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Datasheet for the decision of 30 November 2009

Case Number: T 0898/08 - 3.3.08

Application Number: 96945101.2

Publication Number: 0871754

IPC: C12N 15/85

Language of the proceedings: EN

Title of invention:
Method for obtaining retroviral packaging cell lines producing high transducing efficiency retroviral supernatant

Applicant:
SYSTEMIX, INC.

Opponent:
-

Headword:
Packaging cells/SYSTEMIX

Relevant legal provisions:
EPC Art. 123(2)
RPBA Art. 13(1)

Relevant legal provisions (EPC 1973):
EPC Art. 54(1)(2), 56, 83, 84
EPC R. 28(1)

Keyword:
"Main request: inventive step (no)"
"First auxiliary request: clarity (no)"
"Second auxiliary request: compliance with the EPC (yes)"

Decisions cited:
G 0001/04

Catchword:

-

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Case Number: T 0898/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 30 November 2009

Appellant: SYSTEMIX, INC.
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 13 November 2007 refusing European application No. 96945101.2 pursuant to Article 97(1) EPC 1973.**

Composition of the Board:

Chairwoman: T. Karamanli
Members: T. J. H. Mennessier
M. R. Vega Laso

Summary of Facts and Submissions

I. The applicant (appellant) lodged an appeal against the decision of the examining division dated 13 November 2007, whereby European patent application No. 96 945 101.2 with publication number 0 871 754 was refused. The application, entitled "*Method for obtaining retroviral packaging cell lines producing high transducing efficiency retroviral supernatant*", originated from an international application published as WO 97/21825.

II. The decision was based on the main request (claims 1 to 22), the first auxiliary request (claims 1 to 18) and the second auxiliary request (claims 1 to 8), all filed during the oral proceedings held on 7 February 2007. The main request was refused for reason of lack of novelty (Article 54 EPC 1973) in view of document D12 (see Section XII, *infra*) and the first auxiliary request for reason of lack of inventive step in view of either (i) document D12 in combination with document D1, or (ii) document D11 (see Section XII, *infra*) or document D12 in combination with common general knowledge. In a previous communication under Rule 51(4) EPC 1973, the examining division had considered a second auxiliary request filed during the oral proceedings to be allowable but, since by its letter of 11 July 2007 the appellant maintained its main and first auxiliary requests, the examining division came to the conclusion that the version communicated pursuant to Rule 51(4) EPC 1973 had not been approved. Consequently, the requirements of Article 113(2) EPC 1973 were not fulfilled and the application was refused under Article 97(1) EPC 1973.

III. On 19 March 2008, the appellant filed a statement setting out the grounds of appeal. It requested that a patent be granted on the basis of claims 1 to 18 according to a single request which the appellant considered to correspond to the set of claims according to its previous first auxiliary request filed on 11 July 2007.

IV. The examining division did not rectify its decision and referred the appeal to the board of appeal (Article 109 EPC 1973).

V. On 14 September 2009, the board issued a summons to oral proceedings which was accompanied by a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) containing the board's provisional and non-binding opinion on the issues of added matter, clarity and inventive step.

VI. In reply to the board's communication, the appellant filed on 30 October 2009 further submissions together with a new main request and a new auxiliary request which replaced the previous request on file. A new document (D15; see Section XII, *infra*) was also filed.

VII. By a communication pursuant to Article 17(1) RPBA dated 19 November 2009, the board introduced two further documents (documents D13 and D14; see Section XII, *infra*) into the proceedings.

VIII. At the oral proceedings, which took place on 30 November 2009, the appellant filed three sets of claims, namely a new main request, a new first

auxiliary request and a second auxiliary request (see sections IX, X and XI *infra*).

IX. The set of claims according to the new **main request** consists of 17 claims of which claim 1 reads as follows:

"1. A method for obtaining a recombinant retroviral packaging cell capable of producing retroviral vectors comprising the steps:

(a) obtaining a eukaryotic cell free of endogenous murine leukemia virus retroviral nucleic acid and those sequences closely related to murine leukemia virus which, by recombination, would produce replication competent retrovirus,

(b) preparing a minimal *gag-pol* open reading frame (ORF) insert from a murine leukemia retrovirus, wherein the minimal *gag-pol* ORF is defined by the sequences from the initiation through the termination codon of the *gag-pol* gene with no flanking retroviral sequences;

(c) inserting the minimal *gag-pol* ORF prepared from step (b) into an appropriate expression plasmid;

(d) preparing a minimal *env* open reading frame (ORF) insert from a murine leukemia retrovirus, wherein the minimal *env* ORF is defined by the sequences from the initiation through the termination codon of the *env* gene with no flanking retroviral sequences;

(e) inserting the minimal *env* ORF prepared from step (d) into an appropriate expression plasmid;

(f) inserting the expression plasmids of steps (c) and (e) into the cell of step (a);

(g) propagating the cell obtained from step (f) under conditions favourable for expression of the minimal retroviral *gag-pol* and *env* ORF; and

(h) screening the cell of step (g) for retroviral *gag*, *pol*, and *env* production, thereby obtaining retroviral packaging cell capable of packaging recombinant retroviral vector sequences to produce recombinant, transducing retrovirus."

X. The set of claims according to the **first auxiliary request** consists of 8 claims of which claim 4 reads as follows:

"4. A method of increasing the gene transduction efficiency of a cell, comprising the steps:

(a) obtaining a eukaryotic cell free of endogenous murine leukemia virus retroviral nucleic acid and those sequences closely related to murine leukemia virus which, by recombination, would produce replication competent retrovirus,

(b) preparing a minimal *gag-pol* open reading frame (ORF) insert from a murine leukemia retrovirus, wherein the minimal *gag-pol* ORF is defined by the sequences from the initiation through the termination codon of the *gag-pol* gene with no flanking retroviral sequences;

(c) inserting the minimal *gag-pol* ORF prepared from step (b) into an appropriate expression plasmid;

(d) preparing a minimal *env* open reading frame (ORF) insert from a murine leukemia retrovirus, wherein the minimal *env* ORF is defined by the sequences from the initiation through the termination codon of the *env* gene with no flanking retroviral sequences;

(e) inserting the minimal *env* ORF prepared from step (d) into an appropriate expression plasmid;
(f) inserting the expression plasmids of steps (c) and (e) into the cell of step (a);
(g) propagating the cell obtained from step (f) under conditions favourable for expression of the minimal retroviral *gag-pol* and *env* ORF; and
(h) screening the cell of step (g) for retroviral *gag*, *pol*, and *env* production, thereby obtaining retroviral packaging cell capable of packaging recombinant retroviral vector sequences to produce recombinant, transducing retrovirus. [sic]

transducing said cells with a retroviral-based vector; and subsequently propagating the cells under conditions favorable for the production and secretion of retroviral vector supernatant; and transducing the cell with a retroviral vector supernatant produced from the culture of said retroviral vector producer cell, wherein the retroviral vector supernatant is produced from the co-culture of a first and a second complementary vector producer cell."

XI. The set of claims according to the **second auxiliary request** consists of one claim which is identical to claim 1 of the first auxiliary request and reads as follows:

"1. A recombinant retroviral packaging cell selected from the group consisting of ProPak-A.6 having ATCC Accession No. CRL 12006 and ProPak-X.36 having ATCC Accession No. CRL 12007."

XII. The following documents are referred to in the present decision:

(D1): WO 92/05266 (published on 2 April 1992);

(D6): Y. Soneoka et al., Nucleic Acids Research, Vol. 23, No. 4, 25 February 1995, pages 628 to 633;

(D11): F-L. Cosset et al., Journal of Virology, Vol. 69, No. 12, December 1995, pages 7430 to 7436;

(D12): WO 94/29438 (published on 22 December 1994);

(D13): D. Ott et al., Journal of Virology, Vol. 64, No. 2, February 1990, pages 757 to 766 ;

(D14): S. P. Forestell et al., Gene Therapy, Vol. 4, 1997, pages 600 to 610;

(D15): E. Otto et al., Human Gene Therapy, Vol. 5, May 1994, pages 567 to 575.

XIII. The submissions made by the appellant, in so far as they are relevant to the present decision, may be summarised as follows:

Main request

Article 56 EPC 1973

The use of minimal *gag-pol* and *env* ORFs, which included only those retroviral sequences from the ATG through the stop codon of the genes with no flanking sequences,

allowed the preparation of packaging cells which were both safe, as illustrated in Tables 3 and 8 (see page 49 and 67 of the application, respectively), and efficient, as reported on page 5, lines 15 to 20 and in Example 10 on pages 67 to 69 of the application.

Although it would have been possible for the inventors of document D12 to delete the viral sequences downstream of the *gag-pol* and *env* ORFs in order to obtain minimal ORFs, these helper virus genomes of D12 contained retroviral sequence portions having a length of 20 to 30 base pairs which were suitable for homologous recombination. Thus, at the relevant date, the skilled person had to assume that (i) these 3' sided flanking sequences of *gag-pol* and *env* ORFs were necessary for the production of functional helper viruses with a satisfying packaging efficiency to obtain a retroviral supernatant having a high transduction efficiency, and (ii) the sequences disclosed in D12 already represented the minimum *gag-pol* and *env* ORFs.

Document D15 taught that helper viruses provided in document D12 could not exclude the risk of occurrence of RCR under any conditions, but merely minimised the risk, since a recombination with the recombinant retroviral vectors to be packaged was possible due to the presence of viral sequence portions located downstream of the *gag-pol* and *env* ORFs.

None of the other prior art documents D1, D6 and D11 suggested the complete deletion of retroviral sequences flanking the *gag-pol* and *env* ORFs because it was

important to keep those sequences to balance safety and efficiency.

It had surprisingly been found that a complete deletion of retroviral sequences flanking the *gag-pol* and *env* ORFs resulted in helper viruses which were suitable for an efficient packaging of recombinant retroviral genomes and enabled the production of recombinant replication deficient retroviral vectors after transformation in transducer cells. These vectors had a high transduction efficiency and there were no RCR among them, even if the production of the recombinant retroviral vectors took place under stringent conditions. Therefore, with the claimed method and packaging cells it was possible to exclude the risk of RCR formation without reducing the transduction efficiency of the resulting retroviral supernatant.

Anyway neither document D12 nor document D15 taught that the packaging cell line should be derived from a eukaryotic cell free of endogenous retroviral sequences.

First auxiliary request

Article 84 EPC 1973 (clarity; claim 4)

The person skilled in the art would have been in a position to determine unambiguously from the description the method for which protection was sought in claim 4.

Second auxiliary request

The sole claim was clear and its subject-matter was new and inventive.

XIV. The appellant requested that the decision of the examining division be set aside and a patent be granted on the basis of the main request or, in the alternative, on the basis of the first or second auxiliary request, all filed during the oral proceedings. As a third auxiliary request, the appellant requested that the decision of the examining division be set aside and that the case be remitted to the first instance with the order to grant a patent on the basis of the second auxiliary request filed on 7 February 2007.

Reasons for the Decision

Main request

Admissibility

1. Since the set of claims according to the main request was filed as a direct reaction to objections under Article 84 EPC 1973 raised by the board at the oral proceedings, the board, exercising its discretion under Article 13(1) RPBA, decided to admit it into the proceedings.

Compliance of claim 1 with the requirements of Article 123(2) EPC and Article 84 EPC 1973

2. The board is satisfied that claim 1 does not contain subject-matter which extends beyond the content of the application as filed and that it is clear, concise and supported by the description. Thus, claim 1 complies with the requirements of Article 123(2) EPC and Article 84 EPC 1973.

Compliance of claim 1 with the requirements of Article 54(1) and (2) EPC 1973

3. The board is also satisfied that the subject-matter of claim 1 is new over the cited state of the art. Thus, claim 1 complies with the requirements of Article 54(1) and (2) EPC 1973.

Non-compliance of claim 1 with Article 56 EPC 1973

4. Claim 1 is directed to a method of obtaining a recombinant retroviral packaging cell. The packaging cells are derived from a eukaryotic cell line free of endogenous murine leukemia virus (MLV) retroviral nucleic acid and those sequences closely related thereto which would be capable of producing replication competent retrovirus (RCR) by recombination with transduced retroviral sequences. The minimal *gag-pol* and *env* open reading frames (ORFs) are inserted into dedicated expression plasmids which are then introduced into the cells separately so that they integrate in different positions of the cell genome. The *gal-pol* and *env* sequences, which can be derived from the same MLV or from two different MLVs, are minimal in the sense

that each of the ORFs includes only those sequences from the initiation through the termination codon of the corresponding gene, with no flanking retroviral sequences.

5. For the assessment of whether or not the subject-matter of claim 1 involves an inventive step, document D12 is considered to represent the closest state of the art. D12 describes the preparation of retroviral packaging cells according to a method which differs from the method of claim 1 in that, in order to preclude the generation of RCR, the two expression vectors carrying the *gag-pol* and *env* genes, which are generally referred to in document D12 as "KAT" plasmids, are constructed in such a way that only the protein coding sequences from the retroviral genome are present (see page 11, lines 11 to 13).

6. The plasmids pIK6.1gagpolATG and pIK6.1amenvATG comprise retroviral flanking sequences positioned downstream from the *gag-pol* and *env* ORFs - which are referred to *infra* as 3' flanking sequences - (see document D12, passage from line 10 on page 10 to line 17 on page 12 together with page 15, lines 6 and 7 as well as Example I, pages 35 to 44). The plasmid pIK6.1gagpolATG contains viral sequences of the Moloney MLV extending from the nucleotide position 621, which corresponds to the ATG start codon of the *gag* coding sequence, to the nucleotide position 5869, i.e. it includes 33 flanking nucleotides behind the stop codon at position 5837 (see page 20, lines 15 to 28 together with Figure 1 of document D12). The plasmid pIK6.1amenvATG contains the viral sequence of the MLV 4047A *env* gene extending from the nucleotide at

position 37, which corresponds to the ATG start codon of the *env* coding sequence, to the nucleotide at position 2025, which corresponds to a Nhe.I cleavage site located downstream of the stop codon of the *env* ORF within the 3' LTR region, i.e. it includes 25 flanking nucleotides behind the stop codon at position 2000 (see passage from line 29 on page 20 to line 12 on page 21 together with Figure 1 of document D12). The plasmids are introduced into, *inter alia*, human embryonic kidney 293 cells (see page 32, lines 18 to 26 of document D12). The structure of these plasmids is said to preclude the generation of RCR (see page 11, lines 8 to 28).

7. In view of document D12, the technical problem to be solved may be seen as the provision of an alternative method for obtaining a recombinant safe packaging cell capable of producing retroviral vectors using expression plasmids the structure of which precludes the generation of RCR. The solution to that problem provided in claim 1 is a method which differs from the method disclosed in document D12 in that (i) the recombinant packaging cell is derived from a eukaryotic cell free of endogenous murine leukemia virus retroviral sequences which, by recombination, would produce replication competent retrovirus, and that (ii) **minimal** *gag-pol* and *env* ORFs each derived from a murine leukemia virus are used, each extending from the initiation codon to the termination codon of the gene in question, with no flanking retroviral sequences.

8. In the decision under appeal, the examining division held that, since a person skilled in the art at the priority date of the application would have been aware

that the risk of homologous recombination and the production of replication competent viruses could be minimised by eliminating as much of the homologous retroviral sequences as possible, and by using cell lines free of endogenous sequences with homology to the retroviral vectors, the solution proposed in claim 1 was obvious and did not involve any inventive activity (see point 2.3, second and third paragraphs of the decision under appeal).

9. The appellant contested this finding arguing that the skilled person would have considered the presence of the 3' flanking sequences described in document D12 to be essential for the preparation of safe packaging cell lines and, consequently, would not have tried to eliminate them.

10. This argument fails to convince the board. Nowhere in document D12 is any particular role allocated to the residual 3' flanking sequences present in the illustrated KAT plasmids, nor is there any suggestion that the residual flanking sequences might be essential for minimising the occurrence of replication competent retroviruses. If any, the sole function of the 3' flanking sequences which the skilled person may have inferred from document D12 was to facilitate the construction of the KAT plasmids from the plasmids pMOVpsi and pCRIPAMGAG-2 by using restriction sites available in the flanking sequences, which are indicated on pages 20 (see line 15 onwards) and 21 (see lines 1 to 12) of document D12.

11. The further documents on file do not support the appellant's argument either. On the contrary, document

D15, which was filed by the appellant together with its statement of grounds of appeal, links the occurrence of RCR with the presence of such 3' flanking sequences. The purpose of the study described in this document was to determine whether the RCR detected in three lots of a recombinant retroviral vector obtained using recombinant packaging cells resulted from recombination between the sequences in the vector and the helper sequences including the *gag-pol* and *env* genes in the packaging cells (see the "Introduction" section on pages 567 and 568). The results showed that homologous recombination events occurring between the *env* sequences in the packaging cells and 3' LTR sequences in the viral vector contributed to the creation of RCR (see the paragraph entitled "*Origin of the RCR in GlNa*" bridging pages 573 and 574).

12. While it is true that documents D6 and D11 do not suggest deletion of sequences flanking the *gag-pol* and *env* ORFs, document D1 introduces the concept of using "*minimal sequences other than the protein coding sequences*" to decrease the possibility of homologous generation of replication-competent virus (see page 22, lines 10 to 15) and, thus, paves the way for a complete deletion.

13. The board is convinced that, in view of the above, a person skilled in the art seeking to obtain safe packaging cells would have adopted a cautious attitude and prepared expression plasmids with *gag-pol* and *env* ORFs deprived of any flanking sequences.

14. As concerns the appellant's further argument that neither document D12 nor document D15 described a

method in which the packaging cell line was derived from a eukaryotic cell free of endogenous retroviral sequences, the board concurs with the examining division in that a person skilled in the art working in the field of retroviral vectors at the relevant date was well aware of the risk of recombination between endogenous retroviral sequences and the retroviral vectors introduced into the cells for replication. In the board's view, selecting a eukaryotic cell line free of retroviral sequences was an obvious measure which the skilled person would have taken without applying any inventive skills. In this respect, the board notes that the 293 cells the use of which is recommended in document D12 (see page 32, lines 18 to 24) are the cells which were selected to derive packaging cells in the experiments reported in the application (see page 43, lines 27 to 28, page 44, lines 2 to 3 and page 47, lines 5 to 9).

15. Therefore, the subject-matter of claim 1 does not involve an inventive step and the main request does not comply with Article 56 EPC 1973.

Concluding remark

16. In view of the above remarks, the main request cannot form a basis for the grant of a patent.

First auxiliary request

Admissibility

17. The first auxiliary request was filed as a direct reaction to the conclusion reached by the board that

the main request did not comply with Article 56 EPC 1973.

18. In such circumstances, the board, exercising its discretion under Article 13(1) RPBA, decided to admit the first auxiliary request into the appeal proceedings.

Non-compliance of claim 4 with the clarity requirement of Article 84 EPC 1973

19. Claim 4 is directed to a method which is not unambiguously defined with respect to different aspects:

19.1 The preamble of the claim, which refers to "*[A] method of increasing the gene transduction efficiency of* ***a cell***" (emphasis added by the board), does not account for the fact that, in the process of transducing a target cell population using retroviral particles produced by packaging cells upon transfection with a recombinant retroviral vector, the transduction is not operated by the cells but by the retroviral supernatant recovered from the cell culture (see page 4, lines 9 to 12, page 25, lines 10 to 11, and page 26, lines 28 to 29, of the application).

19.2 In addition, the characterising part of claim 4 is unclearly worded in that it fails to distinguish unambiguously the packaging cells, the producer cells and the target cell population. Furthermore, whereas in the general part of the description the term "complementary" has been used only in association with the term "tropism" (see page 6, lines 7 to 8, page 30, lines 14 to 15, and page 33, lines 8 to 16, of the application), the meaning of that term as used in the

final clause of the claim is obscure. Additionally, claim 4 is unclear in that steps (a) to (h) lead to the preparation of one packaging cell, whereas the above final clause refers to two producer cell lines.

20. According to decision G 1/04 (OJ EPO 2006, 334; see the Reasons, point 6.2), "*Article 84 EPC requires that the claims define the subject-matter for which protection is sought, and that they **must** be clear. It signifies that an independent claim within the meaning of Rule 29 EPC should explicitly specify all of the essential features needed to define the invention, and that the meaning of these features **should be clear** for the person skilled in the art **from the wording of the claim alone**. [..]. These requirements serve the overriding purpose of **legal certainty**.*" (emphasis added by the board). Therefore, the appellant's argument that the skilled person would have determined unambiguously from the description the precise method for which protection is sought in claim 4 is not tenable.

21. Therefore, claim 4 is not clear and the first auxiliary request does not comply with the clarity requirement of Article 84 EPC 1973.

Concluding remark

22. In view of the above remarks, the first auxiliary request cannot form a basis for the grant of a patent.

Second auxiliary request

Admissibility

23. The second auxiliary request, which consists of only one claim corresponding exactly to claim 1 of the first auxiliary request, was filed as a direct reaction to the conclusion reached by the board that the first auxiliary request did not comply with Article 84 EPC 1973.

24. In such circumstances, the board, exercising its discretion under Article 13(1) RPBA, decided to admit it into the appeal proceedings.

Compliance with the requirements of Article 123(2) EPC and of Articles 84, 83 and 54(1) and (2) EPC 1973

25. Claim 1 is directed to two specific recombinant retroviral packaging cells, namely ProPak-A.6 having ATCC Accession No. CRL 12006 and ProPak-X.36 having ATCC Accession No. CRL 12007. Those cells are unambiguously referred to at different places in WO 97/21825 (which is the published version of the application as filed), in particular on page 6, lines 16 to 20, as regards ProPak-A.6 (with a reference to its ATCC Accession number) and on page 47, lines 21 to 25, as regards ProPak-A.6 (with a reference to its ATCC Accession number). Claim 1 does not contain subject-matter which extends beyond the content of the application as filed. It is clear, concise and supported by the description. Therefore, the requirements of Article 123(2) EPC and Article 84 EPC 1973 are met.

26. The board is satisfied that the relevant provisions of Rule 28(1) EPC 1973 with respect to the deposit of biological material have been complied with and that both packaging cells are new over the cited state of the art. Therefore, the requirements of Articles 83 and 54(1) and (2) EPC 1973 are also met.

Compliance with Article 56 EPC 1973

27. The two recombinant retroviral packaging cells ProPak-A.6 and ProPak-X.36 are derived from the human embryonic kidney 293 cell line which has been proved not to contain endogenous retroviral sequences. Their genome contains the *gal-pol* and *env* MLV ORFs which have been integrated separately using two different plasmids. Those ORFs are minimal, in the sense that they extend from the initiation to the termination codon of the respective gene, with no flanking retroviral sequences. Furthermore, the *gag-pol* ORF is expressed from the MLV-LTR promoter in ProPak-X.36.

28. The results in Figure 16A of the application show that both ProPak-X.36 and ProPak-A.6 are able to produce retroviral vector preparations which transduce human hematopoietic stem/progenitor cells with consistently higher efficiency than that produced from the standard mouse packaging PA317 cell line (see page 61, line 25). Table 7 (see page 62) shows that for two different tissues, namely, mobilised peripheral blood and adult bone marrow from a cadaver, the ProPak-A.6 and -X.36 supernatants performed better in terms of transduction efficiency than the PA317 supernatant.

29. RCR generation tests are reported in Example 9 (see pages 66 and 67). Although ProPak-X.36 is not mentioned in Example 9, the board is convinced that the tests were performed using that specific clone which is the sole ProPak-X clone identified in the application (see page 47, lines 18 to 22). Cultures of ProPak-A.6 and co-cultures of ProPak-X.36 with ProPak-X.52 (another cell line in which the *gal-pol* packaging functions are expressed from the MLV-LTR promoter), each cell line carrying BC140revM10, a vector known to rapidly generate RCR in PA317, were maintained for up to 3 months. In no case was RCR detectable in supernatants from ProPak cells cultures (see Table 8 on page 67).

30. The ability of stable cell lines to yield supernatants which mediate such a high-efficiency gene transfer in hematopoietic cell populations without RCR formation would not have been predictable at the relevant date by the skilled person in view of the state of the art, inclusive of document D12.

31. Thus, the subject-matter of claim 1 involves an inventive step and, therefore, the second auxiliary request also complies with Article 56 EPC 1973.

Concluding remark

32. Since the second auxiliary request meets the requirements of the EPC, it forms the basis for the grant of a patent.

Third auxiliary request

33. As the second auxiliary request is allowable, there is no need to consider the third auxiliary request.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division with the order to grant a patent on the basis of claim 1 according to the second auxiliary request filed during the oral proceedings on 30 November 2009, and of a description to be adapted thereto.

The Registrar The Chairwoman

A. Wolinski T. Karamanli