Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 29 January 2018

Case Number: T 0776/12 - 3.3.04

Application Number: 01987765.3

Publication Number: 1334119

IPC: C07K14/135, G01N33/569, A61K38/16, A61K39/155

Language of the proceedings: EN

Title of invention:
Compositions and methods for modulating RSV infection and immunity

Patent Proprietor:
The Government of the United States of America, as represented by the Secretary, Department of Health and Human Services

Opponent:
Sanofi Pasteur, Inc.

Headword:
RSV infection/GOVERNMENT OF THE UNITED STATES OF AMERICA

Relevant legal provisions:
EPC Art. 123(2)
EPC R. 115(1)
RPBA Art. 15(3)

Keyword:
Main request and first to third auxiliary requests - added subject-matter (yes)

Decisions cited:

Catchword:
-

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 0776/12 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 29 January 2018

Appellant: (Patent Proprietor)	The Government of the United States of America, as represented by the Secretary, Department of Health and Human Services Office of Technology Transfer Mail Stop E-67, Suite 1103 Executive Park, Building 4 Atlanta, GA 30333 (US)
Representative:	J A Kemp 14 South Square Gray's Inn London WC1R 5JJ (GB)
Respondent: (Opponent)	Sanofi Pasteur, Inc. 1 Discovery Drive, Knerr Building 1 Swiftwater, PA 18034 (US)
Representative:	Bösl, Raphael Konrad Isenbruck Bösl Hörschler LLP Patentanwälte Prinzregentenstraße 68 81675 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 4 January 2012 concerning maintenance of the European Patent No. 1334119 in amended form.**

Composition of the Board:

Chairwoman	G. Alt
Members:	B. Claes
	P. de Heij

Summary of Facts and Submissions

I. An appeal was lodged by the patent proprietor (hereinafter "appellant") against the interlocutory decision of the opposition division in which it found that, account being taken of the amendments, European patent No. 1 334 119 met the requirements of the EPC. The title of the patent is "*Compositions and methods for modulating RSV infection and immunity*".

II. The opposition division held, *inter alia*, that claim 21 of the main request, filed with a letter dated 26 July 2011, and claim 21 of the first auxiliary request related to added subject-matter (Article 123(2) EPC). Claim 21 of the second auxiliary request was found to concern subject-matter which was not sufficiently disclosed (Article 83 EPC). The opposition division considered that the claims of the third auxiliary request complied with the requirements of the EPC. The auxiliary requests were filed during the oral proceedings.

III. With the statement of grounds of appeal, the appellant filed a new main request and new first to fourth auxiliary requests. Claim 21 of the new main request was identical to claim 21 of the main request considered by the opposition division. The new third and fourth auxiliary requests were identical to the second and third auxiliary requests considered by the opposition division respectively, and so the claims of the new fourth auxiliary request were considered allowable (see section II above). Further, four new documents were submitted and oral proceedings were requested as an auxiliary measure.

Claim 21 of the main request read:

"21. A composition comprising an anti-RSV G glycoprotein antibody, which antibody inhibits binding of respiratory syncytial virus G glycoprotein to a CX3CR1 receptor, for use in treating respiratory syncytial virus infection in a subject infected with respiratory syncytial virus."

Claim 21 of the first auxiliary request read:

"21. A composition comprising an anti-RSV G glycoprotein antibody, which antibody is a monoclonal antibody which blocks binding of respiratory syncytial virus G glycoprotein to a CX3CR1 receptor, for use in treating respiratory syncytial virus infection in a subject infected with respiratory syncytial virus." (emphasis added by the board)

Claim 21 of the second auxiliary request read:

"21. A composition comprising an anti-RSV G glycoprotein antibody, which antibody blocks binding of respiratory syncytial virus G glycoprotein to a CX3CR1 receptor, for use in treating respiratory syncytial virus infection in a subject infected with respiratory syncytial virus, wherein the antibody inhibits the biological activity of a CX3C motif of a RSV G glycoprotein, wherein the biological activity is cell migration." (emphasis added by the board)

