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D E C I S I O N
of 23 February 1999

Case Number: T 0431/96 - 3.3.4

Application Number: 84102916.8

Publication Number: 0122478

IPC: C12P 21/08

Language of the proceedings: EN

Title of invention:
A method for the preparation of monoclonal antibody with specificity for crosslinked fibrin derivatives and an assay procedure using said antibody

Patentee:
Agen Biomedical Limited

Opponent:
Behringwerke Aktiengesellschaft
Innogenetics NV

Headword:
Monoclonal antibody/AGEN

Relevant legal provisions:
EPC Art. 83, 56

Keyword:
"Main request - sufficiency of disclosure (yes)"
"Inventive step (yes)"

Decisions cited:
T 0206/83, T 0223/92, T 0418/89, T 0412/93

Catchword:

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0431/96 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 23 February 1999

Appellant: (Opponent 02)
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Decision under appeal:
Decision of the Opposition Division of the European Patent Office posted 12 March 1996 rejecting the opposition filed against European patent No. 0 122 478 pursuant to Article 102(2) EPC.

Composition of the Board:

Chairperson:	U. M. Kinkeldey
Members:	L. Galligani
	W. Moser

Summary of Facts and Submissions

I. The appeal lies from the decision of the opposition division dated 12 March 1996 whereby the oppositions against the European patent No. 122 478, which had been filed under the terms of Article 100(a)-(c) EPC by two parties, were rejected.

II. The patent in suit contained claims 1 to 16 for all the designated contracting States except Austria (non-AT States) and claims 1 to 16 for AT. Independent claims 1 and 15 for the non-AT States read as follows:

"1. A monoclonal antibody raised against non-denatured D-dimer that may be utilised in a method of diagnosis of disseminated intravascular coagulation (DIC) or other thrombotic states using body fluid, such as lymph, serum, plasma or exudate, said monoclonal antibody having the essential characteristic of reactivity with D-dimer and other cross-linked fibrin derivatives and non-reactivity with fibrinogen or fibrinogen degradation products inclusive of fragment D and fragment E."

"15. A method of detection of cross-linked fibrin derivative in a body fluid, such as lymph, serum, plasma or exudate, including the steps of:

(i) immunising an animal with a non-denatured, cross-linked fibrin derivative or extract containing same;

(ii) removing a spleen from the animal;

(iii) treating the spleen to form a cell suspension;

(iv) purifying the cell suspension to isolate spleen white blood cells or lymphocytes;

(v) forming hybridoma cells containing as one component said spleen white blood cells or lymphocytes;

(vi) cloning or recloning said hybridoma cells using appropriate cell feeder layers;

(vii) carrying out screening assays with antigen selected from cross-linked fibrin derivative or extract containing same or fibrinogen and fibrinogen degradation product so as to isolate hybridoma cells which produce monoclonal antibody as defined in claim 1;

(viii) contacting a fluid sample suspected of containing cross-linked fibrin derivative or antigen derived therefrom with monoclonal antibody prepared from hybridoma cells isolated after step (vii),

and

(ix) subjecting the complex formed in step (viii) to a detection step."

Claim 1 for AT was formulated as a method claim as follows:

"1. A method for the preparation of a monoclonal

antibody raised against non-denatured D-dimer that may be utilised in a method of diagnosis of disseminated intravascular coagulation (DIC) or other thrombotic states using body fluid, such as lymph, serum, plasma or exudate, characterized by

(i) immunising an animal with a non-denatured, cross-linked fibrin derivative or extract containing same;

(ii) removing the spleen from the animal;

(iii) treating the spleen to form a cell suspension;

(iv) purifying the cell suspension to isolate spleen white blood cells or lymphocytes;

(v) forming hybridoma cells containing as one component said spleen white blood cells or lymphocytes;

(vi) cloning or recloning said hybridoma cells using appropriate cell feeder layers;

(vii) carrying out screening assays with antigen selected from cross-linked fibrin derivative or extract containing same or fibrinogen and fibrinogen degradation product so as to isolate hybridoma cells which produce a monoclonal antibody having the essential characteristic of reactivity with D-dimer and other cross-linked fibrin derivatives and non-reactivity with fibrinogen or fibrinogen degradation products inclusive of fragment D and fragment E."

