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Datasheet for the decision of 14 November 2006

Case Number: T 0035/05 - 3.3.08

Application Number: 93114141.0

Publication Number: 0585939

IPC: C12N 15/13

Language of the proceedings: EN

Title of invention:
TNF ligands

Patentee:
YEDA RESEARCH AND DEVELOPMENT Co. Ltd.

Opponent:
Genentech, Inc.

Headword:
TNF ligands/YEDA

Relevant legal provisions:
EPC Art. 123(2), 54(2), 83
EPC R. 88

Keyword:
"Main request - allowability of disclaimer - no"
"Auxiliary request - novelty - sufficiency of disclosure - yes"

Decisions cited:
G 0001/03, T 0019/90, T 0182/89

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0035/05 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 14 November 2006

Appellant I: (Patent Proprietor)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 23 November 2004 concerning maintenance of European patent No. 0585939 in amended form.**

Composition of the Board:

Chairman: L. Galligani
Members: F. Davison-Brunel
C. Heath

Summary of Facts and Submissions

I. European patent EP-A-0 585 939 with the title "TNF ligands" was granted on the basis of the European patent application No. 93 114 141.0 with twenty four claims. Granted claims 1 and 22 read as follows:

"1. A ligand to a member of the tumor necrosis factor/nerve growth factor (TNF/NGF) receptor family which binds to the region of the C-terminal cysteine loop of such a receptor and which is inhibitory to the signaling for the cytocidal effect of said receptor, wherein the cysteine loop includes the amino acid sequence cys-163 to thr-179 in the p75 TNF-R (Fig.5), or a corresponding C-terminal cysteine loop in another member of the TNF/NGF receptor family.

22. Use of a ligand according to any one of claims 1 to 12 or an anti-idiotypic antibody according to claim 20 for the preparation of a pharmaceutical composition for increasing the inhibitory effect of a soluble receptor of the TNF/NGF receptor family."

II. An opposition was filed under Article 100(a) and (b) EPC (in particular, lack of inventive step and of industrial applicability, insufficiency of disclosure). At oral proceedings before the opposition division, the patent proprietor requested the introduction of a new document in the proceedings (document (13); see infra) and amended claim 1 of the main request (granted claim 1) by addition of the following disclaimer: "with the proviso that the ligand is not the monoclonal antibody No.70-2 which was deposited with the deposit number CNCM I-928." This disclaimer was found allowable

under Article 123(2) EPC, yet the opposition division nonetheless concluded that amended claim 1 lacked novelty as not all subject-matter had been disclaimed which ought to have been. The main request was, thus, refused. The first auxiliary request was rejected for lack of sufficient disclosure. The patent was maintained on the basis of the second auxiliary request then on file.

III. Both the patentee and the opponent filed appeals, paid the appeal fees and submitted statements of grounds of appeal. Appellant I's (patentee's) statement of grounds of appeal was accompanied by a new main request and two auxiliary requests.

IV. Each appellant filed further submissions in response to the other's statement of grounds of appeal. Appellant I's submissions were accompanied by a main request and six auxiliary requests to replace the requests on file.

V. The board sent a communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal, indicating its preliminary, non binding-opinion.

VI. Both parties filed submissions in answer to this communication. Appellant I's submissions filed on 13 October 2006 were accompanied by a new main request, three auxiliary requests to replace the requests previously on file and eight new documents.

Claim 1 of the **main request** read as follows:

"1. A ligand to a member of the tumor necrosis factor/nerve growth factor (TNF/NGF) receptor family

which binds to the region of the C- terminal cysteine loop of such a receptor and which is inhibitory to the signaling for the cytocidal effect of said receptor without blocking the binding of TNF or the respective natural ligand to the receptor, wherein the cysteine loop includes the amino acid sequence cys-163 to thr-179 in the p75 TNF-R (Fig.5), or a corresponding C-terminal cysteine loop in another member of the TNF/NGF receptor family,
wherein said ligand is
(a) a protein or a peptide, or
(b) an antibody, a peptide derived therefrom, or a Fab fragment, salt or mutein of said antibody;

with the proviso that the ligand is not the monoclonal antibody No.70-2 which was deposited with the deposit number CNCM I-928 or an Fab fragment, salt or mutein thereof, *[sic]*"

VII. At oral proceedings which took place on 14 November 2006, Appellant I replaced all auxiliary requests on file by a new auxiliary request. Claims 1, 7 and 10 of this request read as follows:

"1. Use of a ligand to a member of the tumor necrosis factor/nerve growth factor (TNF/NGF) receptor family which binds to the region of the C- terminal cysteine loop of such a receptor and which is inhibitory to the signaling for the cytocidal effect of said receptor without blocking the binding of TNF or the respective natural ligand to the receptor, wherein the cysteine loop includes the amino acid sequence cys-163 to thr-179 in the p75 TNF-R (Fig.5), or a corresponding C-terminal cysteine loop in another member of the TNF/NGF

receptor family, for the preparation of a pharmaceutical composition for the treatment of septic shock, cachexia, graft-versus-host disease and autoimmune diseases, in particular rheumatoid arthritis, wherein said ligand is an antibody, a peptide derived therefrom, or a salt or mutein of said antibody.

7. The use according to any one of claims 1 to 3, wherein the ligand comprises the scFv of monoclonal antibody No. 32 (CNCM I-1358) or 70 (CNCM I-928).

10. A ligand as defined in claim 1 comprising the scFv of monoclonal antibody No.32 (CNCM I-1358).

Dependent claims 2 to 6, 8 and 9 were directed to further features of the claimed use. Claims 11 and 12 related to specific ligands and claims 13-14, 15-16 and 17-18 respectively related to DNA molecules, replicable expression vehicles, host cells comprising DNAs encoding the ligands of claims 10 to 12. Claims 19 and 20 respectively related to a process for the production of said ligands and to pharmaceutical compositions comprising them. Claim 21 was directed to the ligands of claims 10 to 12 carrying polyethylene glycol side chains.

VIII. The documents which are mentioned in this decision are the following:

(1): Locksley, R.M. et al., Cell, Vol. 104, pages 487 to 501, 23 February 2001;

(3): Naismith, J.H. and Sprang, S.R., Trends in Biochemical Sciences, Vol. 23, No. 2, pages 74 to 79, February 1998;

(10): Marsters, S.A. et al., The Journal of Biological Chemistry, Vol. 267, No. 9, pages 5747 to 5750, 26 March 1992;

(12): Bodmer, J.L. et al., Trends in Biochemical Sciences, Vol. 27, No. 1, pages 19 to 26, January 2002;

(13): EP-A-0 398 327.

IX. Appellant's I arguments in writing and during oral proceedings insofar as relevant to the present decision may be summarised as follows:

Main request; claim 1
Allowability of disclaimer under Article 123(2) EPC

The monoclonal antibody (mAb) No. 70.2 had been characterised as **prior art** in the patent in suit, in column 2, section [0007], where reference was made to document (13) - which disclosed it - and in column 17, section [0109], where it was defined, in particular, by the date of its deposit which preceded the priority date. It was, thus, obvious that its inclusion in granted claim 1 was fully inadvertent. The situation was equivalent to those dealt with under Rule 88 EPC which allowed for the correction of obvious errors. The disclaimer amounted to such an allowable correction.

As for the disclaimer per se, it did not fall within any of the categories of disclaimers found unallowable under Article 123(2) EPC in the Enlarged Board of Appeal decision G 1/03 (OJ EPO 2004, 413). Indeed, document (13) was an accidental anticipation within the meaning given to this expression in the decision. What document (13) was concerned with was the isolation of antibodies binding to the soluble form of the TNF receptor (TBP-II; example 4). It showed that polyclonal antibodies interfered with the binding of TNF to the receptor, the properties of monoclonal antibodies in this respect had not been characterised. On the basis of this technical teaching, the skilled person would conclude that the antibodies were **TNF** antagonists. In contrast, the principle underlying the present invention was to isolate **TNF receptor** antagonists as the claimed antibodies did not prevent the binding of TNF to the receptor, yet inhibited the cytocidal effect of this receptor.
The possibility that antibodies with such properties would exist was not even suggested in document (13) which did not provide any suitable starting point to the present invention. Accordingly, document (13) had to be regarded as an accidental anticipation which could be disclaimed in accordance with the findings in G 1/03 (supra) without offending the requirements of Article 123(2) EPC.

Auxiliary request; claim 1
Article 54 EPC; novelty

The disclosure of document (13) as regards the properties of the antibodies therein disclosed was found on page 6, lines 36 to 42. This paragraph made it

completely clear that for any one of the antibodies, the multivalent form, i.e. the antibody per se, was being able **to mimic** the effects of TNF. In contrast, the patent in suit disclosed monoclonal antibodies which were able **to inhibit** the cytotoxic effect of TNF-R in the presence of TNF. These also had the property that they did not prevent the binding of TNF to TNF-R. They represented an hitherto undisclosed selection amongst all antibodies capable of binding to the TNF receptor.

