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Datasheet for the decision of 8 May 2007

Case Number: T 0634/05 - 3.3.08

Application Number: 91113267.8

Publication Number: 0466199

IPC: C12N 15/12

Language of the proceedings: EN

Title of invention:
Factor VIIIc encoding DNA sequences and related DNA constructs

Patentee:
Novartis Vaccines and Diagnostics, Inc., et al

Opponents:
Bayer HealthCare LLC
BIOVITRUM AB

Headword:
Factor VIII:C/NOVARTIS

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
"Claim 1 of each of the requests on file: added matter (yes)"

Decisions cited:
T 0194/94, T 0823/96

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0634/05 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 8 May 2007

Appellant: (Patent Proprietor)	Novartis Vaccines and Diagnostics, Inc. 4560 Horton Street Emeryville CA 94608 (US)
Representative:	Goodfellow, Hugh, Robin Carpmaels and Ransford 43 Bloomsbury Square London WC1A 2RA (GB)
Respondent I: (Opponent 01)	Bayer HealthCare LLC 511 Benedict Avenue NY 10591-5097 Tarrytown (US)
Representative:	Taormino, Joseph Paul Hoffmann - Eitle Patent- und Rechtsanwälte Arabellastrasse 4 D-81925 München (DE)
Respondent II: (Opponent 02)	BIOVITRUM AB Lindhagensgatan 133 S-11276 Stockholm (SE)
Representative:	Pohlmann, Sandra M. Dörries Frank-Molnia & Pohlman Triftstrasse 13 D-80538 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted 17 March 2005 revoking European patent No. 0466199 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: F. Davison-Brunel
Members: T. J. H. Mennessier
M. Günzel

Summary of Facts and Submissions

I. The patentee (appellant) lodged an appeal against the decision of the opposition division of 17 March 2005 revoking the European patent No. 0 466 199. The patent, entitled "Factor VIIIc encoding DNA sequences and related DNA constructs", was granted on European application No. 91 113 267.8 which is a divisional application to application No. 85 100 223.8 (publication No. EP-A-0 150 735) filed on 11 January 1985.

II. The patent had been opposed on the grounds as set forth in Article 100(a) EPC that the invention was not novel and not inventive, in Article 100(b) EPC that it was not sufficiently disclosed and in Article 100(c) EPC that the subject-matter of the patent extended beyond the content of the application as filed (Article 123(2) EPC) and of the earlier parental application (Article 76(1) EPC).

III. The basis for the revocation was a main request (claims 1 to 16) filed at oral proceedings on 14 December 2004 which was considered by the opposition division not to fulfil the requirements of Articles 76(1) and 123(2) EPC (claims 1 to 16), and Article 84 EPC.

IV. On 28 July 2005 the appellant filed a statement of grounds of appeal which was accompanied by a main request and auxiliary requests 1 to 5. The main request corresponded to the claims as rejected by the opposition division.

V. Opponent 01 (respondent I) and opponent 02 (respondent II) replied to the statement setting out the grounds of appeal with letters dated 2 February 2006 and 9 February 2006, respectively.

VI. A communication under Article 110(2) EPC dated 20 June 2006 and presenting some of the Board's preliminary and non-binding views was sent to the parties.

VII. In reply to the Board's communication the appellant filed with a letter dated 30 August 2006 new auxiliary requests 2 and 3 to replace the corresponding requests then on file and three new auxiliary requests (dated 16 August 2006) numbered 6, 7 and 8 to be added to the earlier requests 1 to 5.

VIII. Both respondents also replied to the Board's communication with letters dated 30 August 2006.

IX. On 18 October 2006, the Board issued a communication under Article 11(1) RPBA with some further preliminary and non-binding opinions. The proceedings were scheduled to take place on 15 February 2007.

X. Further exchanges of information between the Board and all parties concerned led to postponement of the oral proceedings to 8 May 2007.