III. The opposition division considered that the claims as granted contained no added matter. It also decided that, failing proper experimental evidence to the contrary, there were no reasons to believe that non-denatured D dimer could not be obtained on the basis of the disclosure in the description in the patent in suit. Furthermore, the claimed subject-matter was considered to be novel over the following documents:

(2) Boucheix C. et al., Protides of the Biological Fluids, Vol. 13, 1982, pages 399 to 402;

(4) Soria J. et al., in "Fibrinogen - Structure, Functional Aspects, Metabolism, Vol. 2, 1983, W. de Gruyter & Co., Berlin (DE), pages 227 to 233.

It was also decided that the claimed subject-matter involved an inventive step having in particular regard to the following document, which represented the closest prior art:

(1) Lee-Own V. et al., Thrombosis. Res., Vol. 14, 1979, pages 77 to 84.

In fact, there was no reasonable expectation of success of obtaining antibodies specific enough for native D dimer and thus suitable for clinical assays.

IV. Both the opposing parties (opponents 01 and 02) lodged an appeal, with payment of the fee, against this decision and filed a statement of grounds. Further evidence was filed therewith by the opposing parties.

On 27 August 1996, opponents 01 withdrew their appeal.

V. The respondents (patentees) filed their reply with additional evidence. The appellants (opponents 02) replied thereto with further submissions.

VI. On 30 October 1998, the board issued a communication pursuant to Article 11 of the rules of procedure of the boards of appeal with an outline of the issues to be discussed at oral proceedings.

VII. Both the appellants and the respondents filed further submissions in reply to the board's communication.

VIII. Oral proceedings took place on 23 February 1999. The main request consisted of the claims as granted with the following amendments: item (i) of claim 15 for non-AT States and of claim 1 for AT was changed to read "immunising an animal with a non-denatured, crude fibrin extract, and following this up with administration of pure crosslinked fibrin derivative;". Two auxiliary requests were also filed.

IX. In addition to the already mentioned documents (1), (2) and (4), the following documents were referred to:

(5) Budzynski A. Z. et al., Blood, Vol. 54, No. 4, October 1979, pages 794 to 804;

(6) Wilner G.D. et al., Biochemistry, Vol. 21, 1982, pages 2687 to 2692;

(7) Graeff H. and R. Hafter, Seminars in Thrombosis and Hemostasis, Vol. 8, No. 1, 1982, pages 57 to

68

(8) Olexa S. A. and A. Z. Budzynski, Biochemistry, Vol. 18, No. 6, 1979, pages 991 to 995;

(19) Declerck P.J. et al., Thromb. Haemostas., Vol. 58, No. 4, 1987, pages 1024 to 1029;

(21) Cierniewski C. S. et al., Thromb. Haemostas., Vol. 48, No. 1, 1982, pages 33 to 37;

(23) Kennel S.J. et al., Thrombosis Res., Vol. 22, 1981, pages 309 to 320;

(26) Rylatt D.B. et al., Thrombosis Res., Vol. 31, 1983, pages 767 to 778.

X. The appellants put forward essentially the following arguments:

(a) There was no basis in the application as filed for the feature "raised against non-denatured D-dimer". This was because (i) it was not disclosed how the said non-denatured D-dimer was prepared, reference being made in the specification only to methods in which denaturating conditions were used (eg reference to document (6)), and (ii) the preferred antibodies of the examples were not raised against a non-denatured D-dimer, but against a fibrin lysate followed by a booster D-dimer material which, in view of the way it was prepared (cf. item i), was denaturated.

(b) The expression "pure crosslinked fibrin

derivative" was not clear (Article 84 EPC);

(c) The patent specification misguided the skilled person as the method indicated therein for producing the non-denatured D-dimer (reference to document (6)) was a method in which a long exposure to high concentrations of urea was used, and which therefore could only result in a denatured product (cf. also the declaration of Dr Hurrell, respondents' technical expert). Later description how the antibodies of the examples were prepared (cf. document (26)) showed that the method used did not correspond to that disclosed in the patent specification. The latter contained no indication that, in spite of the references given, only a short term exposure to urea should be used. The sentence "care should be taken..." at the bottom of page 8 did not provide per se sufficient information for the skilled person who was faced with the undue burden of preparing the undenatured D-dimer for boosting and screening. The protocol given in the patent specification was not clearly set out such as to produce any antibody falling within the terms of claim 1 because, apart from the lack of information how to prepare the undenatured D-dimer, it did not provide data on the success rate (cf. the vague sentence "several hundred hybridoma..." on page 9, lines 42 to 43) and it reported misguiding reactivities in respect of the specific antibodies of the examples (cf. in Table 1 cross-reactivity with fibrinogen in spite of claim requirement of no reactivity). Under these circumstances, the skilled person could not repeat the production of

the monoclonal antibodies according to the patent in suit. As the specific hybridomas of the examples had not been deposited under Rule 28 EPC, also this way to reproduce the invention was not available. The situation in the present case had striking similarities with that of decision T 418/89 (OJ EPO 1993, 20) in which a judgement of insufficiency was pronounced.

