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**Datasheet for the decision
of 7 September 2018**

Case Number: T 0503/12 - 3.3.08

Application Number: 99946662.6

Publication Number: 1109937

IPC: C12Q1/68, C07K16/08

Language of the proceedings: EN

Title of invention:

Method of diagnosing, monitoring, staging, and imaging various cancers

Patent Proprietor:

Diadexus, Inc.

Opponent:

Medarex, Inc.

Headword:

Tumour marker/DIADEXUS

Relevant legal provisions:

EPC Art. 54, 83, 113(1)

EPC R. 115(2)

RPBA Art. 12(4), 15(3)

Keyword:

Admission of auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B -
(no)

Sufficiency of disclosure - main request, auxiliary requests 4
and 5 - (no)

Novelty - auxiliary requests 6 and 7 - (no)

Decisions cited:

Catchword:



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Case Number: T 0503/12 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 7 September 2018

Appellant: Diadexus, Inc.
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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
30 December 2011 concerning maintenance of the
European Patent No. 1109937 in amended form.**

Composition of the Board:

Chairman B. Stolz
Members: M. Montrone
J. Geschwind

Summary of Facts and Submissions

- I. An appeal was lodged by the patent proprietor (hereinafter "appellant") against the interlocutory decision of an opposition division concerning European patent No. 1 109 937, having the title "*Method of diagnosing, monitoring, staging, and imaging various cancers*".
- II. The patent was opposed under Articles 100(a) EPC on the grounds of lack of novelty and inventive step and under Articles 100(b) and (c) EPC.
- III. In the decision under appeal the opposition division held that claims 1 to 10 of the main request (claims as granted) complied with the requirements of Articles 123(2) EPC, but that the patent did not sufficiently disclose the claimed invention (Article 100(b) EPC). It further took the view that claims 1 to 10 of auxiliary requests 1A, 2A and 3A, claims 1 to 6 of auxiliary requests 1B, 2B and 3B, claims 1 to 5 of auxiliary request 4, claims 1 to 3 of auxiliary request 5, and claim 1 of auxiliary request 6 did not meet the provisions of Article 83 EPC. Further, it held that the subject-matter of claim 1 of auxiliary request 7 was anticipated by the disclosure of document D2 (Article 54 EPC). Lastly, auxiliary request 8 and pages of the description adapted thereto were considered to comply with the requirements of the EPC.
- IV. With its statement of grounds of appeal, the appellant submitted eleven auxiliary requests. Auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B were new in the appeal proceedings, while the main request (claims as granted) and auxiliary requests 4 to 8 corresponded to the

respective requests dealt with in the decision under appeal.

V. Claim 7 of the main request reads:

"7. Use of an antibody or antibody fragment which binds specifically to the protein encoded by polynucleotide sequence SEQ ID No: 1 or to a fragment of the protein encoded by polynucleotide sequence SEQ ID No: 1, wherein the fragment of the protein encoded by polynucleotide sequence SEQ ID No: 1 is encoded by polynucleotide sequence SEQ ID No: 10, 11, 12 or 13, in the manufacture of a medicament for *in vivo* imaging of a cancer selected from breast, ovarian, endometrial and uterine cancer."

Claim 2 of auxiliary requests 4 and 5 reads:

"2. Use of an antibody or antibody fragment which binds specifically to the protein encoded by polynucleotide sequence SEQ ID NO: 1 or to a fragment of the protein encoded by polynucleotide sequence SEQ ID NO: 1, wherein the fragment of the protein encoded by polynucleotide sequence SEQ ID NO: 1 is encoded by polynucleotide sequence SEQ ID NO: 12 or 13, in the manufacture of a medicament for *in vivo* imaging of a cancer selected from breast, ovarian, endometrial and uterine cancer."

Claim 1 of auxiliary request 6 reads:

"1. An isolated antibody or antibody fragment which binds specifically to a fragment of the protein encoded by polynucleotide sequence SEQ ID NO: 1, wherein the fragment of the protein encoded by polynucleotide

sequence SEQ ID NO: 1 is encoded by polynucleotide sequence SEQ ID NO: 12 or 13."

Claim 1 of auxiliary request 7 reads:

"1. A diagnostic method indicative of the presence of a cancer selected from breast, ovarian, endometrial and uterine cancer in a patient, the method comprising:

(a) measuring levels of a polynucleotide comprising SEQ ID NO: 1, 11, 12 or 13, a native mRNA encoded thereby, or a fragment thereof (CSG) in a sample of cells, tissues or bodily fluids obtained from the patient; and

(b) comparing measured levels of CSG with levels of CSG in a sample of cells, tissues or bodily fluids obtained from a normal human control, wherein a change in measured levels of CSG in the patient versus the levels of CSG in the normal human control is associated with the presence of a selected cancer."

VI. In reply to the appellant's statement of grounds of appeal, the opponent (hereinafter "respondent") submitted arguments *inter alia* as to why the patent did not sufficiently disclose the subject matter of the claims directed to the use of antibodies of the main request (Articles 100(b) EPC), and auxiliary requests 1A, 1B, 2A, 2B, 3A, 3B, and 4 to 6 contravened (Article 83 EPC). Furthermore, it submitted arguments as to why *inter alia* the antibodies as defined in claim 6 of the main request lacked novelty in view of the disclosure of document D2, and submitted that in the decision under appeal the opposition division found that auxiliary request 7 lacked novelty.

VII. The parties were summoned to oral proceedings. In a communication pursuant to Article 15(1) RPBA, the parties were informed of the board's provisional, non-binding opinion on some of the legal and substantive matters of the case. In reply thereto, both parties, without providing substantive arguments, announced that they would not be attending the oral proceedings.

VIII. Oral proceedings before the board were held on 7 September 2018, in the absence of both parties.

IX. The following documents are referred to in this decision:

D2: WO 00/36107, published on 22 June 2000;

D3: WO 99/63088, published on 9 December 1999;

D23: Stryer L., Biochemistry 4th ed., W. H. Freeman and Company New York, 1999, pages 60-61, 110, 140-141 and 975;

D31: Appendix A and B, filed with the letter of 22 September 2011.

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

Main request - claim 7; auxiliary requests 4 and 5 - claim 2

Sufficiency of disclosure (Articles 100(b) or 83 EPC)

The patent in suit reported neither anti-Ovr110 antibodies nor that Ovr110 proteins were expressed in

the various claimed cancer diseases. The suitability of anti-Ovr110 antibodies in the diagnosis of these diseases was nevertheless derivable for the skilled person from the experimental data disclosed in Example 2, because the data showed that the expression of the Ovr110 gene was significantly increased in tissues derived from these cancers.

The protein sequences encoded by the Ovr110 gene and its fragments were also not disclosed in the patent in suit. However, the skilled person knew at the filing date of the patent in suit how to translate a nucleic acid sequence into a corresponding protein sequence. This task was either achieved by hand or by an appropriate software program and would have resulted in a single open reading frame (ORF) for the sequence of SEQ ID NO: 1. Thus, the provision of DNA sequences of the Ovr100 gene and fragments thereof enabled the skilled person to generate corresponding Ovr110 proteins. This did not apply to the nucleic acids of SEQ ID NOs: 10 and 11 which lay within the non-coding region of the Ovr110 gene, and were therefore not translated into corresponding proteins.

Antibodies binding specifically to the Ovr110 protein were not raised at the relevant date of the patent. However, the raising of such antibodies against a known protein required solely routine experimental work of the skilled person. Although the selection of specific anti-Ovr110 antibodies with a sufficient specificity and affinity was needed for a diagnostic use, the generation of such antibodies likewise only required routine work, since ELISA assays for assessing the expression level of the Ovr110 protein were described in the patent in suit (see paragraphs [0039] and [0040]).

Furthermore, despite protein levels of Ovr110 have indeed not been determined in cancer patients or in controls, this did not affect the diagnostic utility of the antibodies, because the skilled person knew at the relevant date that increased mRNA expressions led to increased protein expressions (see e.g. document D23, chapter 37, page 975, lines 14 to 16).

Auxiliary request 7 - claim 1

Novelty (Article 54 EPC)

Document D2 did not anticipate the subject-matter of claim 1, since alignments of the relevant sequences of SEQ ID NOs: 27 and 74 with SEQ ID NO: 1 referred to in claim 1 showed that the sequence of SEQ ID NO: 74 had one additional adenosine at its 3' end and an insertion between positions 2042 and 2043 of SEQ ID NO: 1 (see document D31). Furthermore, the sequence of SEQ ID NO: 27 was the reverse complement of the nucleotide sequence located between positions 2124 to 2585 of SEQ ID NO: 1. Both sequences were identical except for differences at positions 2154, 2219, 2524 and 2544 of SEQ ID NO: 1 (see document D31).

XI. The respondent's submissions, insofar as they are relevant to the present decision, may be summarised as follows:

Main request - claim 7, auxiliary requests 4 and 5 - claim 2

Sufficiency of disclosure (Articles 100(b) or 83 EPC)

Example 2 of the patent in suit disclosed that the expression of the Ovr110 gene was increased in the various claimed cancer diseases. However, Tables 2 and 3 in Example 2 only reported an increased relative level of Ovr110 without indicating which particular sequence was analysed, i.e. whether the data related solely to the full-length nucleotide sequences of SEQ ID NO: 1, its fragments (SEQ ID NOs: 10 to 13), or to all of these sequences. Moreover, the tables were silent on the primers and probes used for the quantitation. Thus, it could not be demonstrated by the data in Example 2 that the expression levels of the nucleotide sequences of SEQ ID NOs: 1 and 10 to 13 were increased in all of the cancer diseases referred to in the claim.

Further, the patent in suit was silent about a protein that might be encoded by the sequences of SEQ ID NOs: 1 and 10 to 13 and hence, whether they encoded an Ovr110 protein at all. Furthermore, information about the protein's basic structure and location was lacking, including expression studies of the protein in the claimed cancer diseases. In other words, the patent in suit did not disclose the generation of an Ovr110 protein or antibodies binding to it. Nor did it disclose that the protein expression correlated with the mRNA expression of the Ovr110 gene and that the protein was over-expressed in the claimed cancers too. Moreover, it was a prerequisite for antibodies being suitable for the claimed diagnostic applications that they bound to regions of the Ovr110 protein exposed on the cell surface. In the absence of all this information, the patent in suit did not plausibly disclose that the anti-Ovr110 antibodies were suitable for the claimed diagnostic use. A subsequent analysis of the sequence of SEQ ID NO: 1 revealed that the

nucleotide sequences of SEQ ID NOs: 10 and 11 related to non-coding regions of SEQ ID NO: 1, i.e. both sequences were not translated into corresponding proteins.

XII. The appellant requested that the decision under appeal be set aside and the patent be maintained as granted, or in the alternative, on the basis of one of auxiliary requests 1A, 1B, 2A, 2B, 3A, 3B, and 4 to 8, all filed with its statement of grounds of appeal.

XIII. The respondent requested that the appeal be dismissed.

Reasons for the Decision

1. The duly summoned parties did not attend the oral proceedings, which in accordance with Rule 115(2) EPC and Article 15(3) RPBA took place in their absence.

Article 113(1) EPC

2. The board in its communication pursuant to Article 15(1) RPBA expressed a reasoned provisional opinion on the issues to be discussed at the oral proceedings, which included the admission of auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B (Article 12(4) RPBA); sufficiency of disclosure in relation to *inter alia* claim 7 of the main request and claim 2 of auxiliary requests 4 and 5 (Articles 100(b) and 83 EPC); and lack of novelty of the subject-matter of claims 1 of auxiliary requests 6 and 7 vis-à-vis the disclosures of documents D2 and D3.

3. None of the parties provided any substantive comments or arguments in reply to the board's communication pursuant to Article 15(1) RPBA (cf. point VII *supra*).

Moreover, by not attending the oral proceedings, the parties decided not to avail themselves of another opportunity to orally address or comment on the issues raised by the board in its communication for defending their case. The present decision is therefore based on the same grounds, arguments and evidence on which the provisional opinion of the board was based.

Admission of auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B into the appeal proceedings

4. Auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B have been submitted by the appellant with its statement of grounds of appeal. According to Article 12(1) and (2) RPBA, these requests are part of the appeal proceedings. The board, however, pursuant to Article 12(4) RPBA, has a discretion to hold inadmissible facts, evidence or requests, which could have been presented or were not admitted into the first instance proceedings.
5. Claims 1 of auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B comprise an amendment restricting the measurement of protein levels to the level of "a native protein encoded by SEQ ID NO: 1". Objections concerning the measurement of protein levels on the ground of opposition under Article 100(b) EPC have been raised in the respondent's (then opponent's) opposition brief (see point 7.6). In its preliminary opinion, the opposition division shared the respondent's view on this issue (see communication attached to the summons to oral proceedings, point 3.5.6).
6. In reply and in preparation of the oral proceedings before the opposition division, the appellant filed several auxiliary requests (auxiliary requests 1A, 1B,

2A, 2B, 3A, 3B and auxiliary requests 4 to 6). However, none of these requests comprised the amendment identified in point 5 above that is contained in claim 1 of the present auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B. At the oral proceedings, the opposition division maintained its view that the patent in suit did not sufficiently disclose the subject matter as defined by the claims of any of these requests (Articles 100(b) and 83 EPC, respectively, see decision under appeal, points 3.4.2.2, 3.4.2.4, 3.5.4, 3.6.2). In reply, the appellant filed two further auxiliary requests (auxiliary requests 7 and 8). Claims 1 of these two requests were amended by deleting any references to measurements of protein levels. Thus, these two requests did not comprise the amendment presented in claim 1 of the afore mentioned requests either.

7. In view of the above, the board cannot see any reason - and the appellant did not provide such reason - why auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B could not have been submitted by the appellant in the first instance proceedings in support of it's case. Their submission now is neither occasioned by issues raised for the first time in the decision under appeal nor by arguments raised by the respondent only at a late stage in the first instance proceedings.
8. Hence, auxiliary requests 1A, 1B, 2A, 2B, 3A and 3B, all filed with the appellant's statement of grounds of appeal are not admitted into the appeal proceedings in accordance with Article 12(4) RPBA.

Main request (claims as granted) - claim 7

Sufficiency of disclosure (Article 100(b) EPC)

9. According to the established case law, if a therapeutic use of a substance is claimed, attaining the claimed therapeutic effect is a functional feature of the claim. Thus, unless this is already known to the skilled person at the priority date, the patent in suit must disclose the suitability of the substance for the claimed therapeutic application (see Case Law of the Boards of Appeal, 8th edition 2016, II.C.6.2).
10. It is the view of this board that the same applies to the diagnostic use of a claimed substance.
11. Claim 7 is directed to the use of an antibody or a fragment thereof binding specifically to a protein encoded by the polynucleotide sequence of SEQ ID NO: 1, or to fragments of this protein encoded by the polynucleotide sequences of SEQ ID NOs: 10, 11, 12 or 13 in the manufacture of a medicament for *in vivo* imaging of a cancer selected from breast, ovarian, endometrial and uterine in a patient.
12. The patent in suit designates the protein encoded by the gene having the sequence of SEQ ID NO: 1 or fragments thereof (SEQ ID NOs: 10, 11, 12 or 13) as "Ovr110" (see title of paragraph [0057]). Thus, claim 1 relates to a diagnostic use of anti-Ovr110 antibodies in detecting the various cancers specified in the claim under *in vivo* conditions in a patient.
13. The *in vivo* imaging of cancer using the antibodies according to claim 7 requires that the Ovr110 protein encoded by the nucleotide sequences of SEQ ID NO: 1 is

expressed in the cancer cells in a manner accessible to antibodies, i.e. as an *in vivo* diagnostic marker it has to be located in the cell membrane and to contain an extracellular domain detectable by antibodies. Further, the protein has to be present on the surface of the cancer cells in amounts significantly increased vis-à-vis non malignant cells.

14. It is common ground between the parties that neither the patent in suit nor the prior art disclose experimental evidence that anti-Ovr110 antibodies detect the claimed cancers by *in vivo* imaging. Thus, the issue to be assessed in the present case is whether or not the patent in suit provides sufficient information which, having due regard of the skilled person's common general knowledge, would put said person in a position to perform the invention across the whole of the claimed scope readily and without undue burden.
15. Example 1 of the patent reports that the Ovr110 gene is a "*cancer specific gene*" (CSG) based on the analysis of EST expression data in the "*LIFESEQ*" database and a comparison of the gene expression level between normal and tumour tissues (see paragraphs [0050] and [0051]).
16. Example 2 of the patent further discloses the relative quantitation of Ovr110's gene expression by real-time quantitative PCR measurements in different tissue samples, including various cancer-derived tissues (see paragraphs [0054], [0057], [0060], and Table 3). The analysis of the data in Table 3 shows that the expression of the Ovr110 gene is higher in samples derived from breast, ovarian, endometrial and uterine cancers, i.e. the cancers referred to in claim 7, compared to normal tissue (see paragraph [0061]).

17. In the board's view, the skilled person would derive from the experimental data disclosed in Example 2 of the patent in suit that the Ovr110 gene is over-expressed in the various claimed cancers.
18. With regard to the proteins encoded by the nucleic acid sequences of SEQ ID NOs: 1 and 10 to 13, it is common ground between the parties that the sequences of SEQ ID NOs: 10 and 11 lie within the non-coding region of the full-length nucleic acid sequence of SEQ ID NO: 1. In other words, both nucleic acid sequences are under *in vivo* conditions not translated into corresponding proteins.
19. Thus, either it is technically not possible to raise anti-Ovr110 antibodies against the protein fragments encoded by SEQ ID NOs: 10 and 11 since they are not translated into corresponding proteins, or if it would nevertheless be possible to raise them, the antibodies generated are unable to detect Ovr110 *in vivo*, since these fragments are absent from the Ovr110 protein. It follows from the considerations above that not all of the anti-Ovr110 antibodies falling within the claimed ambit are suitable for the claimed diagnostic use.
20. In view of these circumstances, the board concludes that the patent in suit does not disclose the invention as defined in claim 7 of the main request in a manner sufficiently clear and complete for it to be carried out by the skilled person over the whole scope claimed (Article 100(b) EPC).

Auxiliary requests 4 and 5 - claim 2

Sufficiency of disclosure (Article 83 EPC)

21. Claim 2 of auxiliary requests 4 and 5 differs from claim 7 of the main request by the deletion of the proteins encoded by the nucleic acid sequences of SEQ ID NOs: 10 and 11.
22. In view of this difference, the board observes that the arguments set out in points 9 to 17 above with regard to sufficiency of disclosure for claim 7 of the main request equally apply to the subject-matter of claim 2 of auxiliary requests 4 and 5.
23. With regard to the proteins encoded by the nucleic acid sequences of SEQ ID NOs: 1, 12 and 13 as recited in claim 2, it is common ground between the parties that the application as filed does not disclose proteins encoded by these sequences. It is further uncontested that the application as filed is silent on the expression of the Ovr110 protein in the various claimed cancers, let alone its over-expression. Moreover, since the protein sequence of the Ovr110 is not disclosed in the application as filed, its structure (absence or presence of an extracellular domain) and its location in the cell (intracellular, secreted or membrane-bound) is unknown. This information is likewise not derivable from the nucleic acid sequence of SEQ ID NO: 1 or its fragments.
24. As set out in point 13 above, the antibodies according to claim 2 are only suitable for the detection of the various claimed cancers *in vivo*, if the Ovr110 protein is located in the cell membrane of the cancer cells in significantly increased amounts compared to non

malignant cells and has an exposed extracellular domain so that the antibodies can bind to it.

25. However, as set out in point 23 above, neither the location of the Ovr110 protein nor the existence of an extracellular domain of the protein can be derived from the information disclosed in the application as filed. Thus, the skilled person, even assumed in the appellant's favour that a protein based on the disclosed DNA sequence of Ovr110 can be obtained and antibodies can be generated against such a protein, has no guidance how to generate antibodies that are necessarily suitable for the claimed diagnostic use. In such a situation, the skilled person has to generate many antibodies and to test them all individually for their binding to cancer cells, if they bind at all. Moreover, if antibodies fail to bind to Ovr110 in such an assay, the skilled person does not know why they fail, because that could be due to the absence of the Ovr110 protein in the cancer cells tested, the protein's intracellular location or its secretion, or the lack of an accessible extracellular domain in the Ovr110 protein.
26. In view of the considerations above, even further assumed in the appellant's favour that the increased gene expression of Ovr110 in the various cancer tissues reported in Example 2 of the application as filed might be correlated with an increased expression of the Ovr110 protein or the presence of a substantial amount of this protein in the cancers recited in claim 2, the skilled person has to find out by trial and error which of the anti-Ovr110 antibodies are suitable, if any, for the claimed diagnostic use. This amounts to a research program for the skilled person and constitutes an undue burden.

27. Thus, the application fails to disclose the invention as defined in claim 2 of auxiliary requests 4 and 5 in a manner sufficiently clear and complete for it to be carried out by the skilled person (Article 83 EPC).

Auxiliary request 6 - claim 1

Novelty (Article 54 EPC)

28. Claim 1 is directed to an isolated antibody or antibody fragment binding specifically to a fragment of the protein encoded by polynucleotide sequence SEQ ID NO: 1, wherein the fragment of the protein is encoded by the polynucleotide sequences of SEQ ID NOs: 12 or 13.
29. It is uncontested that the proteins encoded by the polynucleotide sequences of SEQ ID NOs: 12 and 13 encompass the complete coding region of the polynucleotide sequence of SEQ ID NO: 1, or in other words encode the complete Ovr110 protein (see decision under appeal, point 3.4.2.2 and document D31, alignment disclosed on page 1).
30. It is further common ground between the parties that document D3 is a prior art document pursuant to Article 54(3) EPC.
- 30.1 Document D3 discloses the amino acid sequence of a protein identified as "PR01291" (see e.g. page 188, lines 30 to 33, page 190, lines 5 to 7, Figure 208 and SEQ ID NO: 291) and a fragment thereof that "*retains a qualitative biological activity of a native PR01291 polypeptide*" (see page 190, line 19). Furthermore, the nucleotide sequence of PR01291 corresponds to the

nucleotide sequence of SEQ ID NO: 1 in the patent in suit. This was not disputed by the appellant.

30.2 The document further discloses antibodies that bind to the PR01291 protein or to fragments thereof (see e.g. page 365, line 16 to page 370, line 23, and example 144 on page 494, claim 17). With regard to an antibody binding to a PR01291 protein fragment, page 190, lines 16 to 18 reads as follows: "*In yet another aspect, the invention concerns an isolated PRO 1291 polypeptide, comprising the sequence of amino acid residues 1 or about 29 to about 282, inclusive of Figure 208 (SEQ ID NO:291), or a fragment thereof sufficient to provide a binding site for an anti-PR01291 antibody*" (emphasis added).

31. Thus, since the sequences of SEQ ID NOs: 12 and 13 referred to in claim 1 are both fragments of SEQ ID NO: 1 that encode together the entire Ovr110 protein (see point 29 above), the antibodies disclosed in document D3 being generated against the PR01291 protein or to a fragment thereof fall directly and unambiguously within the ambit of claim 1 and therefore deprive the claimed antibodies of their novelty.

32. Consequently, auxiliary request 6 contravenes Article 54 EPC.

Auxiliary request 7 - claim 1

Novelty (Article 54 EPC)

33. Claim 1 is directed to a diagnostic method indicative of the presence of a cancer selected from breast, ovarian, endometrial and uterine in a patient by

measuring in step (a) levels of a polynucleotide comprising SEQ ID NO: 1 or a fragment thereof. Thus, the claimed method is directed *inter alia* to the measurement of levels of polynucleotides comprising any fragment of SEQ ID NO: 1 as markers in the diagnosis of the cancers recited in claim 1.

34. It is common ground between the parties that document D2 discloses methods for diagnosing ovarian cancer based on the determination of the expression level of various nucleic acid sequences including those encoded by SEQ ID NOs: 27 and 74 (see Examples 1 and 2 and claim 57).
35. Further, it is uncontested that the sequence of SEQ ID NO: 74 of document D2 is identical to the sequence located at positions 1022 to 2587 of SEQ ID NO: 1 according to claim 1, except for one additional adenine nucleotide at its 3' end, the deletion of one guanine nucleotide at position 1833 of SEQ ID NO: 1 and the insertion of one additional cytosine nucleotide at position 2042 (see document D31, page 22 to 25).

Document D2 further discloses the sequence of SEQ ID NO: 27 which is a partial sequence of SEQ ID NO: 74, and thus likewise a partial sequence of SEQ ID NO: 1 (see document D31, page 18 to 21). The sequence of SEQ ID NO: 27 is identical to the reverse complement sequence located at positions 2124 to 2585 of SEQ ID NO: 1 according to claim 1, except for the nucleotides at positions 2154, 2219, 2524 and 2544.

36. As pointed out by the appellant, the sequences of SEQ ID Nos: 74 and 27 do not completely match that of SEQ ID NO: 1 over their full length. However, they comprise subsequences which completely match SEQ ID NO. 1, for

example, a sequence comprising the nucleotides between the positions 1022 to 1800 of SEQ ID NO: 1, or a sequence comprising the nucleotides between the positions 2124 to 2150 of SEQ ID NO: 1. Since claim 1 is directed to measuring the levels of any nucleotide sequence comprising any possible fragment of SEQ ID NO: 1, in other words to polynucleotides comprising any shorter sequence thereof, it encompasses *inter alia* the use of sequences of SEQ ID Nos: 74 or 27 for the diagnosis of ovarian cancer.

37. Therefore, claim 1 is not novel, and hence auxiliary request 7 contravenes Article 54 EPC.

Auxiliary request 8

38. The patent proprietor is the sole appellant. Thus, the principle of the prohibition of *reformatio in peius* applies for auxiliary request 8 and the pages of the description adapted thereto.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



L. Malécot-Grob

B. Stolz

Decision electronically authenticated