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**Datasheet for the decision
of 20 December 2016**

Case Number: T 0679/11 - 3.3.08

Application Number: 01999116.5

Publication Number: 1356071

IPC: C12N15/86

Language of the proceedings: EN

Title of invention:

GENETICALLY ENGINEERED HERPES VIRUS FOR THE TREATMENT OF
CARDIOVASCULAR DISEASE

Patent Proprietor:

The University of Chicago

Opponent:

Virttu Biologics Limited

Headword:

HSV lacking ICP34.5 γ _{134.5} gene treat cardiovascular disease/
UNIVERSITY OF CHICAGO

Relevant legal provisions:

EPC Art. 123(2)

Keyword:

Main and sole request - Article 123(2) EPC - (no)

Decisions cited:

Catchword:



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Chambres de recours

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Case Number: T 0679/11 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 20 December 2016

Appellant:
(Opponent)

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Decision under appeal:

Interlocutory decision of the Opposition
Division of the European Patent Office posted on
20 January 2011 concerning maintenance of the
European Patent No. 1356071 in amended form.

Composition of the Board:

Chairman P. Julià
Members: B. Stolz
 D. Rogers

Summary of Facts and Submissions

- I. The opponent (appellant) filed an appeal against the decision of the opposition division, whereby the European patent No. 1356071 was maintained as amended at the oral proceedings held before the division.
- II. The opposition division decided that the main request, comprising claims 1 to 6, 15 (partially), and 16 to 22 as filed with letter of 23 March 2009, and claims 7 to 14 and 15 (partially) as filed during the oral proceedings, met the requirements of the EPC.
- III. The patent proprietor (respondent) filed a response to appellant's statement of grounds of appeal.
- IV. The parties were summoned to oral proceedings. A communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed to the summons, informed them of the preliminary, non-binding opinion of the board on some of the issues of the appeal proceedings, in particular those related to Articles 123(2), 83, 54 and 56 EPC.
- V. Under cover of a letter dated 17 October 2016, the respondent informed the board that it was not attending the oral proceedings and was not making any further written submissions.
- VI. Oral proceedings were held on 20 December 2016, in the absence of the respondent.
- VII. Claims 1 and 18 of the main and sole request read as follows:

"1. A method for the manufacture of a pharmaceutical composition for expressing a heterologous nucleic acid sequence in a vascular cell comprising mixing a recombinant replicating herpes simplex viral vector lacking at least one expressible $\gamma_134.5$ gene and operably comprising a heterologous nucleic acid, the herpes simplex virus being debilitated for growth in the central nervous system, with a pharmaceutically acceptable carrier, the pharmaceutical composition preferably being for treating or preventing a cardiovascular disease or condition.

18. A method for the manufacture of a pharmaceutical composition for inducing normal physiology in a functionally abnormal vascular cell comprising mixing one of the vectors as defined in claims 1 to 17 with a pharmaceutically acceptable carrier."

Dependent claims 2 to 17 and 19 to 22, respectively, refer to specific embodiments of the subject matter of the preceding independent claims.

VIII. The arguments of the appellant, as far as they are relevant for the present decision, may be summarized as follows:

Claim 1 referred to a vector "*operably comprising a heterologous nucleic acid*". The opposition division's conclusion that this feature merely meant that the heterologous sequence was "*operable*" and thus capable of being put into practice, was not correct.

The term "*operably*" appeared only once in the application as filed (WO 02/45431), namely on page 13,

line 20, in connection with a control sequence (page 13, lines 18-21). The term "*operatively*" was used twice on page 32, line 16, in connection with a promoter. The language used in claim 1 was different from the language used in the description, and it was not clear that it related to the same subject matter. In claim 1, "*operably*" referred to the vector. In the description the terms "*operably*" and "*operatively*", respectively, referred to a control sequence or a promoter, which was, however, not a feature of claim 1.

