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D E C I S I O N
of 22 June 1998

Case Number: T 0498/94 - 3.3.4

Application Number: 81300047.8

Publication Number: 0033578

IPC: C12P 1/00

Language of the proceedings: EN

Title of invention:
Hybrid cell line for producing monoclonal antibody to a human T cell antigen, antibody, and methods

Patentee:
Ortho Pharmaceutical Corporation

Opponent:
Behringwerke Aktiengesellschaft
Novartis Patent- und Markenabteilung
Boehringer Mannheim GmbH Patentabteilung
Becton, Dickinson and Company
F. Hoffmann-La Roche & Co. Aktiengesellschaft

Headword:
Monoclonal antibody (OKT11)/ORTHO PHARMACEUTICAL CORPORATION

Relevant legal provisions:
EPC Art. 83

Keyword:
"Sufficiency of disclosure - (no)"
"Inventive step (no)"

Decisions cited:
T 0418/89, T 0495/89, T 0510/94

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0498/94 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 22 June 1998

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Decision under appeal:

Interlocutory decision of the Opposition Division of the European Patent Office posted 13 April 1994 concerning maintenance of European patent No. 0 033 578 in amended form.

Composition of the Board:

Chairwoman: U. M. Kinkeldey
Members: F. L. Davison-Brunel
S. C. Perryman

Summary of Facts and Submissions

I. European patent No. 0 033 578 with the title "Hybrid cell line for producing monoclonal antibody to a human T cell antigen, antibody, and methods" was granted with 19 claims based on European patent application No. 81 300 047.8.

II. Notices of opposition were filed by five parties. Revocation of the patent was requested on the grounds of Article 100(a) (lack of novelty, lack of inventive step) and 100(b) EPC (insufficiency of disclosure).

III. By a decision within the meaning of Article 106(3)EPC dated 13 April 1994, the Opposition Division maintained the patent in amended form according to Article 102(3) EPC on the basis of the auxiliary request filed during oral proceedings.

Claims 1, 7 and 9 were as granted except for the fact that the expression "(sig^-, E^- cells)" was added at the end of claim 1, and read as follows:

"1. Mouse monoclonal antibody which

(i) reacts with essentially all normal human peripheral T cells;

(ii) reacts with approximately 95% of normal human thymocytes; and

(iii) does not react with any of the normal human cells in the group comprising B cells and Null cells (sIg^-, E^- cells)."

"7. Mouse monoclonal antibody produced by hybridoma ATCC CRL 8027."

"9. Hybridoma ATCC CRL 8027 (OKT11)."

IV. The Opposition Division accepted sufficiency of disclosure. They decided that the growing of the deposited hybridoma did not amount to undue burden of experimentation. Furthermore, the experimental reports submitted by the Opponent to show that the monoclonal antibody (MAb) OKT11 had a different reactivity pattern with null cells from the one claimed, could not be taken into account as the null cells population had not been purified in the same manner as in the patent in suit. Finally, the reactivity pattern of antibodies different from OKT11 but recognising the same CD antigen could not serve to disprove the reactivity pattern of this last antibody.

V. The Appellants (Opponents 3) lodged an appeal against the decision of the Opposition Division, paid the appeal fee and filed the statement of grounds of appeal.

VI. The Respondents (Patentee) answered the Appellants submission.

VII. A communication was sent by the Board according to Article 11(2) EPC of the Rules of Procedure of the Boards of Appeal setting out the Board's provisional, non-binding opinion.

VIII. The Appellants sent a further submission accompanied by ten new documents. One of these documents will be referred to in the present decision:

(1): Talle M.A. et al., Blood, vol. 66, No. 5, 1985, pages 1124 to 1132.

IX. This submission was answered by the Respondents.

X. Oral proceedings were held on 22 June 1998, at which the Respondents had no representative in attendance.

XI. The submissions by the Appellants in writing and during oral proceedings insofar as they are relevant to the present decision are the following:

(a) The new documents were filed as a reaction to what seemed to be the Board's position at oral proceedings in the parallel case T 0510/94 of 21 April 1998 that a convincing way to challenge the claimed reactivity pattern of a monoclonal antibody was to submit evidence from published documents that this reactivity pattern was wrong. The filing of the documents had been done within the time limit set by the Board.