(d) It could not be demonstrated experimentally that the antibody DSB14 described in documents (2) and (4) was different from the antibodies in the patent in suit as the said antibody was not available;

(e) The claimed subject-matter lacked an inventive step having regard to documents (1),(2),(5) or (21). In particular, document (1) described a polyclonal antibody raised against non-denatured D-dimer which allowed to differentiate between D-dimer and fibrinogen. The claimed subject-matter of the patent in suit was the mere replacement of the polyclonal antibodies of this prior art with monoclonal antibodies, i.e. something which the skilled person could achieve with a reasonable expectation of success, unless the difficulties pointed out in relation to the description were acknowledged to exist (cf. item (c) above). Such a replacement was also obvious in the light of document (5), which described an antiserum with high reactivity for the D-dimer and low or very low reactivity with fibrinogen or fragment D, as well as document (21), where an antiserum capable of detecting the crosslinking site on the D-dimer

was described. The replacement was particularly obvious in view of the disclosure of document (2) (but also of documents (4) and (23)) which related to the application of the monoclonal antibody technology to the problem of finding antibodies of high specificity for the D-dimer to be applied to relevant clinical situations. Document (2) suggested also a boosting step in the preparation of the antibodies. However, later document (19) demonstrated that suitable monoclonal antibodies could be obtained also without a boosting step.

XI. The respondents argued that the patent in suit unambiguously taught that care should be taken not to denature the D-dimer material used for boosting in the immunisation protocol. This was very important as it provided in an elegant manner a pre-enrichment step which increased the probability over conventional techniques of obtaining the desired monoclonal antibody. Moreover, a detailed screening procedure was described which allowed the reproduction of the claimed monoclonal antibody without undue burden. Thus, there was no need to deposit the specific hybridomas of the patent in suit.

As for inventive step, the prior art relating to the polyclonal antibodies was not encouraging for the skilled person as it indicated the difficulties in achieving antibodies which could differentiate between crosslinked and non-crosslinked products (cf. documents (1), (5), (21)). Documents (2) and (4), which relied on monoclonal antibody technology, did not succeed in providing antibodies reactive only with the crosslinked fibrin derivatives as those of the patent

in suit, and did not suggest any way how this could be reliably achieved.

XII. The appellants requested that the decision under appeal be set aside and that the patent be revoked.

The respondents requested that the decision under appeal be set aside and that the patent be maintained on the basis of the following documents:

(a) claims 1 to 16 for all designated contracting States except AT, and claims 1 to 16 for AT, submitted during oral proceedings as main request; or

(b) claims 1 to 16 for all designated contracting States except AT, and claims 1 to 16 for AT, submitted during oral proceedings as first auxiliary request; or

(c) claims 1 to 16 for all designated contracting States except AT, and claims 1 to 16 for AT, submitted during oral proceedings as second auxiliary request.

Reasons for the Decision

Main request

Articles 123(2)(3) and 84 EPC

1. The amendment in item (i) of claim 15 for the non-AT States and claim 1 for AT is of a restrictive nature as it added a further feature and process step which specifies how immunisation is carried out. Thus, no objection under Article 123(3) EPC arises.

2. The said amendment finds support on page 9, lines 11 to 14 of the application as filed and, therefore, is in conformity with the requirements of Article 123(2) EPC.

3. Objection was raised against the feature "against **non-denatured** D-dimer" (emphasis added) in claim 1 both for the non-AT States and for AT, as, in the appellants' view, this feature is not unambiguously derivable from the content of the application as filed (cf. Section X, item (a) supra). It is, however, noted that the application as filed, while indicating that immunisation of an animal can be performed either with a substantially pure crosslinked fibrin derivative or, preferably, with a crude fibrin lysate followed by boosting with a substantially pure crosslinked fibrin derivative (cf. page 8 to page 9, first and second paragraphs, page 15, lines 3 to 8), emphasizes that "[w]hen using a pure crosslinked fibrin derivative such as D dimer, care must be taken in its preparation to not denature the molecule as it is susceptible to denaturation fairly easily" (cf. page 8, last

paragraph). In the board's judgement, this as a whole constitutes a fair support for the feature that the monoclonal antibody referred to in the claims in question is raised against a non-denatured D-dimer. Whether the actual teaching of the patent in suit is enabling in respect of this feature is a different question which has to be examined under the heading "Article 83 EPC" (cf. points 5 to 15 infra).