Beyond the definitions on pages 13 and 32, the patent application provided no definition of what an "*operable*" heterologous nucleic acid could be. The term "*operably*" was never used in the application as filed in conjunction with the heterologous nucleic acid. It was only ever used in conjunction with control sequences. Thus, the exclusion of a reference to the control sequences excluded an essential element of the disclosure as regards an operably linked sequence. Indeed, a reference to the control sequence was essential in order to understand what was meant by the term "*operably*" and to avoid the claim being interpreted as not requiring a control sequence of the kind disclosed. Taking the specific language and disclosure of page 13, lines 18-21, and page 32, lines 12-19, and applying it to the heterologous nucleic acid in the absence of a control sequence lead to an intermediate generalisation of the disclosure for which there was no support.

IX. The arguments of the respondent, as far as they are relevant for the present decision, may be summarized as follows:

The information content of a European patent application was determined by (i) the explicit, i.e., literal, disclosure of the invention, namely the description, the claims and the drawings, as well as (ii) the disclosure implicit in the patent application, i.e., what any person skilled in the art would consider necessarily implied by the patent application as a whole (e.g., in view of basic scientific laws).

The patent application was directed to a method for the manufacture of a pharmaceutical composition for expressing a heterologous nucleic acid sequence. In this context, the method of claim 1 required an HSV vector characterized in that it lacked at least one specific gene and operably comprised a heterologous nucleic acid. The skilled person in the field of biotechnology knew that a vector operably comprising a heterologous nucleic acid was a vector capable of expressing a heterologous nucleic acid, i.e. a vector comprising a functional heterologous nucleic acid. The only other option, i.e. a heterologous nucleic acid being non-operably comprised would, under no circumstances, result in expression of said nucleic acid. Consequently, the skilled person took from the specification as a whole, but also from claim 1 alone, that the mentioned heterologous nucleic acid had to be operably comprised in the vector, meaning that it was functional, i.e. capable of being expressed, because otherwise the expression method could not be put into practice. Hence, the subject-matter of claim 1 complied with the stipulations of Article 123(2) EPC.

- X. The appellant requested that the decision under appeal be set aside and the patent revoked.
- XI. The respondent requested that the appeal be dismissed.

Reasons for the Decision

1. As announced in writing (cf. point V, above), the respondent neither attended the scheduled oral proceedings nor did it file substantive arguments in reply to the board's preliminary, non-binding communication pursuant to Article 15(1) RPBA. By not attending the oral proceedings, the respondent effectively chose not to avail itself of the opportunity to comment or present its observations on the board's opinion despite the board announcing in point 13 of said communication that it considered it necessary to discuss, at the oral proceedings, certain issues in relation to the objections raised on the ground of Article 100(c) EPC. Instead, the respondent relied on its written case.

Article 123(2) EPC

2. The method of claim 1 comprises the use of "*a recombinant replicating herpes simplex viral vector [...] operably comprising a heterologous nucleic acid*".
3. The appellant argued that the insertion of the term "*operatively*" into claim 1 resulted in an extension of the claimed subject matter beyond the content of the application as filed (cf. point VIII, above).
4. The sole passage in the published international patent application WO 02/45431 (hereinafter "*the patent application*") making use of the term "*operably*" provides a specific and unambiguous definition of the relation between control elements and a coding nucleic acid sequence. It reads: "*Expression vectors can contain a variety of "control sequences," which refer*

to nucleic acid sequences necessary for the transcription and possibly translation of an operably linked coding sequence in a particular host cell" (page 13, lines 18-21). Similar information is also derivable from page 32, lines 12-19, where "*operatively positioned*" and "*operatively linked*" are defined as meaning that "*a promoter is in a correct functional location and/or orientation in relation to a nucleic acid sequence to control transcription of that sequence*".

5. This is the only explicit use in the patent application of the terms "*operably*" and "*operatively*", respectively. The first passage relates explicitly to the linking of control sequences to a coding sequence, i.e. the linking to a nucleic acid sequence encoding a protein but not to any heterologous nucleic acid sequence in general. The second passage explicitly relates to the positioning of a promoter, but not to the linking of any other control elements, in order to control transcription of a nucleic acid sequence. Therefore, neither of them explicitly discloses the contested feature of claim 1.

6. Moreover, these paragraphs do not provide an implicit disclosure of the subject matter at issue. An implicit disclosure means a disclosure which any person skilled in the art would objectively consider as necessarily implied in the explicit content. It means no more than the clear and unambiguous consequence of what is explicitly mentioned (cf. *inter alia*, T 823/96 of 28 January 1997, point 4.5 of the Reasons). The cited passages refer to the relation between a control sequence and a nucleic acid sequence but they are entirely silent with regard to the relation between a vector and a heterologous nucleic acid sequence. They

can therefore not provide an implicit disclosure of the subject matter of claim 1.

7. The board concludes that neither of the two passages cited above provides a direct and unambiguous disclosure of "*a recombinant replicating herpes simplex viral vector [...] operably comprising a heterologous nucleic acid*".
8. The respondent argued that the skilled person in the field of biotechnology knew that a vector "*operably comprising a heterologous nucleic acid*" was a vector "*capable of expressing a heterologous nucleic acid, i.e. a vector comprising a functional heterologous nucleic acid*". This was the only technically meaningful interpretation since a vector non-operably comprising a heterologous nucleic acid was unsuitable for expressing a heterologous nucleic acid according to the preamble of claim 1 (cf. point IX, above).
9. The board is not convinced by this argument. The respondent's conclusion that a vector non-operably comprising a heterologous nucleic acid would not be fit for the claimed purpose is only correct if the interpretation of this feature is limited to the respondent's interpretation. The feature can however also be interpreted more broadly.
10. Indeed, respondent's interpretation of this feature as "*a vector comprising a functional heterologous nucleic acid*" (underlined by the board) can also be understood to imply therapeutic activity of the heterologous nucleic acid itself. Alternatively, the contested feature can be understood as requiring operability of the vector in the sense of not rendering the replicating herpes simplex virus non-operable/non-

replicable. These interpretations result from the ambiguity of the contested feature and are not technically meaningless. Such subject matter is however not directly and unambiguously disclosed in the patent application. Thus, also when considering the implicit content of the entire patent application, claim 1 encompasses subject matter which extends beyond the content of the application as filed.

11. The board is aware of the case law concerning the presence, in a claim, of an ambiguous technical feature - for which there is no **explicit** disclosure in the application as filed - when assessing the requirements of Article 123(2) EPC (cf. "Case Law of the Boards of Appeal of the EPO", 8th edition 2016, II.E.1.9.7, page 447). According to this case law, the ambiguous nature of such a feature requires the claim to be interpreted.

The board considers however that, if the contested feature is of such an ambiguous nature that the claim does not define - in a straightforward manner - a few, concrete technically meaningful embodiments, then the claim must be considered to contravene Article 123(2) EPC. It is not the board's task to investigate and provide an exhaustive list of all further possible embodiments in an attempt to define the actual borders or limits of the subject-matter embraced by the claim. In the board's view, such an exercise is not to be carried out when assessing the requirements of Article 123(2) EPC.

12. In the present case, however, such an exercise is not required because, as stated in point 10 above, the interpretation of the ambiguous feature in claim 1 already results in some embodiments for which neither

explicit nor implicit support is derivable from the patent application as filed.

13. Thus, the board concludes that neither of the two passages cited in point 4 above nor any other part of the patent application provide a direct and unambiguous disclosure of "*a recombinant replicating herpes simplex viral vector [...] operably comprising a heterologous nucleic acid*".
14. Claim 1, and therefore the main and sole request, does not meet the requirements of Article 123(2) EPC.
15. Since the main and sole request is not allowable, the patent is revoked.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:



A. Wolinski

P. Julià

Decision electronically authenticated