13.2 PCT), has therefore to be answered in the affirmative.

The subject-matter of both groups of claims, defined by the IPEA as invention 1 and invention 2, refers to the provision of recombinant polyclonal anti-orthopoxovirus antibodies with higher complexity and improved potency.

The antibodies of claim 1, which may be prepared by the method of claims 22 to 24, are characterised by **targeting at least three antigens and at least two epitopes on the same antigen.**

15. Therefore, the Board cannot follow the IPEA's reasoning, according to which the searched subject-matter (inventions 1 and 2) does not comply with the requirement of unity of invention. Hence, the invitation provided for in Article 34(3)(a) and Rules 68.2 and 68.3(e) PCT to pay one additional examination fee is not well founded and the inventions are considered as unitary.

Order

For these reasons, it is decided that:

1. The refund of one additional examination fee paid by the Applicant is ordered.

2. The protest fee shall be refunded.

Registrar: Chair:

P. Cremona U. Kinkeldey