4. The appellants' objection under Article 84 EPC to the clarity of the expression "pure crosslinked fibrin derivative" is not considered to be justified as the skilled person knows both from the prior art (cf. document (7), see e.g. page 57) and from the application as filed (cf. page 9, lines 1 to 8) what is meant thereby.

Article 83 EPC

5. In examining the question whether the description of the patent in suit provides enough information and guidance as to enable a person of ordinary skill to obtain without undue burden and without applying inventive skill a monoclonal antibody having the features recited in claim 1 for the non-AT States and for AT, two questions are of particular relevance, namely:

(i) whether it can be accepted that, as submitted by the respondents, the way in which the animal immunisation step was carried out (i.e. immunisation with a crude fibrin lysate followed by a boost immunisation with a non-denatured D-dimer preparation) contributes to reducing the

burden of the skilled person in preparing a monoclonal antibody having the desired features; and, if so,

(ii) whether the description provides sufficient guidance as to the preparation of the booster.

6. The written description of how hybridomas secreting a monoclonal antibody with the desired features have been produced consists basically of the sequence of the widely known routine technical steps where all that is normally called for is perseverance. As the said monoclonal antibody is characterised by its reactivity/non-reactivity with given products (cf. claim 1), this being readily testable in an assay, the skilled person seeking to reproduce the invention will have to produce monoclonal antibodies by routine methods and test them singly in an assay. This may possibly involve some tedious and time-consuming work, but nothing out of the ordinary since the techniques for the production and selection of hybridomas were common routine techniques at the priority date of the patent in suit (i.e. 17 March 1983).

7. It is, however, important to note that the patent specification on page 5, lines 40 to 43 indicates a procedure of immunisation which is said to simplify the task of obtaining the desired monoclonal antibody, this consisting of the steps of immunising first with a crude fibrin extract and then boosting with pure or substantially pure crosslinked fibrin derivative. In respect of the preparation of the latter, on page 5, line 31, reference is made to prior art document (6) and, immediately thereafter, on lines 33 to 34 it is

added that "care must be taken ... not to denature the molecule as it is susceptible to denaturation fairly easily", no further details being given on how this can be achieved.

8. The respondents submit that the boosting step in the immunisation protocol, by stimulating clones already secreting specific antibodies in the animal, facilitates the search for a monoclonal antibody with the desired features. The board accepts this because:

- firstly, it is scientifically credible that such a pre-enrichment step increases the chances of finding a suitable hybridoma; and

- secondly, there is no evidence on file which could lead to a different conclusion.

9. The answer to the question (i) of point 5 above is therefore affirmative. It has thus to be examined now whether the patent specification in any way misguided the skilled person as regards the preparation of the boosting material. In this respect, the appellants pointed to the apparent contradiction between the reference to a prior art method which taught to operate under denaturing conditions, and the recommendation in the specification not to denature the molecule used for boosting. In their view, this contradiction and the missing further information result in the lack of a clear guidance and, thus, in an insufficient disclosure.

10. On page 5, lines 29 to 32, the patent specification indicates that crosslinked fibrin derivatives can be

purified **based** on a technique using gel filtration in combination with ion exchange chromatography as described by Wilner et al., i.e. document (6). In the subsequent sentence (lines 33 to 34), the patent specification informs the reader that "when using a pure crosslinked fibrin derivative as D dimer, care must be taken in its preparation not to denature the molecule as it is susceptible to denaturation fairly easily". In the board's judgment, the latter statement unambiguously instructs a skilled person to operate according to the reference, **but so as to avoid any condition which could lead to the denaturation of the molecule**. The Wilner reference, which as regards the preparation of the D-dimer makes also reference to document (8), describes a chromatography step on CM-cellulose in 8M urea in order to remove the non-crosslinked material (cf. page 2688, passage bridging left and right columns). Document (8) describes the purification by gel filtration of the D-dimer, directly after fibrin digestion, (cf. passage bridging pages 992 and 993 as well as Figure 2) in a buffer which **does not** contain urea, the use of urea being suggested for dissociating the (DD)E complex (D-dimer together with fragment E) in a different experiment (cf. Figure 5).

