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D E C I S I O N
of 28 August 2000

Case Number: T 0588/95 - 3.3.4

Application Number: 85102665.8

Publication Number: 0171496

IPC: C12N 15/00

Language of the proceedings: EN

Title of invention:

Process for the production of a chimera monoclonal antibody

Patentee:

Research Development Corporation of Japan

Opponents:

- (01) Celltech Limited
(02) Roche Diagnostics GmbH

Headword:

Chimera monoclonal antibody/RESEARCH DEVELOPMENT

Relevant legal provisions:

EPC Art. 84, 123(2),(3)

Keyword:

"Main request and auxiliary requests 1, 2 and 3 (broadening of the scope of protection: yes)"

Decisions cited:

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Catchword:



Case Number: T 0588/95 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 28 August 2000

Appellant: Research Development Corporation of Japan
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 30 May 1995
revoking European patent No. 0 171 496 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairwoman: U. M. Kinkeldey

Members: R. E. Gramaglia

C. Holtz

Summary of Facts and Submissions

I. The appeal is against the decision of the opposition division revoking European patent No. 0 171 496 (application No. 85 102 665.8), which had been opposed by the respondents (opponents 01 and 02) on the grounds of lack of novelty and inventive step, insufficiency of disclosure and added subject-matter. The patent had been granted on the basis of the two following claims:

"1. A production process of chimera monoclonal antibody consisting of a variable region derived from mouse and a constant region derived from man, which is characterized by comprising (a) inserting into an expression vector active genes: V_H and V_L isolated from hybridomas as antibody-producing cells of mouse and genes: C_H and C_L , isolated from human DNA, and then (b) introducing an expression vector from (a) into lymphoma as cultured animal cells."

"2. A production process of chimera monoclonal antibody according to claim 1, wherein said vector is pSV2-gpt, pSV2-neo or SV40."

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

(42) National Cancer Institute, Cancer, Vol. 49(10), pages 2112-2135 (1982);

(45) Harris N.L. et al., Blood, Vol. 84(5), pages 1361-1392 (1994).

III. The board issued a communication pursuant to Article 11(2) of the Procedure before the Boards of

Appeal expressing its provisional opinion.

- IV. Oral proceedings were held on 28 August 2000, during which the appellant filed a new main request and auxiliary requests 1, 2 and 3 in replacement of any preceding claim request.

The claims of the main request read as follows (the changes vis-à-vis granted claims 1 and 2 are shown by way of deletions and in bold):

"1. A production process of chimera monoclonal antibody consisting of a variable region derived from mouse and a constant region derived from man, which is characterized by comprising (a) inserting into an expression vectors **active genes** V_H and V_L isolated from **mouse hybridomas as antibody-producing cells of mouse** and genes C_H and C_L , isolated from human DNA, and then (b) introducing an **both** expression vectors from (a) into **a single mouse lymphoma plasmacytoma** as cultured animal cells."

"2. A production process of chimera monoclonal antibody according to claim 1, wherein said vectors **is are** pSV2-gpt, pSV2-neo or SV40."

The claims of auxiliary request 1 read as follows:

"1. **Use of an expression vector comprising either active gene V_L isolated from mouse hybridomas and gene C_L isolated from human DNA or active gene V_H isolated from mouse hybridomas and gene C_H isolated from human DNA for the co-transformation of a mouse plasmacytoma cell for the production of a chimeric monoclonal**

antibody."

"2. Use of claim 1, wherein said vector is pSV2-gpt, pSV2-neo or SV40."

The sole claim of auxiliary request 2 read as follows:

"1. Use of the plasmids pSV2-HC_kV_{D10} and pSV2-HG1V_{D10} as depicted in Fig. 2 of the description for the transformation of a mouse plasmacytoma cell for the production of chimeric monoclonal antibodies."

The sole claim of auxiliary request 3 read as follows:

"1. Use of the plasmids pSV2-HC_kV_{D10} and pSV2-HG1V_{D10} as depicted in Fig. 2 of the description for the transformation of mouse plasmacytoma cell P3U1 for the production of chimeric monoclonal antibodies."

V. The arguments submitted by the appellant were essentially as follows:

(i) with respect to the main request:

Article 84 EPC

- The claims had been reformulated so as to make clear that the process for producing a chimera monoclonal antibody had to occur by transfection with two different vector plasmids to be introduced into a single plasmacytoma.

Article 123(2)(3) EPC

- The alternative of two expression vectors was already understood by the skilled person to be comprised in claim 1 as granted and as exemplified.
- The term plasmacytoma was to be found on page 9, lines 21 and 24 of the application as filed.
- Replacement of the term "lymphoma" in granted claim 1 by "plasmacytoma" as in claim 1 of the main request did not broaden the scope of the claims, since a plasmacytoma cell was known at the priority date of the patent in suit to be one type of lymphoma cell. This was shown inter alia by documents (42) and (45).
- There was thus no infringement of Article 123(2)(3) EPC.