Claim 21 of the third auxiliary request read:

"21. A composition comprising an anti-RSV G glycoprotein antibody, which antibody blocks binding of respiratory syncytial virus G glycoprotein to a

CX3CR1 receptor, for use in treating respiratory syncytial virus infection in a subject infected with respiratory syncytial virus, wherein the antibody inhibits the biological activity of a CX3C motif of a RSV G glycoprotein, wherein the biological activity is selected from chemotaxis, cell migration or virus adherence to cells." (emphasis added by the board)

IV. The parties were summoned to oral proceedings and informed of the board's preliminary opinion on some of the issues to be considered during the oral proceedings. On a preliminary basis the board was, *inter alia*, of the opinion that claim 21 of the main request and of the first to third auxiliary requests did not comply with the requirements of Article 123(2) EPC.

V. The appellant responded to the board's communication and submitted further arguments. With a further letter the appellant withdrew its request for oral proceedings.

VI. Oral proceedings were held in the absence of the duly summoned parties.

VII. The appellant's arguments on the issue of added subject-matter concerning claim 21 of the main request and of the first to third auxiliary requests, as the board understands them from the written submissions, can be summarised as follows:

Main request

Claim 27 as filed was directed to the treatment of RSV infection using a blocking molecule, in accordance with claim 1 as filed, that inhibited the biological

activity of a CX3C motif of a RSV G glycoprotein. On page 8, lines 23 to 27, the application as filed specified that the blocking molecules of the invention could be antibodies, and that such antibodies "*block the biological activity of the CX3C motif, or block the binding of the CX3C G glycoprotein to the CX3C G glycoprotein receptor, which can be the CX3CR1 receptor*". In the following paragraph, bridging pages 8 and 9, monoclonal antibodies were disclosed as ones "*that can be shown to block binding or the activity associated with binding to the CX3CR1 receptor of many or all RSV strains*" and it was discussed that such antibodies *"are useful in the treatment of patients with RSV infection*".

The invention was thus directed to blocking molecules, in particular antibodies, which inhibited or blocked the binding of the RSV G glycoprotein to the CX3CR1 receptor and were useful in the treatment of patients with RSV infection.

Although the application as filed referred to a number of different types of blocking molecules, antibodies were exemplified and extensively discussed. General information on the compositions for the treatment of RSV disease was given on pages 13 and 14 of the application as filed and blocking molecules were described in more detail from page 16 onwards, this description including an additional analysis of useful antibodies (see e.g. page 16, lines 15 to 26). The production of antibodies was discussed on pages 23 to 25 and their use as pharmaceutical compositions on pages 27 and 28. These sections supported the claimed subject-matter.

The claim required only one single activity of the anti-RSV G glycoprotein antibody, i.e. that it inhibit or block binding of the RSV G glycoprotein to the CX3CR1 receptor, and therefore did not require any combination of inhibiting biological activity and blocking binding. The antibody simply needed to inhibit binding.

First auxiliary request

The paragraph bridging pages 8 and 9 of the application as filed disclosed monoclonal antibodies which blocked binding of the RSV G protein to the CX3CR1 receptor and were useful for the treatment of patients with RSV infection. Although this passage related to anti-RSV G protein monoclonal antibodies which were specific for the CX3C motif in the G protein, monoclonal antibodies were also defined, on page 8, in line 31, as ones "*that can be shown to block binding*" to the CX3CR1 receptor. Therefore, the antibodies were defined either as specific for the CX3C motif or, in the alternative, as blocking binding to the receptor. The passage thus provided a basis for the claim.