Document (13) did not mention mAbs for treating the diseases now listed in claim 1. More specifically, the properties of mAb No.70.2 had not been investigated nor, of course, had its potential uses been described.

Claim 27 of document (13) which encompassed the use of antibodies in the treatment of conditions wherein the effects of TNF were to be antagonised was in clear contradiction to the description. It did not reflect any true technical teaching and, therefore, it could not be relevant to novelty.

As for appellant II's argument that the subject-matter of claim 1 was not novel because it encompassed monovalent forms of antibodies such as disclosed in document (13) - as shown by the fact that claim 10 which was dependent on claim 1 related to scFv antibodies, it did not hold because document (13) itself did not disclose an scFv antibody.

For these reasons, the subject-matter of claim 1 was novel and the auxiliary request fulfilled the requirements of Article 54 EPC.

Article 83 EPC; sufficiency of disclosure

Appellant II's argument that it may not be possible to raise antibody ligands such as claimed against all the members of the TNF/NGF family of receptors because, as shown in documents (10) or (12), they were structurally diverse and recognized different natural ligands was a mere assumption without substance.

As for the identification of the epitope relevant for raising the now claimed antibody ligands - the "corresponding C-terminal cysteine loop" in all of the receptors - it could be carried without undue burden by aligning the primary structures of the different receptors. In fact, it was readily apparent from document (3) (Table III) or document (12) (Figure 1) that the loop corresponded to the B1 module which was present in most of the receptors.

In the same manner, it was wrong to argue that a ligand such as claimed would not be determinative of the overall signaling function of a receptor because this function was dependent on the presence of a death domain in the intracellular part of the receptor, whereas not all receptors had this death domain. Indeed, TNF-R itself did not carry a death domain but clearly signaled toxicity. Furthermore, the later document (1) showed that the presence of a death domain in the receptor was not absolutely required for this receptor to modulate cellular death.

Appellant II had failed to provide any experimental proof that the extrapolation from "ligands to TNF-R" to

"ligands of any member of the TNF/NGF receptor family" posed a problem under Article 83 EPC.

X. Appellant II 's (opponent's) arguments in writing and during oral proceedings insofar as relevant to the present decision may be summarised as follows:

Main request; claim 1
Allowability of the disclaimer under Article 123(2) EPC

Appellant I's argument that the disclaimer should be allowed because it amounted to the correction of an obvious error under Rule 88 EPC was flawed. The passage in column 2 of the patent in suit which made reference to document (13) established the prior art relating to polyclonal antibodies; it had nothing to do with monoclonal antibodies such as mAb No.70.2. Furthermore, the rest of the patent unambiguously defined mAb No.70.2 as an example of the claimed invention, the information as regards its deposit (column 18) being given in this context. Thus, no discrepancy existed between the prior art such as described in the patent in suit and the subject-matter of claim 1, which could be taken as evidence that an obvious error had occurred which it would be possible to correct under Rule 88 EPC.

Even if it was concluded that it was an obvious error that claim 1 comprised the mAb No.70.2, it remained that the disclaimer per se was not allowable under Article 123(2) EPC because document (13) was not an accidental anticipation within the meaning given to the expression of G 1/03 (supra), i.e. its teaching was not so unrelated and remote from the claimed invention that

the person skilled in the art would never have taken it into consideration when making the invention. In fact, document (13) related to the same receptor as in the patent in suit and disclosed antibodies which bound to this receptor.

For these reasons, the disclaimer was not allowable and the main request failed to fulfil the requirements of Article 123(2) EPC.

Auxiliary request; claim 1
Article 54 EPC; novelty

Document (13) disclosed antibodies against the soluble TNF receptor (TBP-II) which may be used as pharmaceutical agents for blocking the effect of TNF on cells (page 3, lines 14 and 15 and page 6, lines 36 to 42). Further, claim 27 therein was directed to the medical use of said antibodies in the treatment of conditions wherein effects of TNF had to be antagonized. Furthermore, document (13) disclosed conditions caused by an overproduction of TNF, listing such conditions as including septic shock, cachexia and the like... (page 7, lines 23 and 24). Thus, document (13) disclosed a use which was identical to the claimed use (claim 1).

