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**Datasheet for the decision
of 9 July 2009**

Case Number: T 0001/08 - 3.3.08

Application Number: 92900560.1

Publication Number: 0561890

IPC: C12N 15/86

Language of the proceedings: EN

Title of invention:

DNA expression systems based on alphaviruses

Patentee:

BIOPTION AB

Opponent:

Novartis Vaccines and Diagnostics, Inc.

Headword:

Alphaviruses/BIOPTION

Relevant legal provisions:

EPC Art. 123(2)

Relevant legal provisions (EPC 1973):

-

Keyword:

"Main and first auxiliary requests - added subject-matter
(yes)"

Decisions cited:

T 0157/90, T 0349/01

Catchword:

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Case Number: T 0001/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 9 July 2009

Appellant: BIOPTION AB
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Respondent: Novartis Vaccines and Diagnostics, Inc.
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 19 October 2007
revoking European patent No. 0561890 pursuant
to Article 102(1) EPC 1973.

Composition of the Board:

Chairman: L. Galligani
Members: F. Davison-Brunel
T. Karamanli

Summary of Facts and Submissions

- I. European patent No. 0 561 890 with the title "DNA expression systems based on alphaviruses" was granted with a set of 63 claims for all designated Contracting States except ES and GR and a set of 66 claims for ES and GR, based on European patent application No. 92 900 560.1.

Originally filed claims 1, 3 and 5 read as follows:

"1. An RNA molecule derived from an alphavirus RNA genome and capable of efficient infection of animal host cells, which RNA molecule comprises the complete alphavirus RNA genome regions, which are essential to replication of the said alphavirus RNA, and further comprises an exogenous RNA sequence capable of expressing its function in said host cell, said exogenous RNA sequence being inserted into a region of the RNA molecule, which is non-essential to replication thereof.

3. The RNA of claim 1 or 2, wherein the exogenous RNA sequence encodes a protein, a polypeptide or a peptide sequence defining an exogenous antigenic epitope or determinant.

5. The RNA of any preceding claim, wherein the alphavirus derived RNA molecule regions comprise a 5' terminal portion, the coding region(s) for non structural proteins required for RNA replication, the subgenome promoter region and a 3' terminal portion of said viral RNA."

II. An opposition was filed raising grounds for opposition under Article 100 (a) to (c) EPC 1973. In the course of the proceedings, the patentee amended the claims as granted by filing a new main request and an auxiliary request for all Contracting States except ES and GR as well as a new main request and an auxiliary request for ES and GR. All requests were rejected by the opposition division for failing to fulfil the requirements of Article 123(2) EPC 1973.

III. The appellant (patentee) filed a notice of appeal and paid the appeal fee on 19 December 2007. It submitted on 29 February 2008 a statement of grounds of appeal together with a new main request and a new auxiliary request for all designated Contracting States except ES and GR, and a new main request and a new auxiliary request for ES and GR. The latter corresponded to the main and auxiliary requests for all designated Contracting States except for ES and GR but comprised three additional claims.

IV. Claim 1 of the **main requests** for all designated Contracting States read as follows:

"1. A recombinant RNA molecule derived from an alphavirus RNA genome, which RNA molecule is capable of efficient infection of an animal host cell and can be replicated therein, and which RNA molecule comprises the complete alphavirus RNA genome regions, which are essential to replication of the said alphavirus RNA genome, and further comprises an exogenous RNA sequence capable of expressing its function in said host cell, said exogenous RNA sequence being operatively inserted

into a region of the alphavirus RNA genome, which is non-essential to replication of the recombinant RNA molecule, and at a location such that, when said recombinant RNA is introduced into an animal host cell, the exogenous RNA sequence is expressed from a subgenomic promoter, **at a level of expression which corresponds to the level of expression of viral structural proteins during host cell infection.**"

(emphasis added by the board)

Claim 1 of the **auxiliary requests** for all Designated Contracting States read as follows:

"1. A recombinant RNA molecule derived from an alphavirus RNA genome, which RNA molecule is capable of efficient infection of an animal host cell and can be replicated therein, and which RNA molecule comprises the complete alphavirus RNA genome regions, which are essential to replication of the said alphavirus RNA genome, and further comprises an exogenous RNA sequence capable of expressing its function in said host cell, **which exogenous RNA sequence encodes an amino acid sequence comprising an antigenic epitope or determinant of a pathogen** and is operatively inserted into a region of the alphavirus RNA genome, which is non-essential to replication of the recombinant RNA molecule, and at a location such that the exogenous RNA sequence is expressed from a subgenomic promoter when said recombinant RNA is introduced into an animal host cell." (emphasis added by the board).

- V. On 18 July 2008, the respondent (opponent) submitted observations on the appellant's statement of grounds of appeal.

- VI. On 12 March 2009, the board sent a summons to oral proceedings together with a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) indicating its preliminary, non-binding opinion, in particular that claim 1 of each of the main and first auxiliary requests may not fulfil the requirements of Article 123(2) EPC.
- VII. On 7 May 2009, the appellant informed the board that it would not attend oral proceedings. The respondent announced in a letter dated 26 May 2009 that it would be represented at oral proceedings.
- VIII. On 2 June 2009, the respondent sent a further submission indicating its intention to request that the board orders an apportionment of costs in its favour under Article 104 EPC in case the oral proceedings would go ahead as scheduled, in view of the fact that the appellant had not filed a substantive response to the board's communication, which comprised a preliminary opinion which was favorable to the respondent, but had merely indicated that it would not attend oral proceedings without withdrawing the request for them.
- IX. On 4 June 2009, the appellant informed the board that it withdrew its request for oral proceedings. Oral proceedings were cancelled on that same day.
- X. The appellant's submissions in writing insofar as relevant to the present decision may be summarized as follows:

Article 123(2) EPC; added subject-matter

*Main request for all designated Contracting States
except ES and GR; claim 1*

The basis for the subject-matter of claim 1 was to be found in the application as filed in claim 1, on page 7, lines 24 and 25, and on page 39, lines 4 to 6. More specifically, the expression "at a level of expression which corresponds to the level of expression of viral structural proteins during host cell infection" had a basis on page 39, lines 4 to 6. The paragraph comprising this information was not limited to Semliki Forest virus (SFV) but clearly referred to the present invention generally. This was also clear from the entire section which referred to "major advantages of the present system" from page 38, lines 13 to page 39, line 15.

*Auxiliary request for all designated Contracting States
except ES and GR; claim 1*

The basis for the subject-matter of claim 1 was to be found in the application as filed in claims 1, 3 and 5, on page 5, second paragraph and on page 7, lines 8 to 20, 24 and 25.

For these reasons, amended claim 1 of each of the main and auxiliary requests did not violate Article 123(2) EPC.

*Main and first auxiliary requests for ES and GR;
claim 1*

Claim 1 of each of these requests was the same as claim 1 of the main and auxiliary requests for all designated Contracting States except ES and GR. The same arguments, thus applied, leading to the conclusion that the requirements of Article 123(2) EPC were fulfilled.

- XI. The respondent's submissions in writing insofar as relevant to the present decision may be summarized as follows:

Article 123(2) EPC; added subject-matter

*Main request for all designated Contracting States
except ES and GR; claim 1*

There was no basis in the application as filed for the amendment : "at a level of expression which corresponds to the level of expression of viral structural proteins during host cell infection". More specifically, the teaching on page 39, lines 4 to 6 was not concerned with comparative expression levels of RNA sequences and did not mention the expression level of the "viral **structural** proteins" as now specified. Furthermore, the passage comprising lines 4 to 6 on page 39 formed part of a summary of the advantages of the system identified in the "foregoing experimental results" and could not be taken out of this specific context. Thus, it did not amount to a general statement of the invention.