On the basis of the disclosure on page 16, lines 15 to 21, of the application as filed, the person skilled in the art would have "*seriously contemplated*" monoclonal antibodies which block binding to the CX3CR1 receptor to treat RSV infection. The skilled person would understand the reference in this passage to the use of antibodies "*in conjunction with neutralizing monoclonal antibodies*" to mean that they could be used *in addition to* neutralising monoclonal antibodies, and so as not requiring neutralising monoclonal antibodies in all cases. Indeed, the immediately preceding paragraph, for example, likewise indicated that treatment could be

provided with a molecule that blocked binding of the CX3C G glycoprotein to its receptor without requiring additional neutralising antibodies.

Second and third auxiliary request

The application as filed referred, in the context of blocking molecules, to both inhibiting the activity of the CX3C motif of the G protein and blocking the binding the G protein to the CX3C G protein receptor. Indeed, on page 14, lines 16 to 29 the application as filed disclosed antibodies which bound to and blocked the normal activity of the G glycoprotein CX3C motif and, in an alternative, that the CX3C site was inactivated by binding antibodies or blocking molecules proximal to the CX3C motif in such a way that the normal activity of the motif was inhibited or compromised.

Also on page 7 in lines 9 to 13, the application as filed referred to blocking the activity by binding *inter alia* antibodies. Parts 3) and 4) of this section provided the alternatives of blocking the motif itself, or of blocking binding in this region (see lines 15 to 16 on page 7). Accordingly, there was clear disclosure of "*antibodies which block binding, which also block (or inhibit) the activity associated with binding*" and the skilled person would thus understand that blocking binding to the CX3C motif was associated with blocking or inhibiting the activity and that, therefore, blocking biological activity was described in combination with the feature of blocking binding in the application as filed.

The person skilled in the art "*would seriously contemplate*" using an antibody that blocked binding of the RSV G glycoprotein to the CX3CR1 receptor since this was specifically mentioned in the passage bridging pages 8 and 9. Furthermore, claim 1 as filed specifically disclosed a blocking molecule, such as an antibody, that inhibited the biological activity of a CX3C motif of a RSV G protein. Read in this context the skilled person would understand from the disclosure, for example on pages 7, 8 and 14, that such a blocking molecule was used to block the biological activity of the protein. The claim thus merely set out what was directly and unambiguously derivable for the skilled person from the application as filed.

VIII. The opponent did not make any submissions in these appeal proceedings.

IX. The appellant requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request, or in the alternative, on the basis of one of the first to third auxiliary requests, all filed with the statement of grounds of appeal.

Reasons for the Decision

1. The appeal is admissible.

2. The parties were both duly summoned but did not attend the oral proceedings. The oral proceedings took place as scheduled in accordance with Article 116(1) EPC, first half-sentence, and Rule 115(2) EPC. In accordance with Article 15(3) RPBA the parties were treated as relying on their written cases.

Added subject-matter (Article 123(2) EPC)

3. For each of the main request and the first to third auxiliary requests, the board decided that one of the claims, namely claim 21, related to added subject-matter. The reasons for this are as follows.

Main request - claim 21

4. The claim (see section III) relates to a composition comprising an antibody which recognises the G glycoprotein of the respiratory syncytial virus (RSV) and which inhibits binding of this glycoprotein to a CX3CR1 receptor.

5. The opposition division, when ruling on the same claim, held that the application as filed was being used as a reservoir from which features pertaining to different embodiments had been combined to create newly claimed embodiments.

6. The appellant has referred, in particular, to the following passages in the application as filed and argued that the skilled person would derive the claimed subject-matter directly and unambiguously from these passages.

