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D E C I S I O N
of 23 April 1998

Case Number: T 0513/94 - 3.3.4

Application Number: 80301357.2

Publication Number: 0018795

IPC: C12N 5/00

Language of the proceedings: EN

Title of invention:
Monoclonal-antibody-producing hybrid cell line, antibody and method of preparing it, therapeutic composition containing it and its diagnostic and therapeutic uses

Patentee:
Ortho Pharmaceutical Corporation

Opponent:
Behringwerke Aktiengesellschaft
Becton, Dickinson and Company
Novartis AG Patent- und Markenabteilung
Boehringer Mannheim GmbH Patentabteilung

Headword:
Monoclonal antibody (OKT3)/ORTHO PHARMACEUTICAL CORPORATION

Relevant legal provisions:
EPC Art. 123(2), 83, 56

Keyword:
"Sufficiency of disclosure (yes)"
"Inventive step (yes)"

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

Catchword:
-

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Case Number: T 0513/94 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 23 April 1998

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Decision under appeal: Interlocutory decision of the Opposition Division of the European Patent Office posted 13 April 1994 concerning maintnance of the European Patent No. 0 018 795 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. 0 018 795 with the title "Monoclonal-antibody-producing hybrid cell line, antibody and method of preparing it, therapeutic composition containing it and its diagnostic and therapeutic uses" was granted with 20 claims based on European patent application No. 80 301 357.2

II. Notices of opposition were filed by four parties. Revocation of the patent was requested on the grounds of Article 100(a) to 100(c) EPC (lack of novelty, lack of inventive step, insufficiency of disclosure, added subject-matter).

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 set of claims filed with letter dated 22 July 1992.

Claims 4 and 5 as granted were deleted.

Claims 1, 6 and 9 were claims 1, 8 and 11 as granted and read as follows:

"1. Mouse complement-fixing monoclonal antibody which (i) reacts with essentially all normal human peripheral T-cells but (ii) does not react with any of the normal human peripheral cells in the group comprising B cells, null cells and macrophages."

"6. Monoclonal antibody which is produced from hybridoma ATCC CRL 8001 (OKT3)."

"9. Hybridoma ATCC CRL 8001 (OKT3)."

IV. The Opposition Division considered that the requirements of Article 123(2) EPC were satisfied for the reason that the deletion of two claims could not amount to adding subject-matter to the application as filed.

With regard to sufficiency of disclosure (Article 83 EPC), it was determined that the growing of the deposited hybridoma did not amount to undue burden of experimentation.

The experimental reports from Opponents which showed that the reactivity pattern of OKT3 was not that described in the patent specification were inconclusive. In particular, the reactivity pattern with regard to B cells and monocytes was contrary to that obtained in the experimental reports by the Patentee without any apparent reasons for the discrepancies. The benefit of the doubt thus went in favour of the Patentee. The fact that the Patentee did not perform the experiments on a sample of the hybridoma maintained by the ATCC culture collection but rather on an equivalent sample which had been kept in his laboratory did not negate the results as it could be believed that both samples were identical.

The reactivity pattern of OKT3 could not be challenged on the grounds that other monoclonal antibodies (MAbs) recognizing the same antigen did not show that reactivity pattern.

Novelty (Article 54 EPC) was acknowledged in the absence of any prior art document disclosing a monoclonal antibody with the claimed characteristics.

With regard to inventive step (Article 56 EPC), it was found that in the absence of any prior art disclosing polyclonal or monoclonal antibody preparations which reacted with T cells and of a clear suggestion as to which immunising agent to use to isolate MAbs specific for T cells, the invention was not obvious.

V. The Appellant (Opponent 4) lodged an appeal against this decision, paid the fee and submitted a statement of grounds of appeal. Opponent 3 indicated its support of the arguments provided by the Appellant.

VI. The Respondent (Patentee) answered the Appellants' submissions.

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. Further submissions were made by the parties.

IX. Amongst the more than 200 documents on file, the following documents are mentioned in the present decision:

(3) Barnstable, C.J. et al., Cell, volume 14, 1978, pages 9 to 20,

(5) Williams, A. et al., Cell, volume 12, 1977, pages 663 to 673,

(11) Williams, A et al., TIBS, 1978, pages 272 to 274,

(33) Recent Advances in Clinical Immunology, Edited by R.A. Thompson, Churchill Livingstone, Chapter 7, page 155, 1977,

(37) Köhler, G. and Milstein, C., Nature, volume 256, 1975, pages 495 to 497,

(45) Hämmerling, G.J. et al., Current Topics in Microbiol. and Immunology, volume 81, 1978, pages 100 to 106,

(61) Bibliography of articles describing work done with Becton-Dickinson monoclonal antibodies, submitted with the Respondent's letter dated 29 June 1987.