Claim 1 also lacked novelty because it encompassed monovalent antibodies as could be understood from the fact that claim 10 was at the same time dependent on claim 1 and relating to a monovalent antibody in the form of an scFv antibody. As already above mentioned, monovalent antibodies and their use (as now claimed)

were already known from document (13), page 6, line 40 together with page 7, lines 22 to 24.

The auxiliary request failed to fulfil the requirements of Article 54 EPC.

Article 83 EPC; sufficiency of disclosure

The scope of claim 1 was unduly broad because it comprised ligands to any receptor of the TNF/NGF family of receptors.

Documents (10) or (12) taught that the mere presence of cysteine-rich domains in all receptors of the family needed not provide similarity of structure and function but that, on the contrary, variations in the number and type of these domains conferred heterogeneity upon the family. It was a fact that different receptors had different topologies which, in turn, meant that they would recognize different natural ligands (corresponding to, but different from TNF or NGF). There was, thus, no reason why appellant I's findings as regard ligands to the p75 TNF receptor could be extended to these other receptors.

Furthermore, document (3) highlighted that at the relevant date, the three dimensional structure of the receptors had not yet been determined. To the extent that the knowledge of this structure would be necessary to identify the loops corresponding to the C-terminal cysteine loop of p75 TNF-R, it would be undue burden to put the claimed subject-matter into practise.

Finally, even if ligands having the claimed properties and binding to other receptors could be isolated, it did not mean that they would have the same effects on the overall signaling function of the receptor - i.e. that the claimed use could be implemented. For instance, the cytocidal effect of the p75 receptor depended on the presence of a death domain in the intracellular part of this receptor. In contrast, some other receptors of the TNF/NGF family of receptors lacked a death domain (e.g. OX40 or CD40, Fig. 1 of document (12)). Accordingly, ligands to these receptors, even if they could be isolated, would not be expected to lead to an inhibition of a cytocidal effect. Otherwise stated, they would be unsuitable for the claimed use.

For these reasons, the requirement of sufficiency of disclosure was not fulfilled.

XI. Appellant I requested that the decision under appeal be set aside and that the patent be maintained on the basis of the Main Request comprising claims 1 to 17, filed on 13 October 2006, or on the basis of Auxiliary Request 1 comprising claims 1 to 21 filed in the oral proceedings.

Appellant II requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

Main request, claim 1
Article 123(2)EPC; allowability of the disclaimer

1. The disclaimer was introduced in claim 1 in order that it does not comprise the mAb No.70.2 disclosed in document (13), this monoclonal antibody also being described as part of the now claimed invention. Document (13) is a European patent application with a publication date (22 November 1990) earlier than the earliest priority date of the patent in suit (3 September 1992). It is, thus, relevant to the assessment of novelty under Article 54(2) EPC.

2. The disclaimer as such is not found in the application as filed. Accordingly, the criteria to be applied for assessing its allowability under Article 123(2) EPC are those enounced in point 2.2 of the Enlarged Board decision G 1/03 (OJ EPO 2004, 413) relating to the conditions in which a piece of prior art relevant under Article 54(2) EPC may be disclaimed. In sub-paragraph 2.2.2 of this decision, it is established that it is allowable to disclaim such a piece of prior art if it may be considered as an accidental anticipation.

3. Document (13) describes a soluble form of the TNF receptor (TNF-R) and the isolation of antibodies there against. It teaches on page 6, lines 36 to 42 that these antibodies will either inhibit TNF activity, i.e. the cytocidal effects of TNF-R when bound to TNF, or mimic the effects of TNF depending on whether they are in a monovalent or multivalent form. In comparison, the present invention relates to antibodies to the soluble

form of TNF-R which are, in particular, inhibitory to the cytocidal effect of TNF-R.

4. The board has no doubts that the skilled person wanting to isolate anti-TNF-R antibodies would never disregard a document which discloses the isolation of anti-soluble TNF-R antibodies and, for this reason, has no hesitation in concluding that document (13) is not an accidental anticipation within the meaning given to the expression in G 1/03 (supra), namely a disclosure so unrelated and remote that the person skilled in the art would never have taken it into consideration when working on the invention. Corroborating evidence thereto can be found in the fact that document (13) is mentioned in the "Background of the invention" part of the patent in suit (EP-A-0 398 327, section [007]], which clearly shows that Appellant I did consider the document before making the invention.