(ii) with respect to auxiliary requests 1, 2 and 3:

Article 84 EPC

- The claims of auxiliary request 1 had been reformulated so as to make clear that use is made of two different vector plasmids, one comprising two genes C_H and V_H coding for the heavy chain and the other comprising two genes C_L and V_L coding for the light chain, to be both introduced into a single plasmacytoma. The transfecting plasmids in the claim of auxiliary request 2 had been restricted to plasmids pSV2-HC_kVD₁₀ and pSV2-HG1V₁₀ exemplified in the patent in suit. A further restriction had been effected in the claim of auxiliary request 3, namely the

cell to be transfected had to be mouse plasmacytoma cell P3U1.

Article 123(2)(3) EPC

- The embodiments of the claims of auxiliary requests 1, 2 and 3 found a basis in the example on page 5, line 15 to page 15, line 5 of the application as filed.
- According to claim 1 as granted, all four genes V_H , V_L , C_H and C_L had to go into a single cell. Therefore, the claimed alternatives were already understood by the skilled person to be comprised in claim 1 as granted and as exemplified. There was thus no infringement of Article 123(2)(3) EPC.

VI. The respondents essentially submitted the following arguments:

- (i) with respect to the main request:

Article 84 EPC

- The example of the patent in suit (see pages 3 to 4) disclosed the construction of a first plasmid comprising the heavy chains C_H and V_H and the construction of a second plasmid comprising the light chains C_L and V_L and the transfection of a plasmacytoma cell with both plasmids. The claims of the main request, however, covered a great many possibilities such as eg inserting of the DNA encoding the heavy chain and the light chain in the same plasmid. There was thus a lack

of support in the description for these embodiments.

Article 123(3) EPC

- Replacement of the term "lymphoma" in granted claim 1 by "plasmacytoma" as in claim 1 of the main request broadened the scope of the claims since lymphoma cells were a subgroup of plasmacytoma (myeloma) cells.
- Deletion of the expression "as antibody-producing cells of mouse" from granted claim 1 infringed Article 123(3) EPC.
- According to the process of granted claim 1, all the four genes had to be inserted in one single vector, while in claim 1 of the main request use was made of two vectors. There was thus an unallowed amendment of the scope of the granted claims

(ii) with respect to auxiliary requests 1, 2 and 3:

Article 84 EPC

- These claims also lacked support in the description of the patent in suit.

Article 123(3) EPC

- As for the replacement of the term "lymphoma" in granted claim 1 by "plasmacytoma", the same objections applied as for the main request.

- Deletion of the expression "as antibody-producing cells of mouse" from granted claim 1 infringed Article 123(3) EPC, here as well.
- According to the process of granted claim 1, all the four genes had to be inserted in one single vector, while now use is made of two vectors.

VIII. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained on the basis of either the main request or auxiliary requests 1, 2 or 3, all filed in the oral proceedings.

The respondents (opponents) requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.

All requests

Article 84 EPC

2. While it is true, as the respondents argue, that the wording in claim 1 of the main request "(a) inserting into expression vectors active genes V_H and V_L isolated from mouse hybridomas and genes C_H and C_L , isolated from human DNA, and then (b) introducing both expression vectors from (a) into a single mouse plasmacytoma" covers many possible strategies for producing a chimera monoclonal antibody, this deficiency, if any, relates rather to the breadth of the claims but does not mean

that the claims are unclear in their technical meaning. Consequently, the claims of the main request meet the requirements of Article 84 EPC, as do the claims of auxiliary requests 1 to 3 for the same reason.

Article 123(3) EPC

3. The wording of claim 1 as granted makes it plain that the protection conferred covers a process for producing a chimera monoclonal antibody involving the use of a **single** expression vector including the four genes V_H, V_L, C_H and C_L for transforming the host cell. This view is supported by claim 2 as granted, which also refers to "said expression vector" in the singular and by the counterpart of granted claim 1 in the description (page 2, line 35), wherein the wording "inserting into **an** expression vector" (emphasis added) is to be found. However, claim 1 of the main request now covers a process in which use is made of **two** distinct expression vectors (cf "introducing **both** expression vectors"). The effect of this amendment is that the claims of the main request now cover a different process not comprised within the scope of protection of the granted claims, contrary to the requirements of Article 123(3) EPC. Therefore, the main request has to be refused. The appellant has argued that it was the implicit meaning of the disclosure as a whole that both vectors had to be introduced into the cell to be transformed. However, in the light of the clear wording as quoted above, the board is unable to accept that the skilled person would have unambiguously interpreted the disclosure in the way the appellant argues.

4. The conclusion arrived at by the board in relation to the main request extends to auxiliary request 1,

wherein the term "co-transformation" taken in the context of claim 1, necessarily implies the use of **two** distinct expression vectors for transforming the host cell for the production of a chimera monoclonal antibody, and to auxiliary requests 2 and 3, whose sole claim mentions expressis verbis the two distinct expressions vectors pSV2-HC_kVD₁₀ and pSV2-HG1V₁₀ to be used for the same purpose.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairwoman:

U. Bultmann

U. M. Kinkeldey