(76) Leucocyte typing, Edited by Bernard et al., Springer-Verlag, 1984, page 9 to 60, 114 to 116.

99(75) Leucocyte typing, Edited by Bernard et al., Springer-Verlag, 1984, page 752.

99(76) Leucocyte typing II, Edited by Reinherz et al., Springer-Verlag, 1986, page 18,

99(77) Leucocyte typing III, Edited by McMichael A.J. et al., Oxford University Press, 1987, page 42

(140) First experimental report by the Appellant submitted with letter dated 27 October 1989,

(142) Second experimental report by the Appellant submitted with letter dated 29 January 1991,

(143) Experimental report submitted by Opponent 3 with letter dated 16 August 1991,

(144) Experimental report submitted by the Respondent with letter dated 1 September 1992.

X. Oral proceedings were held on 23 April 1998.

XI. The submissions in writing and during oral proceedings by the Appellant can be summarized as follows:

Article 123(2) EPC

(a) At oral proceedings before the first instance, granted claims 4 and 5 (and the corresponding passages in the patent specification) were deleted, which related to additional reactivity patterns for the antibody of claim 1. This deletion amounted to now claiming an antibody, the characteristics of which were different from those originally disclosed. The patent failed to fulfil the requirements of Article 123(2) EPC.

Article 83 EPC; claims 6 and 9

(b) The deposition of the OKT3 producing hybridoma had not been achieved in a proper way, as a special medium was necessary in which to grow it, to be able to obtain a sufficient quantity of the OKT3 antibody. This medium was not mentioned in the patent specification which led the skilled person to use another unsuitable medium.

(c) Document (143) showed that E-rosette positive cells did not all react with OKT3. As in the patent in suit T cells were isolated as E-rosette positive cells, the reactivity pattern of OKT3 of binding with essentially all T cells could not be correct.

(d) Documents (140) and (142) showed that OKT3 reacted with monocytes and B cells.

(e) The data presented by the Respondent were not to be taken into account as they were not obtained with the deposited, OKT3 producing hybridoma but rather with a supposedly equivalent sample kept by the Respondent. In any case, the protocol used was flawed and even under such circumstances, the results obtained confirmed the conclusion reached by the Appellant.

(f) Documents 99(75) to 99(77) presented compilations of data obtained by more than 55 laboratories involving as many as 21 monoclonal antibodies recognizing the same antigen (CD3) as OKT3. The reagents used were common to all groups. The cell purification was achieved in most laboratories by the same method of E-rosetting which was also the method used in the patent in suit. The data were mostly analysed by the same method. The results obtained provided ample evidence that the antibodies reacted with other cell subsets than the T cells, i.e. with on average 10% of the E rosette negative cells population comprising B cells and null cells and with 10% of macrophages. Thus, the definition of OKT3 as not reacting with these latter cells had to be erroneous.

(g) The facts of the case were analogous to those in decisions T 0418/89 (OJ EPO 1993, 20) and T 0495/89 (of 9 January 1991) where the patents were revoked as the claimed hybridoma could not be grown without undue burden of experimentation (T 0418/89) and the properties of the claimed specific antibodies did not correspond to the written description (T 0418/89 and T 0495/89).

Article 83 EPC; claim 1

(h) Isolating according to the written patent specification further hybridomas possessing the characteristics listed in claim 1 amounted to undue burden of experimentation because insufficient information was provided on how to identify them; in particular, on how to isolate the purified populations of T cells to be tested.

Article 56 EPC

(i) The skilled person would find in document (11) examples of immunisation schemes with cell membranes, for the isolation of MAbs directed against cell populations. Document (5) and document (45) disclosed monoclonal antibodies against rat and mouse T cells respectively. Combining the teachings of document (11) with those of document (5) or (45) rendered the invention obvious.