11. In the board's view, the reference back to the methods of documents (6) and (8) in the context of the patent in suit would not have been interpreted by the skilled person as an invitation to denature the crosslinked fibrin derivatives. On the contrary, in view of the explicit warning against the use of denaturing conditions, the skilled person would have paid attention to the conditions of operation and, being aware of the denaturing effect of urea (cf. also

document (5)), he or she would have taken the appropriate measures not to denature the molecule, these being either the non-use of urea as done in document (8), or the use of low concentrations or shorter exposure thereto. These were measures within the reach of any person of ordinary skill for which no detailed description is considered to be necessary. Therefore, also the answer to the question (ii) of point 5 above is affirmative.

12. None of the other factors mentioned by the appellants, such as the lack of data on the rate of success in the isolation of hybridomas or the apparent slight cross-reactivity with fibrinogen reported in Table 1, would have affected the ability of the skilled person to prepare, without undue burden by way of routine experimentation, a monoclonal antibody within the terms of the claims. This positive finding applies both to the subject-matter of claims 1 and 15 for non-AT States as well as to that of all other claims as they refer to methods of use of a monoclonal antibody according to claim 1. For obvious reasons, the same finding applies to the set of claims for AT.

13. As for the question of the need of a deposit of the particular hybridomas of the examples, this board has already indicated in previous decisions (cf. T 223/92 of 20 July 1993, in particular point 3.2 of the reasons, and T 412/93 of 21 November 1994, in particular point 76 of the reasons) that the prescription of Rule 28(1) EPC cannot be interpreted such that there is an obligation to deposit material to facilitate the reproduction if the invention can be repeated on the basis of the written description, even

if this should be a much more cumbersome way than by merely growing the deposited micro-organism (here: the hybridoma). Such is the case here. There was thus no obligation to assist the disclosure by making the hybridomas of the examples available by way of a deposit, because the best mode requirement is not part of the European Patent system.

14. The circumstances of the case T 418/89 (supra) referred to by the appellants (cf. Section X, item c) supra) were different from those of the present case as there the board found on the basis of the technical situation there that the written description did not provide a sufficient disclosure of a technical teaching withing the meaning of Article 83 EPC. Thus, the rationale of the said decision does not apply to the technical situation of the present case.

15. For these reasons, the board concludes that the requirements of Article 83 EPC are satisfied.

Novelty (Article 54 EPC)

16. In respect of this issue, the appellants stated that, as the monoclonal antibody DSB14 referred to in documents (2) and (4) was not available, it was not possible to carry out the direct comparison with the monoclonal antibody according to claim 1 (non-AT States) of the patent in suit. The board notes that, apart from the fact that a prior art document which does not enable the skilled person to reproduce a given product (here: the monoclonal antibody DSB14) cannot have an anticipatory effect (cf. e.g. T 206/83 OJ EPO 1987, 5), the monoclonal antibody DSB14 has reactivity

with fibrinogen-degradation products (cf. document (2), Table on page 400) which is a feature excluded for the monoclonal antibody according to claim 1 (non-AT States) at issue here. Consequently, the said prior art monoclonal antibody as described does not affect novelty of the said claim. None of the other documents on file prejudices the novelty of the monoclonal antibody of claim 1 for non-AT States. Therefore, novelty is acknowledged for this claim.

The same finding applies to claim 1 for AT, which is a method of preparation of said antibody and to all remaining claims in the two versions for non-AT and AT as they refer to methods of use of the said monoclonal antibody.

Inventive step (Article 56 EPC)

17. The prior art documents (1), (2), (5) or (21) referred to by the appellants are all concerned with the problem of the immunological distinction between the D-dimer and fibrinogen/fibrinogen-degradation products:

- Document (1) describes the preparation of antisera against a D-dimer purified through a series of column chromatographies. One of them allowed some distinction between the D-dimer and fibrinogen, thus pointing to the presence in the antiserum of antibodies against neoantigenic sites on the D-dimer. In the discussion of the results, the document draws the reader's attention to the necessity of differentiating between fibrin and fibrinogen-degradation products, and to the possible influence of the state of denaturation of

the immunogen on the exposure of the relevant determinants;