5. To justify that document (13) was an accidental anticipation, Appellant I analysed in great depth the mechanisms by which the antibodies of document (13) and the presently claimed antibodies were acting upon TNF-R, concluding from the observed differences that document (13) would not even have suggested the existence of the latter antibodies and that, therefore, it was an accidental anticipation. This argument is not found convincing if only because the skilled person would not have known that the recognition patterns were different before the invention was completed and, also, of course, because reaching the conclusion that they are different necessarily implies a comparison which requires that document (13) be taken into account.

6. A further argument made by Appellant I was that it did not make sense that the patent would be filed with a claim comprising subject-matter which was, at the same time, disclosed as being prior art (Background of the Invention, col. 2, section [007] and col. 17, section [0109]). Therefore, the inclusion of mAb No.70.2 in the claim had evidently been an obvious mistake which it should be allowed to correct as other kinds of obvious mistakes were correctable under Rule 88 EPC. The board need not take position on whether or not an obvious mistake occurred because even if it did and even if it can be corrected, it does not change the fact that the means for correction must fulfil the requirements of the European Patent Convention and this is not the case for the present disclaimer.

7. The main request is refused for not complying with Article 123(2) EPC.

Auxiliary request
Articles 123(2)(3) and 84 EPC; formal requirements

8. The subject-matter of claim 1 has its basis in the passage bridging column 8, line 54 to column 9, line 3 of the application as filed together with the passage bridging column 2, lines 21 to 54 to column 3, line 3, alternatively together with claim 24.
The scope of the claim is narrower than that of the corresponding granted claim 22 (see Summary of Facts and Submissions, section I) as the relevant diseases have been identified and the ligand has been limited to an antibody, peptide derived therefrom, a salt or mutein of said antibody.

Claim 1 is clearly worded and the information as regards the deposit numbers of the relevant antibodies added in claims 7 and 10 makes unambiguous which antibodies are contemplated for the claimed use. The requirements of Article 123(2)(3) and 84 EPC are fulfilled.

Article 54 EPC; novelty

9. The teachings of document (13) have been argued to be detrimental to the novelty of the subject-matter of claim 1. The main thrust of this disclosure is towards the isolation of a soluble form of the TNF receptor called TBP-II. It is taught on page 2, lines 2 to 4 that TBP-II is capable of inhibiting the cytotoxic effect of TNF and on page 7, lines 22 to 24 that TBP-II may be made into pharmaceutical compositions to treat

"any condition where there is an overproduction of endogenous TNF, such as in cases of septic shock, cachexia, graft-versus-host reactions, autoimmune diseases like rheumatoid arthritis...".

The document also discloses on page 3, lines 14 to 16 the isolation of

"antibodies specific for TBP-II and F(ab) fragments thereof which may be used ... in pharmaceuticals both for inhibiting the toxic effects of TNF and for mimicking TNF beneficial effects on cells.".

On page 6, lines 37 to 42, the mode of action of these antibodies is further defined:

"These antibodies provide a new approach for the modulation of the TNF activity, and may be used both to inhibit and to mimic effects of TNF on specific subsets of cells, depending on the molecular form of the antibodies, specifically on their valence: monovalent forms of the antibodies (e.g. F(ab) fragments) being inhibitory and multivalent forms being able to mimic at least part of the effects of TNF."

10. Amongst the antibodies intended to illustrate the invention is mAb No.70.2 which was deposited as CNCM-I 928. There is no experimental evidence provided as regards its functional properties. The best which can be done is, thus, to assume that it would exhibit the properties which are generically disclosed i.e. that it would mimic the effects of TNF. Furthermore, there is no explicit disclosure that mAb No.70.2 - or indeed any of the other isolated antibodies - may be of use for treating septic shock, cachexia ... To read into document (13) that it will do so assumes that the antibody would act like TBP-II. The combined teaching on page 2 that TBP-II acts as an inhibitor and on page 6, that it is the monovalent form of the antibodies which is inhibitory makes it unambiguous that this assumption is wrong as regards the antibody per se (multivalent).

11. In summary, document (13) lacks the characterisation of mAb No.70.2, it fails to provide an explicit disclosure as regards the medical use to be made of the mAbs and it teaches that as such, i.e. in a multivalent form, they would have the opposite effect from that needed for treatment. In the board's judgment, this disclosure

does not amount to a clear and unambiguous disclosure of a use such as now claimed.