XII. The Respondent replied essentially as follows:

Article 123(2) EPC:

(j) Deleting two claims could not amount to adding subject-matter to the application as filed. This application disclosed an antibody with the now claimed properties, quite independently from the fact that it may also have other characteristics.

Article 83 EPC; claims 6 and 9:

(k) The medium necessary to grow the OKT3 producing hybridoma was identified in the letter from ATCC accompanying the delivery of the hybridoma. The composition of this medium was part of the state

of the art since 1978. Adding serum to the growth medium of hybridomas was also common practice. As for a different medium being disclosed in the patent, the skilled person would readily have recognized that the recommended medium was to be used for cell fusion, not for the culture of hybridomas. Alternatively, the hybridoma could always be grown in ascites.

(l) Document (143) disclosed the reactivity pattern of OKT3 with E-rosette positive cells, not with T cells. No evidence had thus been provided that the claimed reactivity pattern of OKT3 with T cells was wrong.

(m) The protocol followed by the Appellants to test the reactivity pattern of OKT3 with regard to B cells and monocytes was flawed and, thus, no conclusion could be drawn therefrom that the reactivity pattern of OKT3 was not that described in the patent specification.

(n) It was perfectly justified for the Respondent not to carry out the experiments with MAbs grown from the hybridoma deposited with the ATCC, the ATCC requiring that the depositors keep a batch of the deposited organism, such as was directly used by the Respondent. The experimental reports showed that OKT3 did not react with B cells or monocytes.

(o) Documents 99(75) to 99(77) provided information on the average reactivity pattern of antibodies recognizing the same antigen as OKT3. This average reactivity pattern was in no way indicative of the specific reactivity pattern of OKT3. A large number of laboratories participated in the tests.

No standardized procedure was used: the cell populations tested were not always isolated by the same protocols. The compilation of the results to arrive to the average reactivity pattern did not exclude stray values.

(p) It was important to remember that a considerable number of late publications disclosed making use of OKT3 without ever mentioning that it reacted with other cell subsets than T cells. Nor was there any mention in the late published literature that the CD3 antigen recognized by OKT3 was ever found on other cells than T cells.

(q) The case was not at all analogous to the cases dealt with in T 0418/89 and T 0495/89 (see supra) because there was no problem in growing the hybridoma and also because, in these latter cases, there existed post-published documents which showed that the then claimed antibodies did not have the reactivity pattern to be expected from reading the patent.

Article 83 EPC; claim 1:

(r) The Appellant had not shown that it was not possible to isolate antibodies with the reactivity pattern given in claim 1. The great number of copycat antibodies which were made by different firms, once the isolation of OKT3 had been described, was a very good indication that the disclosure was sufficient in relation to claim 1.

Article 56 EPC:

At the priority date of the application, the technique of making monoclonal antibodies was still very much in its infancy. A polyclonal antiserum specific for T

cells did not exist. Document (5) disclosed the isolation of a monoclonal antibody against rat T lymphocytes using rat thymocyte membranes as immunogen but this monoclonal antibody also reacted with other types of cells. Besides, in document (3), it was shown that the same technique carried out with membranes from human tonsil lymphocytes as immunogen did not work. None of the documents of the art alone or in combination would make the claimed subject-matter obvious.

A secondary indication of inventive step was to be found in very many publications describing the use of OKT3 in clinical experiments.

XIII. The Appellant (Opponent 04) requested that the decision under appeal be set aside and that the European patent No. 0 018 795 be revoked.

The Respondent requested that the appeal be dismissed.

Reasons for the Decision

Article 123(2)(3) EPC:

1. The patent application as originally filed discloses a monoclonal antibody characterized by six different features (claim 1, Table 1). Two of these features are no longer mentioned in the patent specification and claims now on file. The argument was put forward that the now claimed antibody (claim 1) was different from the originally disclosed antibody. Thus, claim 1 was addressed to a monoclonal antibody which had never been described before and therefore the requirements of Article 123(2) EPC were not fulfilled.

2. The Board observes that in the patent application as originally filed (page 7, lines 10 to 13), it is stated: "Not only does this antibody react with essentially all normal human peripheral T cells, but it also does not react with other normal peripheral blood lymphocytes". These features are those found in present claim 1 together with limitations which also have a basis in the application as originally filed. There is, thus, support for the claimed subject-matter in the application as originally filed.

3. It is true that in the claims originally filed more of the antibodies' properties were defined than now. Yet, it was permissible for the Respondent to re-define the matter which it wanted protected within the limits of the original disclosure.

