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Datasheet for the decision of 23 February 2007

Case Number: W 0019/06 - 3.3.04

Application Number: PCT/EP2005/009968

Publication Number: WO 2006/029879

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Title of invention:
Anti-OX40L Antibodies

Applicant:
F. HOFFMANN-LA ROCHE AG

Headword:
Anti-OX40L Antibodies/HOFFMANN-LA ROCHE

Relevant legal provisions:
PCT Art. 17(3)(a)
PCT R. 13, 40, 68.3(c)
EPC Art. 154(3)
EPC R. 105(3)

Keyword:
"Admissiblity of the protest - (yes)"
"Lack of unity a posteriori"
"Partial reimbursement of additional search fees - (yes)"

Decisions cited:
-

Catchword:
-

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Case Number: W 0019/06 - 3.3.04

International Application No. PCT/EP2005/009968

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 23 February 2007

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Decision under appeal: **Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fees) of the European Patent Office (International Searching Authority) dated 19 January 2006.**

Composition of the Board:

Chair: U. Kinkeldey
Members: M. Wieser
T. Bokor

Summary of Facts and Submissions

I. International patent application No. PCT/EP2005/009986 having the title "Anti-OX40L Antibodies" was filed with forty-six claims.

Independent claims 1, 15, 22, 24, 40, 41, 43 and 45 read as follows:

"1. An antibody, characterized in that said antibody binds OX40L, contains a Fc part derived from human origin and does not bind complement factor C1q.

15. An antibody, characterized in that said antibody binds OX40L and that the antibody comprises a variable region combination independently selected from the group consisting of combinations

a) the light chain variable domain defined by amino acid sequence SEQ ID NO:1 and the heavy chain variable domain defined by SEQ ID NO:2;
b) the light chain variable domain defined by amino acid sequence SEQ ID NO:3 and the heavy chain variable domain defined by SEQ ID NO:4;
c) the light chain variable domain defined by amino acid sequence SEQ ID NO:5 and the heavy chain variable domain defined by SEQ ID NO:6;
d) the light chain variable domain defined by amino acid sequence SEQ ID NO:7 and the heavy chain variable domain defined by SEQ ID NO:8;
e) the light chain variable domain defined by amino acid sequence SEQ ID NO:9 and the heavy chain variable domain defined by SEQ ID NO: 10;

f) the light chain variable domain defined by amino acid sequence SEQ ID NO: 11 or 16 and the heavy chain variable domain defined by SEQ ID NO:12;
g) the light chain (V_L) variable domain defined by amino acid sequence SEQ ID NO:1 and the heavy chain (V_H) variable domain defined by SEQ ID NO:17;
h) the light chain variable domain defined by amino acid sequence SEQ ID NO:18 and the heavy chain variable domain defined by SEQ ID NO:19;
i) the light chain variable domain defined by amino acid sequence SEQ ID NO:1 and the heavy chain variable domain defined by SEQ ID NO:20.

22. An antibody binding to OX40L, comprising a variable light chain and a variable heavy chain, characterized in that the variable heavy chain comprises CDR3 selected from SEQ ID NOs : 33-38 and/or the variable light chain comprises CDR3 selected from SEQ ID NOs : 51-57.

24. An antibody, characterized in that it is produced by a cell line selected from the group consisting of cell lines
hu-Mab<hOX40L>LC. 001 , hu-Mab<hOX40L>LC005,
hu-Mab<hOX40L>LC.010, hu-Mab<hOX40L>LC019,
hu-Mab<hOX40L>LC029 and hu-Mab<hOX40L>LC033.

40. Method of modifying the initial amino acid sequence of an parent antibody heavy chain CDR selected from the group consisting of SEQ ID NOs: 21-38 and/or an parent antibody light chain CDR selected from the group consisting of SEQ ID NOs: 39-57, characterized in providing a nucleic acid encoding said initial amino acid sequence, modifying said nucleic acid in that one

amino acid is modified in heavy chain CDRl, 1-2 amino acids are modified in heavy chain CDR2, 1-2 amino acids are modified in heavy chain CDR3, 1-3 amino acid are modified in light chain CDRl, 1-3 amino acids are modified in light chain CDR2, and/or 1-3 amino acids are modified in light chain CDR3, expressing said modified CDR amino acid sequence in an antibody structure, measuring whether said antibody binds to OX40L with a K_D of less than 10^{-8} M and selecting said modified CDR if the antibody binds to OX40L with a K_D of less than 10^{-8} M.