XI. On 5 April 2007 respondent I filed a further submission.

XII. Oral proceedings took place on 8 May 2007. The appellant withdrew its main and five first auxiliary requests and requested a decision based on its previous sixth, seventh and eighth auxiliary requests taken as

its main, first auxiliary and second auxiliary requests, respectively.

XIII. Claim 1 of the main request read:

"1. **A recombinant** nucleic acid **molecule coding for full length human Factor VIII:C protein** or a portion thereof that possesses coagulant activity, said nucleic acid molecule comprising:

a) the nucleotide sequence:

5' TTT CAA AAG AAA ACA CGA CAC TAT TTT ATT GCT GCA GTG GAG AGG CTC TGG GAT TAT GGG ATG 3'; or

b) a nucleotide acid molecule that is complementary to the sequence of part a)."

(emphasis added by the Board to show parts of the preamble which are also found in the two auxiliary requests)

XIV. Claim 1 of the first auxiliary request differs from claim 1 of the main request only in that, in the preamble, the phrase "or a portion thereof that possesses coagulant activity" has been deleted.

XV. Claim 1 of the second auxiliary request differs from claim 1 of the main request in that, in the preamble, the expression "nucleic acid" has been replaced by the term "DNA" and in that, also in the preamble, the expression "or a portion thereof that possesses coagulant activity" has been replaced by the phrase "which includes the specific sequence at or adjacent to the 5'-terminus of the sequence coding for the 67/70kd

doublet, which specific sequence is also present in the 77/80kd doublet".

XVI. The following documents are cited in the present decision:

(D6): M.A. Truett et al., DNA., Vol. 4, No. 5, 1985, Pages 333 to 349;

(D49): Declaration of Dr. S. Rosenberg dated 9 November 2004;

(D55): Declaration of Dr. M. A. Truett dated 11 November 2004;

(D65): Declaration of Prof. C. F. Higgins dated 19 July 2005.

XVII. The appellant's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

Article 123(2) EPC (claim 1; all requests)

The application as filed described in detail the search for the gene encoding full length Factor VIII:C. Taken as a whole, it was intended to identify Factor VIII:C. Ample specific support for full length Factor VIII:C was to be found in the description (see in particular page 2, lines 16 to 20; page 4, lines 16 to 22; and page 4, lines 30 to 35).

As explained in the declaration of Prof. C. F. Higgins (document D65) the skilled person would have considered that the application as filed described directly and unambiguously a nucleic acid molecule coding for full length Factor VIII:C.

Once a genomic clone had been obtained containing non-degenerate sequence corresponding to the N-terminal amino acids of 67/70 kd fragment as shown in the application (see Appendix B on page 53), the skilled person would have been perfectly able to clone the full length gene for Factor VIII:C using only the information given in combination with his/her common general knowledge. Evidence for this point was to be found in the declarations of Dr. S. Rosenberg (document D49; see point 6 thereof) and of Dr. M. A. Truett (document D55; see point 5 thereof) as regards the priority document.

There was no uncertainty about the number of genes encoding Factor VIII:C that would have caused problems in the cloning strategy.

XVIII. Respondent I's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

Article 123(2) EPC (claim 1; all requests)

The term "full length" as used in connection with "human Factor VIII:C" in claim 1 did not appear and was not defined anywhere in the application as filed. Nor did the application as filed contain any implicit disclosure for it (see in this respect decision T 823/96 of 28 January 1997).

It was not derivable from the application as filed that Factor VIII:C was encoded by a single gene and that consequently a recombinant nucleic acid molecule encoding for full length Factor VIII:C could be obtained.

At the filing date the appellant believed that Factor VIII:C might be encoded by more than one subunit, each of the subunits being encoded by a separate gene. This was evident from several passages in the application as filed, in particular the passage on page 4, lines 30 to 35.

As pointed to in the declaration of Dr. S. Rosenberg (document D49), at the filing date it was certainly not proven conclusively in the literature whether there were one or two genes involved (see point 16.1 of D49).

On the basis of the instructions contained in the application as filed which focused on the 77/80 kd doublet obtained upon electrophoresis under denaturing conditions, the skilled person would not have inevitably obtained a recombinant nucleic acid encoding the full length Factor VIII:C.

XIX. Respondent II's arguments, insofar as they are relevant to the present decision, may be summarised as follows:

Article 123(2) EPC (claim 1; all requests)

The inventors might have sought to provide DNA encoding Factor VIII:C but that could not be relevant or sufficient to acknowledge that DNA encoding full length Factor VIII:C would be derivable from the application as filed. Consistent with this position, the

application explicitly left it open whether Factor VIII:C was encoded by a single or by multiple genes (eg. page 4, lines 30 to 35) and consequently used deliberately ambiguous language. This was not surprising - because at the time the priority application was filed, the inventors simply did not know the answer to that question as they had not cloned the gene. The inventors were in fact only able to clone the entire Factor VIII:C gene much later (see document D6).

Following the instructions contained in the description the skilled person would not have inevitably obtained such a nucleic acid molecule coding for full length Factor VIII:C, as he/she would have been misled by the erroneous first 14 amino acids of the polypeptide represented in Appendix B.

XX. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained with the claims of auxiliary request 6 dated 16 August 2006 (main request), alternatively with the claims of auxiliary request 7 dated 16 August 2006 or with the claims of the auxiliary request 8 dated 16 August 2006.

XXI. Respondents I and II (opponents 01 and 02) requested that the appeal be dismissed.

Reasons for the Decision

Article 123(2) EPC

Main request

1. The use of the term "full length" to specify the human Factor VIII:C in the claims has been objected to under Article 123(2) EPC by the respondents.

2. The respondents' objection is to be associated with the fact that the term "full length" is not used in the application as filed. Indeed, it was introduced in claim 1 of the claim request filed with the letter of 25 January 2002 which corresponds to claim 1 of the main request. The support for said amendment in the application as filed had not been indicated.

3. In accordance with established board case law (see in particular T 194/84, OJ EPO 1990, 59) the relevant question to be decided in assessing whether an amendment in a claim - here, the term "full length" in claim 1 - adds subject-matter extending beyond the content of the application as filed within the meaning of Article 123(2) EPC is the question of whether that amendment was directly and unambiguously derivable from the application as filed, here, whether the application indeed discloses a DNA encoding full length Factor VIII:C while not identifying it as such, *expressis verbis*.

4. The phrase "nucleic acid molecule coding for full length human Factor VIII:C protein" implies, in particular, that the protein is encoded by a single gene.

5. A review of the application as filed shows how doubtful the structure of Factor VIII:C was at the filing date. Indeed, the passage referred to by the appellant on page 4, at lines 30 to 35, which reads:

"*The Factor VIIIC gene expression vector (an expression vector carrying* ***one or more genes*** *encoding for all or a portion of Factor VIIIC, precursor,* ***subunits*** *or fragments thereof) may be introduced into a compatible host and the host grown for expression of Factor VIIIC.*" (emphasis added by the Board)

may only lead to the conclusion that the appellant himself had not discarded the possibility that the protein might be composed of subunits, with one gene for each subunit.

6. The other passages specifically referred to by the appellant (see page 2, lines 16 to 20 and page 4, lines 16 to 32) also refer to "subunits". Another illustrative passage is the sentence on page 2, lines 26 to 31 which relates to the provision of a "DNA fragment encoding **a complete subunit**" (emphasis added by the Board).

7. Finally, it cannot be escaped that while discussing the amount of encoding DNA which was isolated by the inventors, the appellant defines it on page 34, lines 13 to 18 as "the total known coding sequence",

which, of course, is not tantamount to "the sequence encoding full length Factor VIII:C".