4. Claims 1 to 18 are identical to the claims as granted except for dependent claims 5, 8, 12 and 13 (former claims 7, 10, 14 and 15) in which the term "human T cells" was replaced by the expression "normal E-rosette positive purified human T cells". This amendment which finds a basis on page 13, lines 4 to 12 of the patent application as originally filed does not amount to an enlargement of their scope.

5. The requirements of Article 123(2)(3) EPC are fulfilled.

Article 83 EPC; claims 6 and 9

Deposition of the hybridoma

6. The Appellants argued that the written description of the patent specification was not sufficient for the skilled person to be able to reproduce the invention and that thus a deposition of the OKT3 producing hybridoma with a recognized depositary institution was

necessary for sufficiency of disclosure. This deposition had not been achieved in the proper way as the medium in which to grow the hybridoma was not disclosed in the patent as filed and also because IL-6 needed to be added to the growth medium in order to make the monoclonal antibody in sufficient quantities.

7. The patent as filed teaches in example IB to multiply the hybridoma in ascites. Furthermore, when delivering the hybridoma upon request, the ATCC recommended a specific growth medium "because it had been published", supplemented with 20% fetal bovine serum (letter from the ATCC submitted by the Appellants with the grounds of appeal). Thus, there are two ways available to grow the deposited OKT3 hybridoma. In fact, in the course of opposition proceedings before the first instance, an expert for Opponent 3 submitted a statutory declaration (document (143)) whereby he acknowledged receiving the OKT3 producing clone from ATCC and growing it in ascites, obviously without difficulties.

8. The objection that the hybridoma could not be grown in such a way that OKT3 could be obtained in sufficient quantities leaves entirely open, which purpose the quantities of OKT3 should be sufficient for. However, it should at least be possible to produce the antibody in such quantities that its properties can be tested. Opponent 3 was able to test the properties of OKT3 grown from ascites (document (143)). The Appellant also tested its properties in two independent experiments (documents (140) and (142)). In each experiment, two preparations of OKT3 were made, one from the OKT3 hybridoma grown in the presence of IL-6, and one, of much higher concentration, of this hybridoma grown from ascites. Thus, the impossibility of producing OKT3 "in sufficient quantities" by culturing the deposited hybridoma has not been shown in a convincing manner.

9. The Appellant submitted that because the patent taught the RPMI 1640 medium which was the medium suitable for cell fusion, the skilled person would have assumed that it was a proper growth medium as well, whereas, in fact, the hybridoma did not satisfactorily grow in RPMI 1640. This argument is not convincing since the depositary ATCC had given advice in which medium to grow said hybridoma.

10. Thus, the facts of the case are different from those dealt with in T 0418/89 (see supra) where there was evidence on file that the then claimed and deposited hybridoma could only be grown after repeated requests by many recipients had been made to the ATCC and by applying techniques considerably more sophisticated than those recommended by the depositary institution.

11. For all of these reasons, the Board sees no evidence that the claimed hybridoma (claim 9) was not properly deposited and did not secrete the claimed antibody in sufficient quantities (claim 6).

Experimental reports:

- on the ability of OKT3 to react with essentially all normal human peripheral T cells (feature (i) of claim 1):

12. The patent specification (Table 1) shows that OKT3 reacts with more than 95% of peripheral T cells when these are isolated as E-rosette positive cells. In the course of the proceedings before the Opposition Division, Opponent 3 submitted an experimental report which showed that OKT3 reacted with on average 80.9% of T cells when these cells are isolated in the same manner as in the patent in suit i.e. as E-rosette positive cells (document (143)). The questions are thus raised whether the skilled person would have understood

the E-rosette positive cell population to be the T cells subset of peripheral blood lymphocytes and, if not, how representative of the reactivity of OKT3 with the T cells subset, the reactivity of OKT3 with E-rosette positive cells might be considered.

13. At the priority date, the E-rosette test was qualified as "the best currently available for counting T lymphocytes" (document (33), page 155). Yet, immature B lymphocytes, K cells and small numbers of non phagocytic but nonetheless monocyte related cells were also known as E-rosette positive (ibidem). Thus, the skilled person was aware that E-rosette positive cells contained some minor cell populations other than T cells although E-rosetting was a convenient way to obtain an enriched population of these latter cells.