41. An antibody, characterized in that said antibody binds OX40L, being of human IgGl class and comprises as γ heavy chain SEQ ID NO: 58, 62 or 66.

43. An antibody, characterized in that said antibody binds OX40L, being of IgGl class containing mutation L234A/L235A and comprises as γ heavy chain SEQ ID NO: 59, 63 or 67.

45. An antibody, characterized in that said antibody binds OX40L, being of IgG4 class containing mutation S228P comprises as γ heavy chain SEQ ID NO: 60, 64 or 68."

II. The European Patent Office (EPO), acting in its capacity as International Searching Authority (ISA) under Article 16 PCT and 154 EPC, informed the Applicant in a communication of 19 January 2006 (Form PCT/ISA/206 (April 2005)) that the application did not comply with the requirement of unity of invention (Rules 13.1 to 13.3 PCT) and invited the Applicant to

pay five additional search fees, in accordance with Article 17(3)(a) PCT and Rule 40.1 PCT.

The invitation was reasoned as follows (see Form PCT/ISA/206 (extra sheet)):

"This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1–14, 16–21(partly), 25–39(partly), 43–46

characterised by the common subject matter of claim 1, i.e. an antibody characterised in that it binds OX40L, contains a Fc part derived from human origin and does not bind complement factor C1q,
characterised by the common subject matter of claim 43, i.e. an antibody that binds OX40L, is of human IgG1 class and contains mutation L234A/L235A and comprises as gamma heavy chain SEQ ID NOS: 59, 63 or 67,
characterised by the common subject matter of claim 45, i.e. an antibody that binds OX40L, is of human IgG4 class and contains mutation S228P and comprises as gamma heavy chain SEQ ID NOS: 60, 64 or 68.

2. claims: 15, 16–21(partly), 25–39(partly)

characterised by the common subject matter of claim 15, i.e. an antibody characterised in that said antibody binds OX40L and comprises a variable region combination independently selected from the groups of sequences of variable regions provided in the list under points a–i. which relate to SEQ ID NOS: 1–12, 16–20.

3. claims: 22, 23, 25—39(partly)

characterised by the common subject matter of claim 22, i.e. an antibody binding OX40L comprising a variable light chain and variable heavy chain, characterised in that the variable heavy chain comprises CDR3 selected from a list of SEQ ID NOS: 33—38 and/or the variable light chain comprises CDR3 selected from SEQ ID NOS: 51—57.

4. claims: 24—35(partly), 39(partly)

characterised by the common subject matter of claim 24, i.e. an antibody that is produced by a cell line selected from the group provided in the claim.

5. claim: 40

directed to a method of modifying the initial amino acid sequence of an parent antibody heavy chain CDR characterised by SEQ ID NOS: 21—38 and/or an parent antibody light chain CDR characterised by SEQ ID NOS: 39—57, by modifying encoding nucleic acid sequence so as to modify 1 amino acid in heavy chain CDR, 1—2 amino acids in heavy chain CDR2, 1—2 amino acids in heavy chain CDR3, 1—3 amino acids in light chain CDR1, 1—3 amino acids in light chain CDR2 and/or 1—3 amino acids in light chain CDR3, expressing said modified sequences in an antibody structure and measuring whether said antibody binds to OX40L with a given value of KD.

6. claims: 41, 42

characterised by the common subject matter of claim 42, i.e. an antibody that binds OX40L, is of human IgG1 class and comprises gamma heavy chain SEQ ID NOS: 58, 62 or 66."

III. The ISA pointed out that the feature of claim 1 according to which the claimed antibody "contains a Fc part derived from human origin and does not bind complement factor C1q" was equivalent to the technical feature disclosed in claim 43 that the antibody is "of IgG1 class containing mutation L234A/L235A" and to the feature disclosed in claim 45 that the antibody "is of IgG4 class". Therefore the subject-matter of claims 43 to 46 was classed with the first invention identified (claims 1-14, 16-21(partly) and 25-39(partly); see section II above).

Moreover, the ISA held that the claims classed with inventions (2), (3), (5) and (6), (see section II above), which referred to amino acid sequences defined by their respective SEQ ID NO, "...do not have any SEQ ID NOS in common, hence said SEQ ID NOS do not represent any common technical features amongst said groups of subject-matters." Since these claims and also the claims classed with invention (4) were not found to refer to antibodies characterised by containing a Fc part derived from human origin and by not binding complement factor C1q, "...there is only one technical feature in common for all the claims: an antibody characterised in that it binds OX40L."

