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**Datasheet for the decision  
of 12 February 2014**

**Case Number:** T 0034/10 - 3.3.08

**Application Number:** 98946321.1

**Publication Number:** 996717

**IPC:** C12N15/00

**Language of the proceedings:** EN

**Title of invention:**  
IMMUNOPROTECTIVE INFLUENZA ANTIGEN AND ITS USE IN VACCINATION

**Patent Proprietor:**  
Vlaams Interuniversitair Instituut voor  
Biotechnologie vzw.

**Opponents:**  
Vaxinnate Corporation  
MERCK + CO. INC.  
Cytos Biotechnology AG

**Headword:**  
Extracellular domain influenza M2 membrane protein/VLAAMS

**Relevant legal provisions:**  
EPC Art. 84  
RPBA Art. 12(4)

**Keyword:**

Admissibility of Main Request and Auxiliary Requests 1 and 2  
(no)

Admissibility of Auxiliary Requests 3 and 4 (yes)

Auxiliary Request 3 - clarity (no)

Auxiliary Request 4 - all requirements of the EPC (yes)

**Decisions cited:**

T 0019/90

**Catchword:**



**Beschwerdekammern  
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Case Number: T 0034/10 - 3.3.08

**D E C I S I O N  
of Technical Board of Appeal 3.3.08  
of 12 February 2014**

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**Decision under appeal:** Interlocutory decision of the Opposition  
Division of the European Patent Office posted on  
13 November 2009 concerning maintenance of the  
European Patent No. 996717 in amended form.

**Composition of the Board:**

**Chairman:** M. Wieser  
**Members:** P. Julià  
D. Rogers

## **Summary of Facts and Submissions**

- I. Three oppositions were filed against the European patent No. 0 996 717 on the grounds of Articles 100(a), (b) and (c) EPC. The opposition division considered the Main Request (granted claims) not to fulfil the requirements of Article 123(2) EPC, Auxiliary Requests 1 and 2 to contravene Article 84 EPC and Auxiliary Request 3 not to fulfil the requirements of Article 54 EPC. Auxiliary Request 4 was found to fulfil all requirements of the EPC. Auxiliary Request 1 was originally filed on 18 April 2007 (as Main Request) and Auxiliary Requests 2 to 4 were filed on 19 March 2009 at the oral proceedings before the opposition division.
- II. The patentee and opponent 01 (appellants I and II, respectively) appealed the decision of the opposition division.
- III. With its Grounds of Appeal, appellant I filed a new Main Request and Auxiliary Requests 1 to 4. Auxiliary Request 3 was identical to the request upheld by the opposition division, except for a correction in the dependency of claim 5.
- IV. In a reply to appellant II's Grounds of Appeal, appellant I raised an objection with regard to the admissibility of appellant II's appeal. Opponents 02 and 03 (parties as of right) did not reply to the statements of Grounds of Appeal of both appellants and did not file any submissions in the appeal procedure.
- V. The board summoned the parties to oral proceedings. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed

thereto, the board informed the parties of its preliminary opinion on the issues of the case.

In particular, the board pointed out that the appeal filed by appellant II was considered to be admissible but that appellant I's Main Request and Auxiliary Requests 1 and 2 seemed to be not admissible. As for Auxiliary Request 3, the board noted that it would assess, in the context of Article 84 EPC, whether claim 1 was open to interpretation. Finally, the board also noted that there were no submissions on file arguing a lack of inventive step of Auxiliary Request 4.

VI. None of the parties filed any substantive submissions in reply to the board's communication and all parties informed the board of their intention not to attend the scheduled oral proceedings.

VII. The board cancelled the scheduled oral proceedings.

VIII. Claim 1 of the patent **as granted** read as follows:

"1. An influenza antigen comprising a fusion product of

(i) an immunogenic extracellular part of an influenza M2 membrane protein of influenza A virus, and

(ii) a presenting carrier."

IX. Claim 1 of the **Main Request** read as follows:

"1. An influenza antigen in isolated form for use in the preparation of a vaccine against influenza A for humans and/or animals comprising a fusion product of

(i) an immunogenic extracellular part of an influenza M2 membrane protein of influenza A virus, and

(ii) a presenting carrier which is a presenting (poly)peptide,

wherein when said immunogenic extracellular part is a fragment of the extracellular domain of said M2 protein said fragment is immunoprotective."