(b) One of the inventors of the patent in suit was coauthor of document (1). This document disclosed in Table 1 and Figure 3 that OKT11 reacted with about 40% of null cells and, consequently, did not conform to the claimed reactivity pattern. Thus, the facts of the case were analogous to those of the cases T 0418/89 (OJ EPO 1993, 20) and T 0495/89 (of 9 January 1991) where the patents were revoked for insufficiency of disclosure as the properties of the claimed specific antibodies did not correspond to those expected from the written description, as shown in later published scientific papers.

XII. The Respondents objected in writing to the new documents being allowed into the proceedings at so late a stage. Furthermore, they drew the Board's attention to the fact that all newly filed documents were dated after the priority date. As the art progressed, null

cells had been identified by the presence of specific CD clusters on their surface. This definition could not have applied at the priority or filing date because these clusters had not yet been identified. Any argument the Appellants tried to make based on a new definition of null cells had to be considered as irrelevant.

XIII. The Appellants (Opponents 3) requested that the decision under appeal be set aside and that the European patent No. 0 033 578 be revoked.

The Respondents (Patentee) requested that the appeal be dismissed.

Reasons for the Decision

Late filing of documents

1. One of the grounds for the appeal is that the requirements of Article 83 EPC are not fulfilled, more specifically, that the reactivity pattern with null cells of OKT11 as claimed in claim 7 and secreted by a hybridoma as claimed in claim 9 is different from that described in the patent specification and claim 1. The Appellants filed ten new documents in support of this ground of appeal only a month before the oral proceedings. It was explained that the necessity for filing them had only become evident after the proceedings in the parallel case T 510/94 of 21 April 1998 made it likely that they could have a determining influence on the Board's decision in this case.

2. The documents deal with the reactivity pattern of OKT11 with cell populations which prima facie fall within the group of null cells. Their potential relevance to the

assessment of whether OKT11 as deposited has the reactivity pattern defined in the patent specification cannot be ignored. The Board, thus, decides to admit them into the proceedings on the basis of Article 114(2) EPC.

Article 83 EPC (sufficiency of disclosure)

3. According to the patent specification Table 1, page 8, OKT11 does not react with E^- cells. These cells are isolated by E resetting the Ig^- subset of peripheral blood cells as described in Example II A. It can thus be said that OKT11 does not react with E^-, Ig^- cells, the E^-, Ig^- phenotype being defined on page 6, lines 36 and 37 as that of null cells.

4. In document (1) which was published inter alia by one of the inventors at a later date than the priority date of the patent in suit, the reactivity pattern of OKT11 was once more investigated. As in the patent in suit, the null cells are defined as E^-, Ig^- cells. The protocol for their isolation involves the same two biological steps as in Example II A. Thus, the objection by the Respondents that the reactivity pattern of OKT11 with null cells isolated by immunological means are not indicative of its reactivity pattern when it is isolated by biological means, does not apply to the results obtained in document (1).

5. The null cell population is said to contain less than 10 cells expressing the T3 antigen (T cells) which according to the patent in suit (E^+ cells, Table 1) would be expected to react with OKT11 and less than 20% of SmIg positive cells (B cells) which would not be expected to do so. Under these conditions, it is found that OKT11 reacts with 40% of null cells, subject to a standard deviation of 11%.

6. From these results the Board concludes that the later investigation of the claimed OKT11 carried out inter alia by one of the inventors shows a reactivity pattern with null cells which is different from that given in the patent specification and claim 1.

7. The Respondents who must have been aware of these data and of their possible consequences for sufficiency of disclosure of the patent in suit did not comment on them. The facts of this case are thus analogous to those in decisions T 0418/89 and T 0495/89 (see supra) where there also existed post-published documents from the inventors which contradicted the reactivity pattern of the then claimed OKT antibodies, and where the Respondents (Patentee) did not contest the differences in the characteristic features of said antibodies. In these earlier cases, sufficiency of disclosure was denied as "the Respondents themselves were not able to carry out the invention according to their own written disclosure" (T 0418/94, point 3.11 of the reasons). This conclusion equally applies to the present case. Neither the written description disclosing in general terms the features of the MAb of claim 1 nor the deposition of the hybridoma (claim 9) nor the MAb OKT11 (claim 7) secreted by the deposited hybridoma provides a sufficient disclosure within the meaning of Article 83 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. European patent No. 0 033 578 is revoked.

The Registrar: The Chairwoman:

A. Townend U. Kinkeldey