14. Moreover, document (143) shows that the reactivity pattern of OKT3 with E-rosette positive cells varies from 97% to 62% depending on the blood samples the E-rosette positive cells are isolated from. Faced with such widely ranging values and aware of the heterogeneity of the E-rosette positive cells, the skilled person could not disregard the possibility that the results were due, at least to some extent, to different relative amounts of T cells and the minor cell populations in the E-rosette positive populations depending on their origin. Thus, he/she would take any results obtained with regard to the reactivity pattern of OKT3 with E-rosette positive cells as the best available approximation of the reactivity of OKT3 with the T cell subset but not as its exact reactivity with this subset.

15. Accordingly, the Board concludes that the experiments of document (143) do not provide an unambiguous proof that OKT3 does not react as described in the patent in suit, namely, with essentially all normal human peripheral T cells.

- on the inability of OKT3 to react with B cells or macrophages (feature (ii) of claim 1):

16. The Appellant submitted experimental reports on the ability of OKT3 to bind to B cells present in a population of lymphocytes, and to macrophages (i.e. monocytes). The techniques used are those of double staining flow cytometry or of single antibody fluorescence marking. The problems associated with, and the limitations of these techniques were extensively discussed by both parties. It appears that the binding conditions, in particular the antibodies' concentration, their origin and subclass are of critical importance. In the same manner, many different and apparently essential parameters seem to have to be taken into account when setting up the flow cytometer because of their impact on the interpretation of the data. It does not seem possible to consider the results as meaningful unless many controls are carried out. The overall impression which the Board gets from the submissions on file is that these techniques are highly sophisticated techniques, the results of which should be interpreted with the greatest caution.

17. The data from the Appellant relative to the reactivity pattern of OKT3 with B cells and monocytes are presented in documents (140) and (142). The amount of OKT3 used is not clearly stated in either of these documents. There are, furthermore, many departures from a "satisfactory protocol" as suggested by the submissions from both parties: it is not sure that unspecific binding has been avoided in the experiments

described in document (140)), the isotype of the monoclonal antibodies used as negative controls in document (142) is not specified and a positive control staining has not been carried out which would appear to be indispensable to evaluate the results.

18. Taking into account these findings and the fact that the survey of the scientific literature presented in document (61) shows that OKT3 was made use of, in more than one hundred and fifty scientific publications within the next two years of it being available, without its reactivity pattern ever being challenged, the Board considers that the experimental reports presented cannot be given decisive significance.

19. Thus, the Appellant has not provided satisfactory evidence by its experimental reports that OKT3 as claimed in claim 6 and secreted by the deposited hybridoma of claim 9 does not possess the claimed properties. To the contrary, OKT3 has been much used for testing the presence of T cells in populations of lymphocytes (document (61)). The facts of this case are, thus, fundamentally different from those dealt with in decisions T 0418/89 and T 0495/89 (see supra) where evidence existed that the then claimed monoclonal antibodies had a different reactivity pattern from that disclosed in the patent specification.

Experimental reports from the Respondents:

20. In answer to the Appellant's experimental reports, the Respondent also provided an experimental report using the double staining, flow cytometry technique (document (144)). In view of the above finding that the Appellant

was not able to show that the deposited hybridoma does not fulfil the requirements of Article 83 EPC, there is no burden of proof on the Respondent to show that it does. Thus, the validity of the Respondent's experiments need not be discussed.

The Leukocyte Typing workshops:

21. Documents 99(75) to 99(77) are excerpts of the post-published Leukocyte Typing Workshops which disclose studies of monoclonal antibodies for the characterisation of normal and malignant leukocyte populations. The purpose of these studies carried out by 55 laboratories in 14 countries is defined on page 9 of document (76): a joint effort was to be made "to prevent that the rapidly increasing number of monoclonal antibodies being produced would result in a plethora of individual systems of nomenclature being adopted which would create complete confusion and render impossible any coherent dialog...". Thus, the monoclonal antibodies were regrouped in clusters, the clusters being defined statistically, a monoclonal antibody being classified to one of the already delineated cluster if its distance to the furthest monoclonal antibody in the group was the least (passage bridging pages 29 and 30). Eight clusters were, thus, identified. Both parties agree that OKT3 falls within the CD3 cluster including 21 other monoclonal antibodies.