Passage (i) - on page 8, lines 23 to 27:

"*A blocking molecule is defined herein as a drug, chemical compound, antibody, peptide, polypeptide or other molecule that blocks the biological activity of the CX3C motif, or blocks the binding of the CX3C G glycoprotein to the CX3C G glycoprotein receptor, which can be the CX3CR1 receptor.*" (emphasis added by the board);

Passage (ii) - the subsequent paragraph bridging pages 8 and 9:

"*Monoclonal antibodies which are specific for the RSV G glycoprotein CX3C motif or for the receptor to which the CX3C motif binds (particularly the CX3CR1 receptor), or that can be shown to block binding or the activity associated with binding to the CX3CR1 receptor of many or all RSV strains are useful for the treatment of patients with RSV infection...*" (emphasis added by the board);

Passage (iii) - on page 16, lines 15 to 21:

"*Monoclonal antibodies, specific for the RSV G glycoprotein CX3C motif or for the receptor to which the CX3C motif binds (particularly the CX3CR1 receptor) or for other parts of the RSV G glycoprotein such that they block RSV G glycoprotein binding to CX3CR1 or the activity associated with RSV G glycoprotein binding to CX3CR1 for all RSV strains, are useful, in conjunction with neutralizing monoclonal antibodies, to treat patients with disease or to use prophylactically to prevent RSV infection in subjects who are at risk of acquiring RSV disease.*" (emphasis added by the board); and

Passage (iv) - the subsequent passage on page 16 in lines 21 to 26:

"*Polyclonal antibodies, concentrated sera or immunoglobulin preparations containing high titers of antibodies specific for the RSV G glycoprotein CX3C motif or for the receptor to which the CX3C motif binds are also useful for treatment or prevention of RSV disease*.".

7. The board notes, however, that, in fact, none of these passages in the description of the application as filed that the appellant has referred to, discloses antibodies characterised by the feature that they inhibit binding of respiratory syncytial virus G glycoprotein to a CX3CR1 receptor as required by the claim. Rather, these passages refer to compounds which block binding of respiratory syncytial virus G glycoprotein to a CX3CR1 receptor. However, from a technical perspective, and considered by a person skilled in the technical field of protein interaction, the notions of "inhibition" of binding and "blocking" of binding are not equivalent or interchangeable but rather technically distinct. Indeed, whereas the "blocking" of binding of two molecules relates to a rigorous, preventive effect on binding, the more general effect of "inhibiting" the binding of two molecules does not necessarily exclude the binding of those molecules as such.

8. The appellant has referred, in addition, to pages 13, 14, 23 to 25, 27 and 28 of the application as filed, which, in its view, supported the claimed subject-matter. The board notes, however, that also these references similarly do not disclose antibodies having the features as required by the claim.

9. The board notes furthermore that claim 27 as filed is directed to the treatment of RSV infection using a blocking molecule that inhibits the biological activity of a CX3C motif of a RSV G glycoprotein defined in claim 1 as filed. Accordingly, claim 27 as filed also cannot be accepted to disclose the inhibition of the binding of the RSV G glycoprotein to a CX3CR1 receptor as required by the claim.

10. Consequently, in view of the above considerations, the board holds that the claim relates to added subject-matter and does not comply with the requirements of Article 123(2) EPC.

First auxiliary request - claim 21

11. As compared to claim 21 of the main request, this claim now specifies (see section III) that the anti-RSV G glycoprotein antibody in the composition is monoclonal and blocks binding of the RSV G glycoprotein to a CX3CR1 receptor.

12. To substantiate that the claim complies with the requirements of Article 123(2) EPC, the appellant has referred to the sole two passages in the application as filed that relate to monoclonal antibodies, i.e. the paragraph bridging pages 8 and 9 and the paragraph on page 16, lines 15 to 21 (for both see point 6 above, passages (ii) and (iii), respectively).

13. The passage bridging pages 8 and 9, however, discloses anti-RSV G glycoprotein monoclonal antibodies (i.e. which bind to the G glycoprotein) which are specific for the CX3C motif in the RSV G protein. These antibodies therefore do not provide a basis for the amendment to anti-RSV G glycoprotein monoclonal antibodies in general.

14. Furthermore, although the board concurs with the appellant that the passage also refers to monoclonal antibodies that "*can be shown to block binding* [...] *to the CX3CR1 receptor*", this does not necessarily involve an anti-G protein antibody as the blocking of the binding to the receptor could also be achieved e.g. by an antibody directed to the receptor itself. The

passage thus discloses monoclonal antibodies which block the binding in general, but not the specific blocking of the binding to the receptor with an anti-G protein antibody. As these features of the claim are thus not directly and unambiguously derivable from the passage bridging pages 8 and 9 of the application as filed, that passage cannot support the claim.