Each of the six inventions identified by the ISA was found to represent a separate solution to the underlying technical problem, namely the provision of anti-OX40L antibodies and methods for their production. No other problem forming a basis for a single general inventive concept in the sense of Rule 13.1 PCT could be seen.

However, the provision of anti-OX40L antibodies did not represent a contribution over the prior art as such antibodies were already disclosed in document

(1) The Journal of Immunology, vol.166, no.3, 2001, pages 2108 to 2115.

As no other technical feature could be identified that could be considered as a special technical feature within the meaning of Rule 13.2 PCT, and as the application, moreover, did not allow to group together any of the antibodies of inventions (2) to (6) (see section II above) to claims related to six different inventions.

IV. The communication of 19 January 2006 also contained the results of the partial international search, wherein document (1) was cited and its abstract was indicated as relevant passage.

V. With letter dated 27 January 2006 the Applicant requested the debiting of five additional search fees from his deposit account. The payment was made under protest and it was requested that the fees should be reimbursed. The protest was reasoned as follows:

Invention (2), as identified by the ISA, referred to antibodies against OX40L comprising the variable reasons of antibodies LC.001, LC.005, LC.010, LC.019, LC.029, LC.033, LC.059, LC.060 and LC.063.

Invention (3) referred to anti-OX40L antibodies comprising the CDR regions of these antibodies which could be easily recognised by a sequence comparison of the SEQ ID NOS referred to in the claims.

Invention (4) referred to the deposited antibodies LC.005, LC.010, LC.019, LC.029, LC.033.

Invention (5) was directed to a method of modifying the initial amino acid sequence of a parent antibody CDR selected from the CDRS of the nine specific antibodies mentioned above (see invention (2)).

Invention (6) referred to sequences of antibodies LC.001, LC.005 and LC.060.

Moreover, also the subject-matter of claims 43 to 46, which the ISA grouped with invention (1), referred to sequences of antibodies LC.001, LC.005 and LC.060.

VI. On 23 June 2006 the ISA invited the Applicant to pay the protest fee according to Rule 40.2 PCT (see Form PCT/ISA/228 (April 2005)). Together with the invitation, in the Annex of this Form, the ISA communicated to the Appellant the following results of a review of the protest:

The Applicant in the letter setting out the reasoning for his protest had neither provided arguments with

regard to invention (1) as defined by the ISA, nor with regard to the prior art cited by the ISA. There was also no discussion of the objective technical problem underlying the invention.

It was not clear from a reading of said letter whether the reimbursement of all additional search fees was requested.

Applicant's argument that all claims grouped by the ISA with inventions (2) to (6), plus claims 43 to 46, referred to nine antibodies identified by "LC numbers" was considered to be of no value, as "no common special technical feature of said antibodies was identified in the letter from the applicant. The antibodies are known from the description to be monoclonal and to bind OX40L in a specific manner." As antibodies having these technical features were known from the disclosure in document (1), the features did "not fulfil the requirement of the special technical feature of Rule 13.2 PCT, and as such, cannot form the unitary link amongst the groups of inventions identified by the ISA."

Moreover, the independent claims of the application were not restricted to the antibodies defined by the "LC numbers", but also referred to antibodies characterised by combinations of sequence elements derived from these antibodies, like variable regions or CDRS.

Therefore, the invitation to pay five additional search fees was justified. No refund of these fees was ordered.

VII. With letter dated 14 July 2006 the Applicant requested the debiting of the protest fee from his deposit account.

In said letter he submitted further arguments wherein he held that the nine anti-OX40L antibodies (LC.001, LC.005, LC.010, LC.019, LC.029, LC.033, LC.059, LC.060 and LC.063), which were the subject-matter of all claims grouped by the ISA with inventions (2) to (6), were antibodies against human OX40L. Contrary to this document (1) referred to a neutralizing monoclonal antibody against murine OX40L.

Reasons for the decision

The Protest-procedure according to Article 17(3)(a) and Rule 40 PCT in general

1. The International application was filed on 16 September 2005. Therefore, in the present case, the 1 April 2005 version of the Regulations under the PCT is applicable.