- X. Claim 1 of the **Auxiliary Request 1** was identical to claim 1 of the Main Request except for the last paragraph, which read:

"1. *[As claim 1 of the Main Request]* ...

wherein said antigen is obtainable by preparing a gene construct encoding said antigen comprising a first coding sequence encoding said immunogenic extracellular part of an influenza M2 membrane protein, and a second coding sequence for said presenting (poly)peptide operable linked thereto,

and wherein when said immunogenic extracellular part is a fragment of the extracellular domain of said M2 protein said fragment is immunoprotective."

- XI. Claim 1 of the **Auxiliary Request 2** was identical to claim 1 of the Main Request except for the last paragraph, which read:

"1. *[As claim 1 of the Main Request]* ...

wherein said immunogenic extracellular part is the extracellular domain of said influenza M2 membrane protein."

XII. Claim 1 of the **Auxiliary Request 3**, the Auxiliary Request on which the opposition division decided to maintain the contested patent, read as follows:

"1. A vaccine against influenza comprising an influenza antigen comprising a fusion product of

(i) the 23 amino acid extracellular part of an influenza M2 membrane protein of influenza A virus, and

(ii) a presenting carrier."

XIII. Claim 1 of the **Auxiliary Request 4** read as follows:

"1. A vaccine against influenza comprising an influenza antigen comprising a fusion product of

(i) an amino acid sequence as represented by SEQ ID NO 1, 2 or 3, and

(ii) a presenting carrier which is a presenting (poly)peptide."

XIV. Appellant I's submissions, insofar as relevant to the present decision, may be summarised as follows:

*Admissibility of appellant II's appeal*

In its Grounds of Appeal, appellant II had raised objections under Articles 83, 84 and 123(2), (3) EPC against the claims upheld by the opposition division



insofar as they were not limited to naturally occurring sequences. As for naturally occurring sequences, objections were only raised under Articles 83 and 84 EPC. Whereas all these objections were substantiated, there was however no reasoning explaining the alleged lack of compliance of non-naturally occurring sequences with Articles 54 and 56 EPC.

At least to the extent of these unsubstantiated objections under Articles 54 and 56 EPC, appellant II's statement of Grounds of Appeal was ineffective and insufficient to justify the pursuit of the appeal in these respects. Insofar as the statement of Grounds of Appeal was incomplete and did not set out all reasons why the decision under appeal had to be reversed, it did not comply with the requirements of Article 12(2) RPBA.

*Admissibility of the Main Request and Auxiliary Requests 1 and 2*

No reply was filed in this respect in response to the communication pursuant to Article 15(1) RPBA in which the parties were informed of the board's preliminary opinion that the Main Request and Auxiliary Requests 1 and 2 should not be admitted into the appeal proceedings (cf. point V *supra*). In the Grounds of Appeal, the subject-matter of claim 1 of the Main Request and of Auxiliary Requests 1 and 2 was described as being essentially derivable from a combination of claim 1 as granted with several dependent claims.

*Auxiliary Request 3  
Article 84 EPC*

Claim 1 required the presence of an influenza antigen. The claimed subject-matter involved only materials that were capable of raising an immune system response against influenza A virus. Part (i) of claim 1 did not comprise any arbitrary 23 amino acid peptide, let alone non-immunogenic 23 amino acid peptides, but it was specifically directed to the 23 amino acid extracellular part of an influenza M2 membrane protein of influenza A virus.

*Auxiliary Request 4*

No evidence was on file to show that carriers other than hepatitis B core protein would not be suitable for carrying out the invention. On the contrary, there was evidence showing that at least a fusion product with another presenting carrier (TLR5 ligand flagellin) was also suitable. Hepatitis B core protein was just one amongst many potential polypeptide presenting carriers known to the skilled person. It was credible that a large number of these carriers could potentiate immunogenicity and provide an immunoprotective response.

- XV. Appellant II's submissions, insofar as relevant to the present decision, may be summarised as follows:

*Admissibility of appellant II's appeal*

No submissions were on file from appellant II in reply to the objections raised by appellant I as regards the alleged deficiencies under Article 12(2) RPBA of appellant II's statement of Grounds of Appeal.

*Admissibility of the Main Request and Auxiliary Requests 1 and 2*

No reply was filed to the communication pursuant to Article 15(1) RPBA in which the parties were informed of the board's preliminary opinion that the Main Request and Auxiliary Requests 1 and 2 should not be admitted into the appeal proceedings (cf. point V *supra*).

*Auxiliary Request 3*

*Article 84 EPC*

Claim 1 was open to interpretation and thus unclear. This claim could be read as not being restricted to naturally occurring sequences of the extracellular domain of the M2 membrane protein of influenza A virus, but also as referring to a sequence comprising any arbitrary 23 amino acid peptide, even non-immunogenic sequences, fused to a polypeptide presenting carrier.

*Auxiliary Request 4*

In its reply to appellant I's Grounds of Appeal, appellant II accepted that Auxiliary Request 4 provided a clear definition of part (i) of the fusion protein of claim 1. With regard to this Auxiliary Request, the letter of reply did not refer to any of the objections raised under Articles 84, 123, 83, 54 and 56 EPC against the Main Request and Auxiliary Requests 1 and 2 or to any of the objections raised against the claim request upheld by the opposition division (Auxiliary Request 3 in the present appeal proceedings). In its statement of Grounds of Appeal, appellant II argued that it was not reasonable on the basis of the disclosure in the patent, which showed an immunoprotective response when an hepatitis B core protein was used as the polypeptide presenting carrier,

to believe that such an immunoprotective response could be generated with generally all polypeptide presenting carriers (Article 83 EPC).

XVI. The appellant I (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of its Main Request or, in the alternative, of Auxiliary Requests 1 to 4, all requests filed with its statement of Grounds of Appeal on 23 March 2010.

XVII. The appellant II (opponent 01) requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

## **Reasons for the Decision**

### *Admissibility of the appellant II's appeal*

1. Appellant I argued that appellant II's statement of Grounds of Appeal does not fulfil the requirements of Article 12(2) RPBA (cf. point XIV *supra*).
2. The statement of Grounds of Appeal of appellant II is understood by the board as being based on a broad interpretation of claim 1 of the request upheld by the opposition division (i.e. Auxiliary Request 3 in the present appeal proceedings). It contains objections against the subject-matter of this claim which, in appellant II's view, allows two possible interpretations (cf. point XV *supra*). Appellant I's allegations that these arguments are incomplete and flawed do not prejudice the admissibility of the appeal itself. Equally the requirements of Article 12(2) RPBA are not contravened since the objections raised by

appellant II are clear and comprehensible. Moreover, also the alleged presence of non-substantiated objections under Articles 54 and 56 EPC in appellant II's statement of Grounds of Appeal, does not *per se* render appellant II's appeal inadmissible, since there is no doubt that other, fully substantiated, objections have been provided with regard to Articles 84, 83 and 123(2), (3) EPC.

3. In consequence, the requirements of Article 12(2) RPBA are fulfilled and the appeal filed by appellant II is admissible.

*Admissibility of the Main Request and of Auxiliary Requests 1 and 2*

4. According to Article 12(4) RPBA, it is within the power of the board to hold inadmissible facts, evidence or requests which could have been presented in the first instance proceedings. Thus, for the board to reach a decision on the admissibility of the new claim requests, it is important to decide whether reasons have been given for their introduction at this stage of the proceedings and for not introducing them in opposition proceedings, whether their filing is a direct reply to the arguments of the opposition division raised in the decision under appeal or whether they address arguments or issues raised in earlier stages of the opposition proceedings (cf. "Case Law of the Boards of Appeal of the EPO", 7th edition 2013, IV.C.1.2.3, page 810).
5. Regarding appellant I's arguments on this issue (cf. point XIV *supra*), the board notes that:

Claim 1 of the **Main Request** contains features of claims 1 and 4 as granted (the presenting carrier is a (poly)peptide), of claim 16 as granted (for use in the preparation of a vaccine) and claim 19 as granted (wherein the antigen is in isolated form). However, claim 1 further requires the immunogenic extracellular part to be an immunoprotective fragment. As such, this feature was not present in claim 1 as granted (cf. point VIII *supra*). It is arguable whether it may be derivable from the use claims 16 and 27 and/or the product claim 17 as granted. Although in a different context, this feature was present in claim 1 of Auxiliary Request 1 before the opposition division which read: "*1. An influenza antigen comprising a fusion product of (i) an immunoprotective extracellular part of an influenza M2 membrane protein ...*".

Claim 1 of **Auxiliary Request 1** reads as claim 1 of the Main Request but further contains the subject-matter of granted claim 13 (product-by-process feature).

Claim 1 of **Auxiliary Request 2** reads as claim 1 of the Main Request but defines the immunogenic extracellular part as being the extracellular domain of the influenza M2 membrane protein. This definition was present in claim 1 of Auxiliary Request 2 before the opposition division which read: "*1. An influenza antigen comprising a fusion product of (i) the extracellular part of an influenza M2 membrane protein ...*".

6. Moreover, the amendments introduced into claim 1 of the Main Request and Auxiliary Requests 1 and 2 raise issues and objections that were not considered at first instance proceedings.

In particular, the feature "*in isolated form*" was not present in claim 1 of any of the claim requests filed during the first instance proceedings. Objections under Articles 123(2) and 84 EPC have been raised by appellant II against *inter alia* the introduction of this feature into claim 1 of the Main Request and of Auxiliary Requests 1 and 2. Without entering into the merit of these objections, the board notes that none of these objections could have been considered and examined at the proceedings before the opposition division. A similar situation arises for the introduction of the product-by-process feature into claim 1 of Auxiliary Request 1 which, since it was not present in claim 1 of any of the claim requests before the opposition division, also could not be considered and examined at the proceedings before the opposition division.

7. All three requests, the Main Request and Auxiliary Requests 1 and 2, were filed in appeal proceedings only and no reasons have been given either to explain their filing at this late stage, or why they could not have been filed earlier, i.e. at the first instance proceedings. The objections that these requests intend to overcome were present throughout the opposition proceedings. Thus, the patentee/appellant I could have addressed them during these proceedings.
  
8. Thus, in view of the above considerations, the board, exercising its discretion, does not admit the Main Request and Auxiliary Requests 1 and 2 into the appeal proceedings (Article 12(4) RPBA).

*Admissibility of Auxiliary Requests 3 and 4*

9. Auxiliary Request 3 is identical to the set of claims upheld by the opposition division, except for a correction in the dependency of claim 5 (there is also an uncorrected error in the dependency of claim 7). Claim 1 of Auxiliary Request 4 is a combination of claims 1 and 3 of Auxiliary Request 3.
10. None of these auxiliary requests raises issues or objections that were not considered by the opposition division during the opposition proceedings. Thus, these auxiliary requests are admitted into the appeal proceedings.

*Auxiliary Request 3*

*Article 84 EPC*

11. Appellant II raised a clarity objection against the feature of claim 1(i) of Auxiliary Request 3. In particular, with regard to the feature defining the extracellular part in claim 1 as being "... *the 23 extracellular part of an influenza M2 membrane protein of influenza A virus ...*" (cf. point XII *supra*), it was considered not to be clear whether this embraces only naturally occurring sequences of 23 amino acids or also artificially mutated or engineered sequences (cf. point XV *supra*).
12. A similar clarity objection was raised in opposition proceedings against the subject-matter of claim 1 of Auxiliary Request 2 then on file, which read as follows: "*1. An influenza antigen comprising a fusion product of (i) the extracellular part of an influenza M2 membrane protein ...*" (cf. point 5 *supra*). The opposition division considered this objection to be relevant since, in its view, "... *the term "extracellular part" encompasses more embodiments than*



*the sequence of aminoacids 1-23 of M2 ... (t)he claim encompasses sequences which may be shorter or longer than the 23 residues identified in the description, or include inserted aminoacids ...".* The opposition division considered that "*... (i)t is not clear what qualifies a sequence to fall under the definition of "extracellular part"..."*" (cf. page 8, point 5 of the decision under appeal).

13. The analysis of the opposition division in respect of this subject-matter is also relevant for the subject-matter of claim 1 of present Auxiliary Request 3 in which the length of this extracellular part has been limited to 23 amino acid residues (cf. point XII *supra*).
- 13.1 Although the extracellular domain of the influenza M2 membrane protein is highly conserved, a certain degree of variability cannot be excluded, as shown by the sequences disclosed in the patent itself (cf. Table 1 of the patent). Thus, the naturally occurring sequence of "*the 23 amino acid sequence of the extracellular domain of the M2 membrane protein of influenza A virus*" is not a single, unique, defined amino acid sequence but, in view of Table 1 of the patent, comprises several - at least three - different amino acid sequences. For this reason alone, there is already a certain degree of ambiguity in the subject-matter of claim 1 of Auxiliary Request 3.
- 13.2 Moreover, there is no limitation in part (i) of claim 1 of Auxiliary Request 3 to naturally occurring sequences of the influenza M2 membrane protein of influenza A virus. The wording of claim 1(i) does not clearly and unambiguously exclude other artificially mutated or engineered sequences derived from any of the possible

naturally occurring sequences of "*the 23 amino acid extracellular part of an influenza M2 membrane protein of influenza A virus*". Therefore part (i) of claim 1 includes non-naturally occurring amino acid sequences. This interpretation is in line with the interpretation of the opposition division, which considered the term "*the extracellular part*" to encompass minor changes, in particular the substitution of amino acid residues.

13.3 Thus, it is not clear what qualifies a sequence to fall within the definition of "*the 23 amino acid extracellular part of an influenza M2 membrane protein*". It is questionable whether sequences of 23 amino acids comprising three, two or only one of the epitopes present in (known) naturally occurring sequences of an extracellular domain of the M2 membrane protein of influenza A virus fall within the wording of claim 1(i). In addition, it is unclear which degree of structural homology/identity and of functional similarity/identity is required for a sequence of 23 amino acids to be covered by the the wording of the claim.

13.4 This is all the more important since the preamble of claim 1 generally requires the claimed vaccine to comprise an "*influenza antigen*" without indicating any limitation to a particular type of influenza antigen and/or influenza virus type, not even to the influenza A virus (cf. page 2, paragraph [0002] of the patent).

14. In view of the above considerations, the board decides that the claims of Auxiliary Request 3 do not fulfil the requirements of Article 84 EPC.

*Auxiliary Request 4*

15. The objection under Article 84 EPC against Auxiliary Request 3 raised above, is overcome by the introduction into claim 1 of the three specific 23 amino acid sequences of the extracellular domain of the influenza M2 membrane proteins of influenza A virus, i.e. SEQ ID NO 1, 2 or 3 (cf. point XIII *supra*). This was also acknowledged by appellant II in its letter of 10 August 2010 (cf. point XV *supra*), in which no explicit objection was raised against the subject-matter of Auxiliary Request 4. Moreover, appellant II in its Grounds of Appeal did not raise any objection under Articles 123(2), (3), 54 and 56 EPC with regard to the claim request upheld by the opposition division (Auxiliary Request 3 in appeal proceedings), when claim 1 of this request was interpreted as being limited to the naturally occurring sequences of 23 amino acids of the extracellular domain of the influenza M2 membrane protein of influenza A virus (cf. page 4, paragraph (a) of appellant II's statement of Grounds of Appeal). Thus, as regards this embodiment, the decision of the opposition division was not contested by appellant II. By introducing the three specific SEQ ID NO's disclosed in the patent-in-suit into claim 1 of Auxiliary Request 4, there is no doubt that the claim is limited, only and exclusively, to naturally occurring sequences. The board sees no reason to differ from the findings of the opposition division as regards Articles 123(2), (3), 54 and 56 EPC.

16. In its Grounds of Appeal, appellant II raised an objection under Article 83 EPC against claim 1 of the claim request upheld by the opposition division (Auxiliary Request 3 in appeal proceedings), when the claim is interpreted as being limited to the naturally occurring sequences of 23 amino acids of the extracellular domain of the influenza M2 membrane

protein of influenza A virus (cf. page 4, paragraph (a) of appellant II's statement of Grounds of Appeal). The fact that an immunoprotective response was demonstrated in the patent with a specific polypeptide presenting carrier (hepatitis B core protein) was not considered to render it credible that a similar response could be obtained with all possible polypeptide presenting carriers (cf. point XV *supra*). The same objection was raised in opposition proceedings against Auxiliary Request 3 then on file, but was considered not to be relevant by the opposition division (cf. page 10, last paragraph of the decision under appeal).

17. According to the established case law, a patent may only be objected to for lack of sufficient disclosure if there are serious doubts, substantiated by verifiable facts (cf. "Case Law", *supra*, II.C.6.1.4, page 318 and T 19/90, OJ EPO 1990, page 476). The board shares the view of the opposition division that the allegations put forward by appellant II do not suffice to raise serious doubts on the possibility of using polypeptide presenting carriers in general as defined in claim 1. In any case, the board fails to see any convincing verifiable fact on file to support the allegations of appellant II. Thus, the board sees no reason to differ from the findings of the opposition division as regards Article 83 EPC.
18. It follows from the above, that Auxiliary Request 4 fulfils all the requirements of the EPC.

## Order

### For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to maintain the patent as amended on the basis of claims 1 to 15 of Auxiliary Request 4 filed with letter dated 23 March 2010 and a description to be adapted thereto.

The Registrar:

The Chairman:



A. Wolinski

M. Wieser

Decision electronically authenticated