12. It was also argued that claim 27 of document (13) directed, in particular, to "The antibody according to any one of claims 18 to 25 or F(ab) fragments thereof ...., for use in the treatment of conditions wherein effects of TNF, either endogenously formed or exogenously administered, are to be antagonized." together with the information on page 7 that septic shock, cachexia... were diseases involving an overproduction of TNF constituted an expressis verbis disclosure of the now claimed use. However, it is readily apparent that interpreting claim 27 as directed towards the use of monoclonal antibodies (multivalent) for antagonizing the effect of TNF is fully contradictory to the technical teaching provided in the description (page 6). The drafting of the claim encompassing **all** forms of antibodies for treating **each of** the opposite effects of TNF simply does not reflect the invention then described. Therefore, claim 27 does not have any bearing on the novelty of present claim 1.

13. Finally, the argument was made that present claim 1 could be understood as comprising monovalent antibodies at least in the form of scFv fragments (claim 10 dependent on claim 1) and, therefore, that the monovalent antibodies disclosed in document (13) would be novelty destroying for said claim 1. This argument is not convincing insofar as document (13) does not disclose monovalent antibodies in the form of scFv fragments.

14. For these reasons, novelty is acknowledged.

Article 83 EPC sufficiency of disclosure

15. No objections were raised as regards the feasibility of isolating ligands to the TNF receptor with the claimed properties, in the form of antibodies, peptides derived therefrom, salts and muteins thereof. The board is also of the opinion that these ligands could be obtained without undue burden on the basis of the information given in the patent specification.

16. In fact, lack of sufficient disclosure was argued in relation to the scope of the claim, namely that there was no technical evidence available that ligands could be isolated which would bind to the further members of the TNF/NGF family of receptors. An in depth study of document (10) as well as of documents (1), (3) and (12) (to be taken as experts documents) was carried out. The conclusions which were drawn therefrom were as follows:

- the receptors being widely diverse in terms of their sequences, they **may not** all give rise to antibodies such as claimed,

- **if** the tri-dimensional structure of the receptors was necessary to identify the region corresponding to the C-terminal cysteine rich loop in TNF-R (epitope), it would not be possible to raise the antibody ligand;

- some receptors did not carry an intracellular death domain, which domain was instrumental in triggering the cytocidal effect. One would not **expect** to be able to

raise antibodies against these receptors, which would inhibit the cytocidal effect.

17. In accordance with the case law (T 19/90, OJ EPO 1990, 476, point 3.3 of the decision), "the mere fact that a claim is broad is not in itself a ground for considering the application as not complying with the requirement of sufficiency of disclosure under Article 83 EPC. Only if there are serious doubts, substantiated by verifiable facts, may an application be objected to for lack of sufficient disclosure". Furthermore, the burden of proof is upon an opponent to establish that the skilled reader would be unable to reproduce the invention (T 182/89, OJ EPO 1991, 391).

18. No technical evidence was provided to show either that a ligand could **not** be obtained in respect of any one of the TGF/NGF receptors, or that a subcategory of receptors would **not** be suited for the isolation of antibodies such as claimed. Appellant I submitted that the epitope can be identified without undue burden on the basis of comparing the primary structures of the various receptors. Document (1) (page 494) teaches that the cytocidal effect on cells will be modulated by the members of the family which do not comprise a death domain.

19. For these reasons, and in the absence of any evidence to the contrary, the board concludes that the requirement of Article 83 EPC is fulfilled over the scope of the claim.

Article 56 EPC; inventive step

20. At oral proceedings, Appellant II indicated that its main concern as regard inventive step had been in relation to the much broader claim 1 of the main request including ligands in the form of proteins or peptides in general, and that it did not have any comments as regards the inventive step of the now claimed subject-matter. In the board's judgment, document (13) which is the closest prior art does not make it obvious that monoclonal antibodies such as now claimed, i.e. binding to a receptor of the TNF/NGF family of receptors without hindering TNF/NGF binding, could be isolated, and a fortiori, it does not make it obvious that these monoclonal antibodies may be of use in fighting such diseases as mentioned in the claim, by inhibiting cytoxicity. There is no other document on file which, when combined with document (13) would deprive the claimed subject-matter of inventive step. The requirements of Article 56 EPC are fulfilled.

Adaptation of the description

21. Appellant I proposed amendments to the description which were not objected to by appellant II. The board considers that those amendments result in an appropriate adaptation of the description to the claims of the auxiliary request and are in compliance with the requirements of Article 123(2) EPC.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted back to the previous instance with the order to maintain the patent in the form of Auxiliary Request I, with an amended description, both filed in the oral proceedings, and drawings as granted.

The Registrar The Chairman

A. Wolinski L. Galligani