2. According to Rule 40.2(c) PCT an Applicant may pay additional search fees, required by the ISA under Rule 17(3)(a) PCT, under protest. Such protest shall then be examined by **a review body constituted in the framework of the ISA**, which to the extent that it finds the protest justified, shall order the total or partial reimbursement of the additional fees to the Applicant.

3. According to Rule 40.2(e) PCT the examination of such protest **may** be subjected by the ISA to the payment of a

protest fee. In this case the Applicant, according to Rule 40.1(iii) PCT, shall pay this fee within one month of being invited to do so. According to Rule 40.1(ii) this invitation shall be made together with the invitation to pay the additional search fees.

The implementation of the Protest-procedure by the EPO acting as ISA

4. Due to its filing date the present application has to be treated by the EPO acting as ISA according to the procedure set out in the "Notice from the European Patent Office dated 1 March 2005 concerning the protest procedure under the PCT (lack of unity)" (OJ, EPO 3/2005, 226 - hereinafter: Notice).

5. According to the Notice, in derogation from Rule 40.1(iii) PCT, the invitation to pay the protest fee is not made together with the invitation to pay additional search fees, but at a later point in time. Pending entry into force of the EPC as revised in 2000, where additional fees for international search or international preliminary examination are paid under protest according to Rule 40.2(c) or Rule 68.3(c) PCT, the EPO will continue to subject any invitation to pay such additional fees to an internal review, prior to submission of the protest to the Board of Appeal. The Notice further states that this review is in the nature of a service from the EPO and the previous procedure described in Rule 105(3) EPC - which provision implemented for the EPO the protest procedure according to the earlier version of the PCT - "is no longer applicable". In order to allow the Applicant to consider the result of the review the EPO will, by way

of concession, not require payment of the protest fee until one month after the date of notification of the review to the applicant (see point (3) of the Notice).

It must be noted that the formulation in the Notice that the previous procedure according to Rule 105(3) EPC is "no longer applicable" is quite misleading, when considering the fact that the Notice actually confirms that the previous procedure in fact will be further applied. What is probably meant is that even though the present version of Rule 40.2(e) PCT does not explicitly foresee an interlocutory revision before the final decision on the protest - and in this sense the procedure according to Rule 105(3) EPC is indeed no longer considered as a **mandatory provision** which finds its legal basis in the PCT - , such an interlocutory revision is actually performed by the EPO acting as ISA.

6. When following this procedure, the Applicant is invited to pay the protest fee only after having received the communication of the ISA, in which he is informed of the result of the "internal review". The time limit for the payment of the protest fee starts at the date of said communication. In the present case this invitation to pay the protest fee was given in the "Form PCT/ISA/228 /April 2005)", (see especially points (1) and (2) of this Form).

7. Thus, the EPO acting as ISA does not strictly follow all of the provisions of Rule 40.1 PCT. However, it is clear that the application of a less strict procedure that derogates from the exact wording of the PCT is **to**

the advantage of the Applicant (see point (3) of the Notice, last sentence: "... by way of concession, ...").

8. According to Rule 40.2(e) PCT a protest shall be considered not to have been made, where an Applicant has not, within the time limit under Rule 40.1(iii) PCT, paid the required protest fee. However, it has to be noted that Rule 40.1(iii) PCT not only lays down the time limit for the payment of the protest fee, but also the obligation of the ISA to call the Applicant's attention to his liability to pay this fee and to prescribe the time limit. Thus, the term "... from the date of the **invitation** ..." in Rule 40.1(iii) PCT refers not only to the date of the invitation according to Article 17(3)(a) PCT and Rule 40.1(ii) PCT, but also to the invitation to pay the protest fee itself (see Rule 40.1(iii) PCT, first sentence: "**invite** the applicant to pay, ..."). Therefore, the legal effect foreseen in Rule 40.2(e) PCT when an Applicant has not, within the given time limit, paid the protest fee (protest shall be considered not to have been made), cannot occur without a preceding, explicit invitation for payment of the protest fee and the setting of a time limit by the ISA.

9. The procedure according to the Notice corresponds with the provisions of Rule 40.1(iii) PCT in so far as the Applicant is invited **to pay the protest fee** within a **time limit of one month.** However, it does not correspond with the provisions of Rule 40.1 PCT with regard to the point in time at which the invitation has to be made. Pursuant to Rule 40.1 PCT the invitation provided for in Article 17(3)(a) PCT contained both an invitation to pay the protest fee together with an

invitation to pay additional search fees. The position under the Notice is that these invitations are now made separately.