- Document (2) describes the preparation of monoclonal antibodies whose reactivity varied greatly between fibrinogen, fibrinogen-degradation products and soluble fibrin derivatives (e.g. D-dimer). One of them (DSB14) displayed high reactivity with soluble fibrin derivatives (e.g. D-dimer), no reactivity with fibrinogen and fragment E, but some reactivity with fragment D and fibrinogen-degradation products (cf. Table on page 400);

- Document (5) deals with the study of markers on the D-dimer with antisera and recognises that a structurally intact D-dimer should bear determinants which should be useful in distinguishing it from the fibrinogen-degradation products;

- Document (21) describes the preparation of antisera from animals immunised with purified D-dimer which allow the detection and quantitation of D-dimer in the presence of fibrinogen and fragment D. The reactivity with fragment E is not reported. The document states at the end of the discussion that the system was not yet proven to be effective for the study of clinical material.

18. The appellants made also reference to documents (19) and (23). The first is post-published evidence that was not available to the skilled person, which, in any case and contrary to the appellants' submissions (see

Section X, item e), last sentence supra), makes use of a boosting step in the protocol for making monoclonal antibodies (cf. page 1025, left column, first paragraph). The second document reports the preparation of monoclonal antibodies from rats immunised with fragment D of human fibrinogen, some of them reacting equally well with fibrinogen and fragment D, and others reacting preferentially, but not absolutely with fragment D. This document is thus less relevant than the documents cited under point 17 above.

19. In the board's judgement, of the quoted prior art documents, document (1) represents the closest prior art for the evaluation of inventive step because it addresses also the issue of a possible influence of the conformational state of the immunogen on the specificity of the antibodies.

20. In the light of the said prior art, the problem to be solved is seen in the finding of antibodies capable of providing a marked immunological distinction between the D-dimer and fibrinogen/fibrinogen-degradation products.

21. As a solution thereto, the claims at issue propose a monoclonal antibody displaying reactivity with D-dimer and other cross-linked fibrin derivatives and non-reactivity with fibrinogen or fibrinogen-degradation products inclusive of fragment D and fragment E (cf. claim 1 for non-AT States and for AT) as well as assay procedures making use of it (cf. claim 15 for non AT-States). The description indicates how such a monoclonal antibody can be prepared and provides examples of specific monoclonal antibodies which have

been obtained.

22. The finding of an antibody reacting exclusively with the crosslinked fibrin derivatives, and thus displaying the reactivity features recited in claim 1, was for the skilled person an obvious desideratum. However, the question here is whether the skilled person in the light of quoted prior art documents would have reasonably expected to be able to prepare it. In the board's view, documents (1), (5) and (21), which deal with polyclonal antibodies, did not foster his or her expectations in this respect as all of them indicated that further work was necessary in an area where the achievement of a result was by no means certain (cf. document (1), "Discussion", in particular the last two paragraphs; document (5), "Discussion", in particular the last paragraph; document (21) "Discussion"). An obvious option for the skilled person was to go to the monoclonal antibody technology as done in document (2) (or document (4)). However, also the disclosure in the latter documents would not have fostered the expectations of the skilled person who would have realised from the results reported therein that obtaining a monoclonal antibody reactive only for the crosslinked fibrin derivative was not a straightforward matter. In view of this, the use in document (2) of a booster in the protocol for the production of monoclonal antibodies would have gone unnoticed. It is in any case observed that such boosting step was not carried out in the same manner as described in the patent in suit as the same early fibrin degradation products were used both for the first immunisation and for the subsequent boosting.

23. Thus, in the board's view, the skilled person would not have reasonably expected, on the basis of the quoted prior art documents, taken alone or in combination, to be able to isolate a hybridoma secreting an antibody having the property of the monoclonal antibody of claim 1 (non-AT States and AT) at issue. Furthermore, nothing in the art provided any hints towards the particular immunisation protocol described in the patent in suit which, as stated, facilitated such an endeavour.

24. For these reasons, the monoclonal antibody of claim 1 for non-AT States as well as its method of preparation (cf. claim 1 for AT) involve an inventive step. For obvious reasons, the same finding applies to all other claims in the two versions for non-AT States and AT, as they all refer to methods of use of the said monoclonal antibody.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to maintain the patent on the basis of the following documents:

   (a) claims 1 to 16 for all designated contracting States except AT, and claims 1 to 16 for AT, submitted during oral proceedings as main request; and

   (b) description as granted.

The Registrar: The Chairperson:

U. Bultmann U. M. Kinkeldey