Auxiliary request for all Designated Contracting States except ES and GR; claim 1

There was no basis in the application as filed for the amendment: " encodes an amino acid sequence **comprising** an antigenic epitope or determinant". Indeed, originally filed claims 3 and 7 related to "a peptide sequence **defining** an exogenous antigenic epitope or determinant" and in the description, mention was made of an exogenous RNA sequence that **consisted** of an epitope or determinant rather than of an exogenous RNA sequence that comprised an epitope or determinant.

For these reasons, the main request and the auxiliary request violated Article 123(2) EPC.

Main and first auxiliary requests for ES and GR; claim 1

Claim 1 of each of these requests was the same as claim 1 of the main and auxiliary requests for all designated Contracting States except ES and GR. The same arguments, thus applied, leading to the conclusion that the requirements of Article 123(2) EPC were not fulfilled.

XII. 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 the auxiliary request for all designated Contracting States except ES and GR and on the basis of the main request or the auxiliary request for ES and GR, all filed on 29 February 2008.

The respondent requested that the appeal be dismissed.

Reasons for the decision:

Article 123(2) EPC; added-subject-matter

Main request for all designated Contracting States except ES and GR; claim 1

1. Claim 1 (section IV supra) is directed to a recombinant RNA molecule which ... comprises an exogenous RNA sequence..., at a location such thatthe exogenous RNA sequence is expressed **from** a subgenomic promoter **at a level of expression which corresponds to the level of expression of viral structural proteins during host cell infection.** The appellant refers to originally filed claim 1, to the passage in the application as filed on page 7, lines 24 and 25 and to the passage on page 39, lines 4 to 6 as basis for this subject-matter.

2. It is readily apparent from reading originally filed claim 1 (section I, supra) that the claim does not relate to a recombinant RNA molecule defined, in particular, by the expression level of the exogenous RNA it carries. The passage of the original description on page 7, lines 21 to 30 encompassing lines 24 and 25 reads:

"To that end, according to the present invention there is provided an RNA molecule derived from an alphavirus RNA genome and capable of efficient infection of animal host cells, which RNA molecule comprises the complete alphavirus RNA genome regions, which are essential to replication of the said alphavirus RNA, and further

comprises an exogenous RNA sequence capable of expressing its function in said host cell, said exogenous RNA sequence being inserted into a region of the RNA molecule, which is non-essential to replication thereof."

This passage, also, does not identify the level of expression to be expected from the exogenous RNA carried by the molecule according to the invention.

In view of the above, neither the cited passage nor the originally filed claim 1 constitute a sufficient basis for the acknowledgement that the now claimed subject-matter was originally disclosed.

3. The teaching on page 39, lines 4 to 6 is part of a passage which is itself comprised within Example 8 illustrating the "present in vivo packaging system" isolated starting from **SFV** (page 37). The passage is intended to describe the advantages linked to "**the present system**" as derivable "**from the foregoing experimental results**" (page 38, lines 13 to 18). One such advantage is, thus, identified in lines 4 to 6 as:

"(4) The level of protein expression obtained is extremely high, the level corresponding to those of the viral proteins during infection."

4. The board understands the overall teaching in Example 8 as defining the properties of the **specific SFV** recombinant RNA system exemplified. It is not meant to describe the properties of all recombinant RNA molecules which may be derived from alphaviruses. Furthermore, the teaching in said point (4) is a

teaching about the amount of **proteins** which may be produced using this specific system. In contrast, in the above mentioned feature of claim 1 (point 1, supra), the "level of expression" referred to is that of an **RNA** rather than of proteins since it is said to be obtained **from** a promoter. Accordingly, in the board's judgment, the information provided in the passage including point (4) does not correspond to the now claimed subject-matter.

5. The presently claimed recombinant RNA molecule is not disclosed either implicitly or explicitly in any other passages of the application as filed taken as a whole.
6. The main request is rejected for not fulfilling the requirements of Article 123(2) EPC.