10. In effect, the discrepancy outlined above only arises from the fact that the EPO continues to perform the interlocutory revision even when it is no longer mandatory. Otherwise the two cornerstones of the procedure, namely the invitation to pay further search fees and the genuine second instance review of the invitation by the Board remains unchanged. It may be noted that these two instances were the pillars of the protest procedure even in the previous version of the PCT Regulations, considering that the intermediate level of the interlocutory revision (the "prior review" in Rule 40.2(e) PCT, version in force before 1 April 2005) was only required if the ISA availed itself of the possibility to require a protest fee from the applicant. Thus the present practice does not appear to be contrary to the basic principles underlying the protest procedure. Furthermore, to what extent the implementation of the protest-procedure according to the Notice corresponds to the legal obligations on an ISA under the procedure laid down in the Regulations under the PCT need not to be answered. The Board as a review body according to Rule 40.2(c) PCT (see also Article 154(3) EPC) does not consider itself to be competent to approve or prohibit this practice of the EPO acting as ISA. Rather, the responsibility of the Board (when examining the admissibility of the protest) is restricted to the examination of the formal requirements for filing a protest. The Board - in the absence of competence and of a directly applicable legal basis in the PCT itself - cannot deduce any

further legal effect from this unilateral amendment of the protest-procedure by the EPO acting as ISA.

11. The Board takes it that the Applicant, in view of the Notice, could proceed from the assumption that the procedure of the ISA in the present case would lead to the entrustment of the Board with the examination of the protest, as long as the protest fee was paid on time.

12. Therefore, considering the generally established principle of protection of legitimate expectations, the Board takes the view that it has only to be examined if the payment of the protest fee was made on time within the framework of the procedure according to the Notice.

13. In the present case the Applicant was invited with the communication of 23 June 2006 ("Form PCT/ISA/228 (April 2005)") to pay the protest fee within one month. In a letter dated 14 July 2006 the Applicant requested the debiting of the protest fee from his Deposit Account. Thus, the payment was made in time, and the protest is considered to have been made (Rule 40(2)e PCT).

Admissibility of the Protest

14. The protest, which has been reasoned by the Applicant (see section (V) above), is therefore admissible.

Examination of the protest

15. The ISA has identified six groups of inventions, each "characterised by the common subject-matter" of a different independent claim, with the exception of

invention (1) which was found to be characterised by the subject-matter of three independent claims, namely claims 1, 43 and 45 (see section (II) above).

Claim 1 (invention (1)) refers to an antibody **binding to OX40L**, which contains a **human Fc part** and **does not bind to complement factor C1q**.

Independent claim 15 (invention (2)) refers to an antibody **binding to OX40L,** which comprises a combination of variable regions selected from a group of nine indicated combinations of sequences characterised by their respective SEQ ID NO.

Independent claim 22 (invention (3)) refers to an antibody **binding to OX40L,** which comprises a variable light chain and a variable heavy chain comprising CDR3 selected from different sequences characterised by their respective SEQ ID NO.

Independent claim 24 (invention 4)) refers to an antibody produced by a cell line selected from a group of six different cell lines. It is evident from the designation of these cell lines that they are hybridoma cell lines producing an antibody **binding to OX40L.**

Independent claim 40 (invention (5)) refers to a method for modifying the initial amino acid sequence of a parent antibody heavy chain CDR and/or a parent antibody light chain CDR selected from different sequences characterised by their respective SEQ ID NO. The ability of the modified antibody for **binding to OX40L** is measured.

Independent claim 41 (invention (6)) refers to an antibody **binding to OX40L** being of human IgG1 class and comprising a γ heavy chain selected from different sequences characterised by their respective SEQ ID NO.

Independent claim 43 (invention (1) refers to an antibody **binding to OX40L** being of human IgG1 class, containing a defined mutation and comprising a γ heavy chain selected from different sequences characterised by their respective SEQ ID NO.

Independent claim 45 (invention (1)) refers to an antibody **binding to OX40L** being of human IgG4 class, containing a defined mutation and comprising a γ heavy chain selected from different sequences characterised by their respective SEQ ID NO.

16. It can be seen from the above analysis that the only technically characterising feature which is common to the antibody according to claim 1 (invention (1)) and the antibodies claimed by the various other independent claims is the capability of **binding to OX40L.**

17. The antibodies according to claims 15, 22, 40, 41 (inventions (2), (3), (5) and (6)) are moreover characterised by referring to specific sequences characterised by their respective SEQ ID NO. The SEQ ID NOS contained in said claims are SEQ ID NOS 1 to 12, 16 to 58, 62 and 66. Claims 43 and 45, which the ISA grouped with invention (1) refers to SEQ ID NOS 59, 60, 63, 64, 67 and 68. According to the "Description of the Sequence Listing" on pages 39 to 40 of the application SEQ ID NOs 1 to 12, 16 to 20 refer to the light and heavy chain variable regions of a group of nine

antibodies designated LC.001, LC.005, LC.010, LC.019, LC.029, LC.033, LC.059, LC.060 and LC.063. SEQ ID NOS 58 to 60, 62 to 64 and 66 to 68 refer to the heavy chains of LC.001, LC.005 and LC.060 and mutants thereof.

According to page 40, line 4, SEQ ID NOS 21 to 57 refer to CDR sequences. The Applicant, in the letter dated 27 January 2006, setting out the reasons for the protest, states that these CDRS are parts of the variable chains of antibodies LC.001, LC.005, LC.010, LC.019, LC.029, LC.033, LC.059, LC.060 and LC.063. He argues that this could be "easily recognized by a sequence comparison".

The Board has performed a sequence comparison and came to the result that Applicant's argument is correct (SEQ ID NO 21 equates amino acid residues (31) to (35) of SEQ ID NO 10; SEQ ID NO 22 equates amino acid residues (31) to (35) of SEQ ID NO 2; SEQ ID NO 23 equates amino acid residues (31) to (35) of SEQ ID NO 4, and so on).

The hybridoma cell lines mentioned in claim 24 have been deposited with "Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ)" according to the requirements of the Budapest Treaty. It is evident from page 24 and from the examples of the present application that the antibodies produced by these cell lines, which are the subject-matter of claim 24 (invention (4)), are the antibodies LC.001, LC.005, LC.010, LC.019, LC.029 and LC.033.

18. According to page 41, lines 27 to 31 of the present application, antibodies LC.001, LC.005, LC.010, LC.019, LC.029, LC.033, LC.059, LC.060 and LC.063 are **human**

anti-human OX40L monoclonal antibodies (see also example 1).

Thus, the independent claims "characterising" inventions (2) to (6) identified by the ISA share the technically characterising feature that they refer to **human anti-human OX40L monoclonal antibodies,** respectively to antibodies comprising fragments thereof.

19. Document (1) discloses a neutralizing monoclonal antibody against **murine OX40L**, designated RM134L (see abstract).

Human and murine OX40L are different proteins, which when used as antigen for the production of antibodies give rise to the production of different antibodies.

Example 18 of the present application shows that antibody LC.001 binds to human OX40L but is unable to bind to murine OX40L. In this experiment RM134L, the rat anti-murine OX40L antibody described in document (1) is used as positive control for murine OX40L expression.

20. Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution

which each of the claimed inventions, considered as a whole, makes over the prior art (Rule 13.2 PCT).

21. The Board agrees with the ISA in so far, as the only technically characterising feature which is common to the antibody according to claim 1 (invention (1)) and the antibodies according to the independent claims "characterising" inventions (2) to (6), namely their capability to **bind to OX40L,** is known from the disclosure in document (1), and does not therefore define a contribution over the prior art.

22. However, the five different groups of inventions defined by the ISA as inventions (2) to (6) (see section (II) above) all refer to **human anti-human OX40L monoclonal antibodies,** respectively to antibodies comprising fragments thereof.

This feature defines a contribution which each of the claimed inventions (2) to (6), as defined by the ISA, considered as a whole, makes over the prior art, namely document (1), which discloses an anti-**murine OX40L** antibody. The feature, thus, fulfils the requirement of a "special technical feature" as defined in Rule 13.2 PCT, and as such forms an unitary link between inventions (2) to (6), as defined by the ISA.

23. To summarise, the Board agrees with the ISA that the present application does not relate to one invention only or to a group of inventions so linked as to form a single general inventive concept as required by Rule 13.1 PCT. However, the Board, in the light of the above findings, is convinced that claims 1 to 46 refer to **two**

different inventions only, and not to six different inventions as found by the ISA.

Order

For these reasons it is decided that:

Four additional search fees shall be reimbursed.

Registrar: Chair:

P. Cremona U.Kinkeldey