22. Document 99(75),(Table T26) reports the testing of 4 MAbs, but not of OKT3, against cell populations identified as T-PBL and non-T PBL. The medium reactivity with non-T PBL cells is given as about 20% (the lowest percentage being 0% and the highest, 52%). In document 99(77), the reactivity with B cells is given as 16.8% and with monocytes as 11.7%. In document (76) the overall median reproducibility of the

experiments is said to be of 6% to 8% (page 22). It was this scattering of the results which caused serious concern of the scientific community as it is discussed in document 99(76) on pages 114 to 116 together with figures TEC 1 and TEC 2.

23. The Appellant interprets these results as meaning that OKT3 reacts with B cells and monocytes. Yet, as already stated, OKT3 was not part of the studies. Furthermore, the scientists themselves while allocating each monoclonal antibody to a statistically defined group did not draw any firm conclusion as to the reactivity pattern of any specific anti-CD3 antibodies. As above stated, they rather tried to understand why the results obtained for anyone monoclonal antibody and for anyone cluster of monoclonal antibodies could so vary from laboratory to laboratory. For these reasons, the Board is not convinced that documents 99(75) to 99(77) are proof that the reactivity pattern of OKT3 (claim 6), as secreted by the deposited hybridoma (claim 9) is not such as described in the patent in suit and claimed in claim 1.

24. In view of what precedes the Board decides that there is no insufficiency of disclosure with regard to the properties of the specific hybridoma and monoclonal antibody of claims 6 and 9.

Article 83 EPC, claim 1:

25. In the light of the above findings, the arguments by the Appellant that the experimental protocol provided in the patent specification for the production of the monoclonal antibody of claim 1 was not reproducible, need not be discussed. The deposited hybridoma and its secreted antibody ensure the reproducibility of the subject-matter of this claim, which thus fulfil the requirements of Article 83 EPC.

Article 56 EPC, inventive step

26. Document (5) discloses that monoclonal antibodies to differentiation antigens carried by subpopulations of lymphocytes are useful tools in purifying the antigens and studying the functionality of these subpopulations. To illustrate this concept, a monoclonal antibody is produced using rat thymocyte membranes as the immunogen in the myeloma hybrid technique of Köhler and Milstein (document (37)), and this antibody reacts with rat thymocytes and rat T cells but does not react with rat B cells.

27. Starting from this document as the closest prior art, the objective technical problem to be solved is the production of a monoclonal antibody specific for human T cells.

28. A monoclonal antibody is provided which reacts with human T cells but not with B cells, null cells and macrophages. The above mentioned problem has thus been solved.

30. The monoclonal antibody is produced by the method of Köhler and Milstein using human T cells as an immunogen. This method is the one used in document (5). No inventive step could be attributed to applying a known method for the isolation of MAbs to human antigens. The question which remains to be answered is whether the skilled person would have had a reasonable expectation of success that an antibody such as claimed could be produced because it had been possible to produce an antibody such as described in document (5), in 1979.

31. Documents (11) and (45) have been cited in this context. They relate to the production of monoclonal antibodies directed to mouse or rat antigens. These

antibodies react with antigens which may be common to different cells subsets (document (11): (L-C antibody to the Leukocyte common antigen; document (45): R3-11) or to antigens which may be present on one specific type of cells (document (11): Thy-1, document (45): R3-1). At the priority date, in 1979, it was, thus, known that monoclonal antibodies could be produced, which were specific in their recognition of subsets of rat or mouse lymphocytes but that they needed not necessarily be so.

32. There are no documents of the state of the art which disclose a polyclonal antiserum specific for human T cells or monoclonal antibodies reacting with a specific subset of human lymphocytes. In fact, document (3) discloses that the monoclonal antibodies which are produced by using human tonsil lymphocytes as immunogen recognize tissue-common antigens rather than any specific cell subset. The authors point out that "the reasons for the differences obtained in the rat and human experiments are not known" (page 16). On the basis of this failure of a highly skilled scientific team (the inventor of the hybridoma technique and Nobel Prize laureat Milstein is one of the authors of document (3)), to produce any MAbs to specific cell subsets, the Board is convinced that the isolation of the claimed antibody was not obvious. The requirements of Article 56 EPC are fulfilled.

Order

For these reasons it is decided that:

The appeal is dismissed

The Registrar: The Chairwoman:

A. Townend U. M. Kinkeldey