8. The appellant argued that, if the skilled person had followed the instructions contained in the description, he/she would have inevitably obtained the whole sequence encoding Factor VIII:C and, thus, would inevitably had come to the conclusion that a single gene encoded Factor VIII:C, presumably implying by such an argument that the application provided an unambiguous if implicit disclosure of a single gene encoding Factor VIII:C. In the Board's view, that position is not tenable. The case law established in T 823/96 (supra, point 4.5 of the decision) in relation to Article 123(2) EPC appears to be particularly relevant:

"*... the term "implicit disclosure" should not be construed to mean matter that does not belong to the content of the technical information provided by a document but may be rendered obvious on the basis of that content. In the Board's judgment, the term "implicit disclosure" relates solely to matter which is not explicitly mentioned, but it is a clear and unambiguous consequence of what is explicitly mentioned.*"

In the Board's judgement, the provision of the partial sequence of a gene encoding a polypeptide involved in Factor VIII:C activity does not have as a clear and an unambiguous consequence, the provision of the DNA encoding the full length Factor VIII:C, taking into account that the very nature of this factor was simply not known (see page 3, lines 15 to 21 of the application as filed: "*Human Factor VIIIC is a complex*

protein which can be isolated in substantially pure form exhibiting an apparent molecular weight of about 460kd. Upon electrophoresis under denaturing conditions, a large number of fragments result of varying molecular weights: 240, 160, 140, 115, 92.5, 80 and 77kd, the latter two being found to migrate as a doublet.").

9. Corroborating evidence that this way of reasoning has to be correct may be found in the fact that when the DNA encoding full length Factor VIII:C was finally identified (see document D6, Figure 8), it turned out to be different from that given in Appendix B of the present application.

10. Neither the declaration of Dr. M. A. Truett (document D49) nor the one of Dr. S. Rosenberg (document D55), each of which to the avail that the content of the earliest priority document is sufficiently complete to allow the skilled person to clone the gene coding for Factor VIII:C without undue difficulty, are relevant to support the appellant's argumentation. Indeed, the content of the earliest priority document is restricted compared to the content of the application as filed (Appendix A et B are absent) and focuses on preliminary experimental results concerning a particular fragment, the 67/70 kd as isolated by preparative SDS electrophoresis, while leaving open the possibility that Factor VIII:C was composed of several subunits each of which being encoded by a separate gene.

11. If, as stated at point 11 of the declaration of Prof. C. F. Higgins (document D65), the 63 nucleotide sequence represented in claim 1 was the only DNA sequence in which the inventors could be completely confident, until the cDNA encoding full length Factor

VIII:C gene had been isolated, it is not at all unambiguous that the skilled person, following the instructions contained in the description including Appendix A and B, would have inevitably obtained a recombinant nucleic acid molecule coding for full length human Factor VIII:C.

12. In view of the afore-mentioned remarks, the Board concludes that the introduction of the term "full length" in claim 1 as an amendment which is not directly and unambiguously derivable from the application as filed and that, therefore, the application has been amended in such a way that it contains subject-matter which extends beyond the content of said application.

13. Therefore, the main request does not comply with the requirements of Article 123(2) EPC. For this reason alone, it cannot be allowed. At oral proceedings, much discussion also took place as to whether or not replacing the term "coagulant" by the term "anticoagulant" in claim 1 of the main request was a correction which could be allowed under Rule 88 EPC. Yet, in view of the decision under Article 123(2) EPC, this issue need not be addressed here.

First and second auxiliary requests (auxiliary requests 7 and 8 both dated 16 August 2006)

14. Claim 1 of the first auxiliary request also contains in its preamble the wording "A recombinant nucleic acid molecule coding for full length human Factor VIII:C protein". Therefore, this request does not comply with the requirements of Article 123(2) EPC, for the same reasons as given in respect of the main request.

15. In claim 1 of the second auxiliary request, the claimed nucleic acid is identified as being DNA. This restriction does not affect the reasoning made with respect to the main request, the only nucleic acid referred to in the experimental part being DNA. Therefore, also the second auxiliary request does not comply with the requirements of Article 123(2) EPC.

16. As none of the requests on file comply with the requirements of Article 123(2) EPC, there is no basis for the maintenance of the patent in an amended form.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

A. Wolinski F. Davison-Brunel