15. The passage referred to on page 16 of the application as filed also discloses, in addition to anti-RSV G glycoprotein monoclonal antibodies which are specific for the CX3C motif in the RSV G protein, anti-RSV G glycoprotein monoclonal antibodies which are specific for other parts of the RSV G protein, such that they block the binding of the G protein to the CX3CR1 receptor, but the passage specifies that they can be used - when (also prophylactically) treating patients - "*in conjunction with neutralizing monoclonal antibodies*". The latter feature is however lacking from the wording of claim 1.

16. The appellant has argued in this context that the fact that the monoclonal antibodies were disclosed as being used in conjunction with neutralising monoclonal antibodies was merely an optional feature. This was derivable from the immediately preceding paragraph, which did not disclose additional antibodies.

Passage (v) - on page 16, lines 8 to 13 reads:

"*RSV treatment is provided by administration, to an RSV infected human or animal, of an effective amount of a CX3C blocking molecule in a pharmaceutically acceptable carrier. A blocking molecule is defined herein as a drug, chemical compound, antibody, peptide, polypeptide or other molecule that blocks the biological activity*

of the CX3C motif or blocks the binding of the CX3C G glycoprotein to the CX3C G glycoprotein receptor, which is most preferably the CX3CR1 receptor." (emphasis added by the board)

17. The board notes, however, that passage (v) relates in general to "*blocking molecules*" which can block the binding of the G glycoprotein to its receptor for the treatment of RSV. Antibodies are stated as examples of such molecules, as are drugs, or a chemical compound, peptide, polypeptide or other molecule, but not monoclonal antibodies. It is only the subsequent paragraph (here numbered (iv)) of the description which refers to the specific use of monoclonal antibodies, but it requires that they be used in conjunction with neutralising antibodies. Accordingly, the board cannot concur with the appellant that these two passages, when read in combination, provide a basis for claim 21.

18. Accordingly, the claim does not comply with the requirements of Article 123(2) EPC.

Second and third auxiliary requests - claim 21

19. As in the higher-ranking requests the claim of these requests (see section III) is for a composition comprising an anti-RSV G glycoprotein antibody for use in treating RSV infection in a subject infected with RSV. The antibody is now further specified by the feature that it blocks binding of RSV G glycoprotein to a CX3CR1 receptor *and* by the feature that it inhibits the biological activity of a CX3C motif of a RSV G glycoprotein.

20. In order for this claim to comply with the requirements of Article 123(2) EPC, it is required, *inter alia*, that the application as filed discloses an anti-RSV G glycoprotein antibody having both these functional features.

21. The board considers, however, that such antibodies are not disclosed in the paragraphs referred to in points 6 and 16 above. Indeed, in passages (i) and (v), for example, the antibody is not specified as specific for the RSV G protein (i.e. an anti-RSV G glycoprotein) and the biological activity is specified not as inhibited but blocked. Passages (ii) and (iii) relate to monoclonal antibodies, while passage (iv) relates to, *inter alia*, antibodies that are specific for the RSV G glycoprotein CX3C motif but do not necessarily block binding between the motif and the receptor.