Auxiliary request for all designated Contracting States except ES and GR; claim 1

7. Claim 1 (section IV supra) is directed to a recombinant RNA molecule comprising an exogenous RNA sequence... which exogenous RNA sequence **encodes an amino acid sequence comprising an antigenic epitope or determinant of a pathogen**. The appellant refers to originally filed claims 1, 3 and 5 (section I, supra), to page 5, second paragraph and page 7, lines 8 to 20, 24 and 25 of the application as filed as basis for the claimed subject-matter.
8. The second paragraph on page 5 is part of a discussion of the prior art starting on page 2, relative to the use of viruses comprising RNA genomes to develop DNA expression systems with a specific reference to members

of the alphavirus genus. Mention is made of the previously developed Sindbis DNA expression systems. The problems inherent to their use are described and, immediately thereafter, in the second paragraph on page 5, it is stated:

"Another important aspect of viral DNA expression vectors is use thereof to express antigens of unrelated pathogens and thus they can be used as vaccines against such pathogens."

The statement is followed by a discussion on the properties of safe and effective vaccines. This disclosure certainly does not amount to a disclosure of the subject-matter of present claim 1.

9. On page 7, the necessity for developing improved DNA expression systems is emphasized (lines 8 to 20). Furthermore, as already above mentioned (point 2, supra), the passage from line 21 to line 30 discloses a recombinant RNA molecule having structural features used to define the now claimed recombinant. Yet, the information is missing that the exogenous RNA sequence encodes an amino acid sequence comprising an antigenic epitope or determinant of a pathogen and that it should be expressed from a subgenomic promoter. This passage on page 7 of the application as filed, thus, does not disclose the claimed subject-matter.

10. As for originally filed claim 3 - dependent in particular on claim 1 - and originally filed claim 5 - dependent in particular on claim 3 -, they relate to a recombinant RNA molecule wherein the exogenous RNA sequence encodes "... a peptide sequence **defining an**

exogenous antigenic epitope or determinant". This feature of the exogenous RNA is at the same time narrower and wider than that of the corresponding feature of exogenous RNA sequence of the presently claimed recombinant RNA molecule ("defining" rather than "comprising", no pathogen mentioned). Otherwise stated, the subject-matter of present claim 1 is simply different from that of the originally filed claims.

11. Thus, for the reasons explained in points 7 to 10 supra, the auxiliary request is rejected for not fulfilling the requirements of Article 123(2) EPC.

12. One last remark : it may be that by citing "side by side" the claims and passages of the application as filed alleged to provide a basis for claim 1 of either request, the appellant wished to imply that it was the combination of these claims and passages which was relevant to compliance with Article 123(2) EPC. In case it was intended so, the board will point out that, in accordance with the case law (eg. T 349/01 of 28 January 2004 and T 157/90 of 12 September 1991), it is not permissible under Article 123(2) EPC, to claim subject-matter which combines elements scattered throughout the application as filed unless it would be totally clear and unambiguous that they were meant to be combined. Nor is a generalisation allowable unless it finds a basis. This is not the case here as above explained.

Main and auxiliary requests for ES and GR

13. Claim 1 of these main and auxiliary requests is identical to claim 1 of the main and auxiliary requests

filed for the other designated Contracting States.
Therefore, the same reasoning applies and the requests
are refused for failing to comply with the requirements
of Article 123(2) EPC.

Respondent's request for apportionment of costs

14. The respondent requested that the board orders an
apportionment of costs in its favour in case oral
proceedings were to take place. Since oral proceedings
were cancelled due to the withdrawal of the appellant's
request for oral proceedings, the respondent's
conditional request for apportionment of costs became
irrelevant.

Order:

For these reasons, it is decided that:

The appeal is dismissed.

The Registrar

The Chairman

A. Wolinski

L. Galligani