22. The appellant has argued that the application as filed referred, in the context of blocking molecules, to both the blocking of the binding of the G protein to the CX3C G protein receptor and to the inhibition of the activity of the CX3C motif of the G protein. In particular, the application disclosed antibodies which bound to and blocked the normal activity of the G glycoprotein CX3C motif, and, in an alternative, that the CX3C site was inactivated by binding antibodies or blocking molecules proximal to the CX3C motif in such a way that the normal activity of the motif was inhibited or compromised. The appellant based this argument on the paragraph on page 14, lines 16 to 29 of the application as filed (passage (vi)):

"Drugs, antibodies, peptides, polypeptides or other blocking molecules that bind to and thereby block the normal activity of the G glycoprotein CX3C motif of an

infecting RSV virus are administered to treat RSV infection. The CX3C site is also inactivated by binding drugs, antibodies, peptides, polypeptides or other blocking molecules proximal to the CX3C motif of an infecting RSV virus in such a way that the normal activity of the motif is inhibited or compromised. The preferred antibodies do not specifically recognize the CX3C domain, thus limiting the possibility of inducing autoimmunity to structurally similar endogenous chemokines, such as fractalkine.

The normal biological activities of the live, wild-type RSV virus that are inhibited, terminated or modulated by the compositions and methods provided herein include but are not limited to, chemotaxis, cell migration and virus adherence to cells." (emphasis added by the board)

23. The board notes, however, that the antibodies disclosed in this passage (vi) are antibodies that either bind to the CX3C motif of the G glycoprotein - as opposed to the G glycoprotein in general as in the claim - and block its normal activity or, in an alternative, are antibodies that bind proximal to the CX3C motif of the G glycoprotein - again as opposed to the G glycoprotein in general, as in the claim - and thereby compromise or inhibit the activity of the CX3C motif. Accordingly, the claim also encompasses antibodies that bind to the G glycoprotein outside (the proximity of) the CX3C motif and yet block the binding of RSV G glycoprotein to a CX3CR1 receptor. This passage therefore cannot provide a disclosure for the antibody referred to in point 19 above.

24. In a further line of argument, the appellant referred to another passage in the application as filed, namely

Passage (vii) - on page 7, line 3 to 17 which reads:

"*Basically, immunity and treatment are achieved by* [...] *3) blocking the activity of the CX3C motif by binding drugs, antibodies, peptides, polypeptides or other blocking molecules to the motif of an infecting virus; 4) inactivating the CX3C site by binding drugs antibodies, peptides, polypeptides or other blocking molecules proximal to the CX3C motif of an infecting virus (preferably the binding of blocking molecules proximal to the motif occurs in regions that alter the secondary structure of the motif, thereby changing biological activity, or that sterically prevent RSV G glycoprotein binding to CX3CR1 or the biological activity associated with RSV G glycoprotein binding to CX3CR1 by a non-live virus vaccine); and/or 5) ...*".

25. The appellant has argued that parts (3) and (4) of the passage provided the alternatives of blocking the motif itself or of blocking by binding in its region. There was thus a clear disclosure of "*antibodies which block binding, which also block (or inhibit) the activity associated with binding*" and the skilled person would thus understand that blocking binding to the CX3C motif was associated with blocking or inhibiting the activity and that therefore blocking biological activity was disclosed in the application in combination with the feature of blocking binding.

26. The board notes that, like the antibodies disclosed in passage (vi), the antibodies referred to in part (3) of passage (vii) bind to the CX3C motif of the G glycoprotein and block its activity, while the

antibodies referred to in point 4) are antibodies that bind proximal to the CX3C motif of the G glycoprotein. Both alternatives are opposed to binding to the G glycoprotein in general, as allowed in the claim. Accordingly, this passage too cannot provide a disclosure for the antibody referred to in point 19.

27. In view of the above considerations, claim 21 of the second auxiliary request does not comply with the requirements of Article 123(2) EPC.

28. The board notes that the opposition division was of the opinion that claim 21 of the third auxiliary request met the requirements of Article 123(2) EPC. The board, however, considers that it relates to added subject-matter and does not comply with the requirements of Article 123(2) EPC, for the same reasons as claim 21 of the second auxiliary request, as its subject-matter is one of the alternatives defined in that claim (see section III).

29. In view of the fact that for each of the main request and the first to third auxiliary requests, at least one claim, i.e. claim 21, fails to comply with the requirements of Article 123(2) EPC, the claim requests are not allowable.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated