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Datasheet for the decision of 17 November 2011

Case Number: T 1277/08 - 3.3.08

Application Number: 96944531.1

Publication Number: 815263

IPC: C12Q 1/68

Language of the proceedings: EN

Title of invention:
Methods for the detection of clonal populations of transformed cells in a genomically heterogeneous cellular sample

Patentee:
Esoterix Genetic Laboratories, LLC

Opponent:
Roche Diagnostics GmbH

Headword:
Detection of transformed cells/ESOTERIX

Relevant legal provisions:
EPC Art. 54, 56, 83, 84, 123(2)(3)
RPBA Art. 12(4), 13(1)(3)

Keyword:
"Amended claims - admitted"
"Requirements of the EPC - met"

Decisions cited:
T 0411/98, T 0548/03

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1277/08 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 17 November 2011

Appellant I: (Patent Proprietor)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 3 March 2008 concerning maintenance of European patent No. 815263 in amended form.**

Composition of the Board:

Chairman: M. Wieser
Members: M. R. Vega Laso
J. Geschwind

Summary of Facts and Submissions

I. European patent No. 0 815 263 with the title "Methods for the detection of clonal populations of transformed cells in a genomically heterogeneous cellular sample" is based on European patent application No. 96944531.1 which was filed as international application under the PCT and published as WO 97/23651. The patent was granted with 14 claims.

II. An opposition to the grant of the patent was filed. The opposition was based on the grounds mentioned in Article 100(a), (b) and (c) EPC 1973, in particular that the claimed subject-matter lacked novelty (Article 54 EPC 1973) and inventive step (Article 56 EPC 1973), that the granted claims encompassed added matter which went beyond the content of the application as filed, and that the claimed invention was not disclosed in a manner sufficiently clear and complete for a person skilled in the art to carry it out.

III. In an interlocutory decision under Articles 102(3) and 106(3) EPC 1973 posted on 3 March 2008, the opposition division found that, while the maintenance of the patent as granted was prejudiced by the ground for opposition of Article 100(c) EPC, a set of amended claims and a description adapted thereto filed as auxiliary request 1 during the oral proceedings met the requirements of the EPC.

IV. The patent proprietor (appellant I) and the opponent (appellant II) each lodged an appeal against the interlocutory decision of the opposition division.

V. Together with its statement of grounds of appeal, appellant I filed five sets of amended claims as auxiliary requests 1 to 5. The claims as granted were maintained as the main request.

VI. Appellant II filed a statement setting out its grounds of appeal together with new evidence (documents (10), (11) and (12)).

VII. As a subsidiary request, both parties requested oral proceedings.

VIII. Each party was given the opportunity to reply to the grounds of appeal of the other party. Only appellant I filed observations.

IX. The parties were summoned to oral proceedings. In a communication under Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) attached to the summons to oral proceedings, the board expressed its provisional opinion on some issues concerning Article 123(2) EPC which arose from the claims then on file.

X. The patent was transferred to the present patent proprietor and the transfer was recorded in the Patent Register.

XI. In response to the board's communication, appellant I filed six sets of amended claims as, respectively, main request and auxiliary requests 1 to 5, which replaced its previous requests. Appellant II submitted observations.

XII. Oral proceedings were held on 17 November 2011. During the oral proceedings, appellant I filed a new set of amended claims as main (and sole) request replacing all the requests previously on file.

XIII. Claim 1 of the main request reads:

"1. A method of detecting the presence of a subpopulation of transformed cells in a biological sample obtained from an organism comprising the steps of:

a) determining from the biological sample a number X of a first wild-type polynucleotide characteristic of a genomic region that is not mutated, in said subpopulation of transformed cells;

b) determining from the biological sample a number Y of a second wild-type polynucleotide in a genomic region of said organism suspected of being mutated in said subpopulation of transformed cells; and

c) determining whether a statistically significant difference exists between said number X wherein said number X is indicative of the amount of a reference allele in said sample and said number Y wherein said number Y is indicative of the amount of wild-type target allele in said sample, the presence of a statistically significant difference being indicative of the presence of a subpopulation of transformed cells in said biological sample."

Dependent claims 2 to 4 relate to particular variants of the method according to claim 1.

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

(1): O.-P. Kallioniemi et al., June 1992, Proc. Natl. Acad. Sci. USA, Vol. 89, pages 5321 to 5325;

(2): J. A. Macoska et al., 15 July 1994, Cancer Research, Vol. 54, pages 3824 to 3830;

(3): WO 95/09928, published on 13 April 1995;

(10): A. L. Hubbard et al., 1994, Br. J. Cancer, Vol. 70, pages 434 to 439;

(11): H.-X. An et al., 1995, Int. J. Cancer (Pred. Oncol.), Vol. 64, pages 291 to 297;

(12): J. E. Stickland et al., 1993, Oncogene, Vol. 8, pages 223 to 227.

XV. The submissions made by appellant I, as far as they are relevant to this decision, may be summarized as follows:

Admission of a new set of amended claims into the proceedings

The new set of amended claims did not give rise to additional issues, but overcame objections under Article 123(2) EPC on which the board had expressed an adverse opinion. The amendments were straightforward and did not require further discussion.

Article 123(2) EPC

Numerous passages in the application as filed, for instance, on page 6 lines 8 to 17 described methods according to the invention without the restriction to a "clonal" subpopulation. Even though on line 18 of the same page the wording "clonal" was used, the passage concerned to a "preferred embodiment". Thus, the omission of the feature "clonal" in claim 1 did not offend against Article 123(2) EPC.

Article 84 EPC

The amended claims were clear and concise within the meaning of Article 84 EPC. In the context of mammalian cells, the wording "*transformed cells*" meant "cancerous" or "precancerous" cells.

Article 83 EPC

There was no statement in the application as filed to the effect that the claimed methods would not work using PCR.

Admission of documents (10) to (12) into the proceedings

Documents (10) to (12) could have been submitted in opposition proceedings. Their content was not more relevant than the content of other documents already on file. Thus, in accordance with the jurisprudence of the Boards of Appeal documents (10) to (12) should be disregarded.

Article 54 EPC

Documents (1) to (3) were not prejudicial to the novelty of the claims because they described a different method used for a different purpose.

Article 56 EPC

Documents (1) to (3) addressed the problem of finding a suitable method of determining the level of amplification of oncogene sequences in tumour cells. This problem differed from the problem underlying the present invention. In the experiments described in the prior art documents, only isolated tumour cells were used. The method of the prior art would not be suitable for detecting the presence of a small subpopulation of tumour cells in a sample containing mainly normal cells. It would be difficult, if not impossible to adapt the method of document (1) for the purpose of the present invention.

XVI. The submissions by appellant II, as far as they are relevant to this decision, were as follows:

Admission of a new set of amended claims into the proceedings

The new set of claims should not be admitted into the proceedings because it was filed at a very late stage of the proceedings.

Article 123(2) and (3) EPC

Claim 1 as filed was directed to a method of detecting the presence of a clonal subpopulation of transformed cells. The subject-matter of amended claim 1, in which the wording "clonal" had been omitted, had no basis in the application as filed. Thus, Article 123(2) EPC was contravened.

Article 84 EPC

The claims did not comply with Article 84 EPC. The feature "*polynucleotide characteristic of a genomic region*" was not clear, because the skilled person was in doubt whether (i) DNA or (ii) DNA and RNA (see page 8, line 49 of the patent) was meant. The wording "*transformed cells*" could be understood as referring to cells in which DNA had been introduced.

Article 83 EPC

Except for the link between mutation or loss of the p53 gene and colon cancer, the specification of the patent did not disclose which mutation pertaind to cancer or a metabolic disease, in particular to which specific kind of cancer or metabolic disease.

The specification was totally silent on the determination of the number X and Y. The skilled person did not know what the numbers X and Y meant and was not able to determine them. Moreover, the specification did not teach how a reference gene was identified. It was very doubtful whether a small amount of transformed

cells present in a sample such as stool would indeed be sufficient to allow detection.

The scope of the claims was extremely broad and encompassed also PCR methods. It was apparent from paragraphs [0005] and [0027] of the patent that PCR methods would not allow detecting the presence of a subpopulation of transformed cells in a biological sample.

Admission of documents (10) to (12) into the proceedings

Documents (10) to (12), which related to methods using PCR, had not been filed during the opposition proceedings because, in view of the statements in the patent in suit, it had been believed that the claimed invention was not enabled for methods involving PCR. Thus, for the sake of efficiency of procedure PCR-related documents were not submitted. The finding in the decision under appeal that methods involving PCR were in fact enabled had been surprising.

Documents (10) to (12) were submitted together with the statement of grounds of appeal, i.e. right at the beginning of the appeal procedure, as an immediate response to the opposition division's finding. Since the evidence they provided was highly relevant with respect to novelty of the invention, they should be admitted into the appeal proceedings.

Article 54 EPC

In the decision under appeal, the opposition division found that a difference between the methods described in the prior art documents (1) to (3) and the claimed method was that the latter required the sample to be analyzed completely. It was not apparent which of the features in the claims supported this understanding. Since the sample was not defined in the patent by a particular minimum size or any other feature, it could be any part of a complex plant or animal, for example tumour cells as described in documents (1) to (3). The wording of claim 1 explicitly allowed for further steps to be performed before or after any of the steps a) to c), which could also be a particular treatment of the sample, resulting e.g. in a reduction of the biological material of the sample. Thus, the claimed method did not require that the whole sample be analyzed.

Furthermore, the opposition division found that documents (1) to (3) addressed a different problem, namely analysis of genetic alterations rather than detecting a subpopulation. However, for the assessment of novelty it was only relevant whether all features of the respective claim were disclosed in the prior art. This was the case here. Documents (1) to (3) described subpopulations, particularly in line 18 of the abstract and in the passage on page 5324, left column, second paragraph, first sentence in document (1); on page 3829, first sentence in the first paragraph of the left column in document (2); and on page 15, line 28 in document (3).

Consequently, in the light of the content of documents (1) to (3) the subject-matter of claim 1 lacked novelty.

Article 56 EPC

The subject-matter of the claims did not involve an inventive step within the meaning of Article 56 EPC. Document (1), which was considered as the closest state of the art, taught that an increased copy number of a certain oncogene was associated with cancer. It would be obvious to a skilled person seeking to detect the presence of tumour cells to determine the copy number of an oncogene and compare it to a reference gene.

XVII. Appellant I (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained on the basis of claims 1 to 4 of the main request filed at the oral proceedings.

XVIII. Appellant II (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

Admission of a new set of amended claims into the proceedings

1. The amended claims of the present main request were filed at the oral proceedings after discussion of the requests previously on file. The amendments introduced into the claims are intended to overcome objections under Article 123(2) EPC. While it is true that the

pertinent objections had been raised by the opponent already in the notice of opposition, in the decision under appeal the opposition division considered that the objections in question were not justified. Thus, there was no motivation for the proprietor to amend the claims at the onset of the appeal proceedings, i.e. with its statement of grounds of appeal.

2. Only from the board's communication sent in preparation for the oral proceedings (see paragraph IX above) did appellant I learn that the board was, provisionally, not inclined to share the opposition division's view on Article 123(2) EPC with respect to the term "*transformed*" omitted in claim 1. In response to the board's communication, appellant I addressed this issue by filing a set of amended claims as auxiliary request II. This set of claims differed from the claims of the present main request only in that it included a clerical error ("*... of an amount of a reference allele ...*" instead of "*... of the amount of a reference allele ...*") and further dependent claims which have now been deleted.

3. Under Article 13(1) RPBA, any amendment to a party's case after it has filed its grounds of appeal or reply may be admitted and considered at the board's discretion. Although the submission of the claims at the oral proceedings must be regarded as a "very late" submission which should be accepted and considered only in exceptional situations, in the present case the board has decided to admit the amended claims of the main request into the proceedings. In exercising its discretion, the board has taken into account that the introduced amendments are in fact straightforward,

neither raise new issues nor take the other party by surprise, and can be dealt with without adjournment of the oral proceedings (see Article 13(3) RPBA).

Article 123(2) and (3) EPC

4. Present claim 1 is derived from claim 1 of the application as filed. A basis for the features introduced into step c) of the claim to define the numbers X and Y is found on page 6, lines 20 to 25 of the application as filed.

5. As regards the basis for the omission of the feature "clonal", which in claim 1 of the application as filed characterized the subpopulation of transformed cells ("*A method for detecting the presence of a clonal subpopulation of transformed cells ...*"), the board observes that the feature "clonal" is specified in some passages of the application as filed describing the claimed methods, whereas it is missing in other passages. For instance, in the first sentence under the heading "Summary of the invention" (see page 4, lines 5 and 6) it is stated that: "*The present invention provides methods for detecting a subpopulation of genomically transformed cells ...*", while the following sentence reads: "*Such methods detect the presence in a biological sample of a clonal subpopulation of cells which have a genome different from that of the wild type ...*". Similarly, in the passage on page 6, lines 8 and 9 of the application as filed it is stated that "*... the present invention provides methods for detecting genomic changes in a subpopulation of cells in a sample of biological material*", while in the subsequent paragraph describing a preferred embodiment

(see lines 18 and 19 of the same page) the detection of a "clonal subpopulation" is specified. Thus, the application as filed discloses both the detection of a subpopulation of transformed cells generally, and specifically the detection of a clonal subpopulation, the latter being merely a possibility, but not an absolute requirement.

6. The board cannot accept appellant II's allegation that the feature "clonal" is disclosed in the application as filed as an essential feature of the method. In the board's judgement, there are no technical reasons which may induce a skilled person reading the application as filed to assume that the methods described therein can be applied only to the detection of a **clonal** subpopulation of transformed cells. Appellant II did not put forward any arguments in this respect either. Hence, the omission of the wording "clonal" in present claim 1 is considered not to contravene the requirements of Article 123(2) EPC.

7. No objections were raised by appellant II under Article 123(2) EPC in respect of either dependent claim 2, which differs from claim 5 as granted in that the feature "*transformed*" has been introduced to characterize the cells, or dependent claims 3 and 4, which correspond to claims 6 and 7 as granted.

8. Nor did appellant II raise any objections under Article 123(3) EPC, and the board sees no reason to raise any of its own motion.

9. The amended claims are considered to conform to Article 123(2)(3) EPC.

Article 84 EPC

10. It was appellant II's view that amended claim 1 offended against Article 84 EPC because the features "*polynucleotide characteristic of a genomic region*" and "*transformed cells*" were unclear. However, in the board's judgement a person skilled in the art reading claim 1 will understand the term "*characteristic of*" to mean that the polynucleotide to be determined in step a) of the claimed method not necessarily has to be the genomic region suspected of being mutated, but that it can also be a polynucleotide derived from the genomic region in question, e.g. a transcription product. This is supported by the statement in the patent that "*DNA or RNA may optionally be isolated from the sample ...*" (see page 8, line 49 of the patent as granted).

11. As concerns the term "*transformed cells*", a skilled person in the field of diagnostic methods for detecting genetic mutations - the technical field of the present patent - will understand this term when applied to animal cells as meaning that the cells have progressed towards a cancerous state. This is supported by the numerous references to cancerous or precancerous cells in the patent specification. Thus, also in respect of this wording there is no ambiguity in claim 1.

12. Consequently, the requirements of Article 84 EPC are considered to be met.

Article 83 EPC

13. In the decision under appeal, the opposition division found that the invention claimed according to auxiliary request 1 then on file met the requirements of Article 83 EPC (see point 6.3 of the decision under appeal). In its submissions in appeal proceedings, appellant II reiterated the objections under Articles 100(b) and 83 EPC raised in opposition proceedings, but did not put forward any arguments with regard to the specific reasons on which the opposition division based its decision on sufficiency of disclosure.

14. In particular, appellant II did not dispute that, at the relevant date, a person skilled in the art was able to obtain information on specific mutations associated with certain types of cancer from public databases. Nor did it dispute that the technical information provided in paragraphs [0056] to [0059] of the patent as granted, which corresponds to the disclosure on pages 21 and 22 of the application as filed, does put a person skilled in the art in the position to determine the numbers X (reference allele) and Y (target allele). The opposition division's finding that, as was apparent from documents (1) to (3), the use of specific reference alleles was well-established in the art, has not been contested by appellant II either. Finally, the opposition division's finding that the determination of the number of events needed for statistical significance was exemplified in paragraphs [0033] to [0036] of the patent as granted (see the passage from line 25 on page 12 to line 18 on page 14) remained uncontested in appeal proceedings. Each of these

findings in the decision under appeal is, in the board's view, valid, *mutatis mutandis*, also in respect of the present claims.

15. The sole issue concerning sufficiency of disclosure raised by appellant II during the discussion of the present claims at the oral proceedings was the alleged unsuitability of PCR methods for carrying out the claimed invention, which, in its view, was substantiated by the statements in paragraphs [0005] and [0027] of the patent as granted (see page 2, second paragraph; and page 10, first paragraph under the heading "Detailed description of the invention" in the application as filed). However, the board observes that the statements indicated by appellant II do not concern the methods as claimed, but rather PCR-based methods known in the art at the filing date purportedly having particular drawbacks. Since appellant II has not put forward any reasons why the claimed method may suffer from the same drawbacks, the statements on which it relies cannot be accepted as evidence for the alleged lack of sufficient disclosure in respect of the claimed invention.

16. In view of the above, the board is not persuaded that appellant II's objections concerning the requirements of Article 83 EPC are justified.

Admission of documents (10) to (12) into the proceedings

17. The board is empowered to hold inadmissible facts, evidence or requests which could have been presented in opposition proceedings (see Article 12(4) of the Rules of Proceedings of the Boards of Appeal).

18. Documents (10) to (12) were filed by appellant II together with its statement of grounds of appeal to support further objections of lack of novelty. In the board's judgement, there is no apparent reason why these documents could not have been filed in opposition proceedings. The submission of the fresh documents for the first time in appeal proceedings cannot be accepted as a reaction to statements in the decision under appeal because, contrary to appellant II's argument, there is no statement in the decision to the effect that methods according to the invention which involve PCR are enabled. Rather, the sole statement of the opposition division in this respect reads: "*The fact that the application cites one method that would not work (PCR) is not relevant for* [sic] *question of sufficiency of disclosure*" (see decision under appeal, section 6.3, second paragraph, first sentence).

19. Moreover, the board observes that none of the newly filed documents seems to describe the detection of the presence of a subpopulation of transformed cells in a biological sample. Thus, the content of documents (10) to (12) is not more relevant to the issue of novelty than the content of documents which were already on file.

20. For these reasons, the board, exercising its discretion, decides to disregard the late-filed documents (10) to (12).

Article 54 EPC

21. In the decision under appeal, the opposition division regarded the subject-matter of claim 1 of the auxiliary request 1 then on file as novel because none of documents (1) to (3) described a method for detecting the **presence** of a subpopulation of cells in a biological sample. In the view of the opposition division, it was a prerequisite of the studies reported in documents (1) to (3) that cells known to be cancerous were provided, while the method of claim 1 then on file was aimed at detecting whether such cells were present or not (see last two paragraphs of section 4.3 of the decision under appeal.

22. The board shares the opposition division's view. Document (1) describes a two-colour fluorescence *in situ* hybridization (FISH) method used for the analysis of the level of amplification of the ERBB2 oncogene, and the distribution of amplified genes in breast cancer cell lines and uncultured primary breast carcinomas. The level of amplification is defined as the ratio of ERBB2 copy number (target) to copy number of chromosome 17 centromeres (reference) (see first sentence of the Abstract on page 5321). Subject of the analysis were ten established breast cancer cell lines and primary breast cancer samples obtained by mechanical disaggregation of fresh tumour tissues, or by touching a freshly cut tumour surface to a microscope slide (see page 5321, right-hand column, last paragraph).

23. According to the jurisprudence of the Boards of Appeal, for the subject-matter of a claim to lack novelty it

must be clearly and directly derivable from the prior art and **all** its features must be known from the prior art (see decision T 411/98 of 11 January 2000). As stated in the decision under appeal, document (1) does not disclose a method of detecting the presence of a subpopulation of transformed cells, in particular cancer cells in a biological sample, but rather a method of analyzing oncogene amplification which is a characteristic feature of tumour cells that seems to have an important role in the progression of many tumours. Hence, at least the feature "*... detecting the presence of a subpopulation of transformed cells in a biological sample ...*" specified in claim 1 is not disclosed in the prior art document (1).

24. While appellant II's remark that the wording "cell subpopulations" is used in the Abstract (see lines 16 to 19) and on page 5324 (see left-hand column, first full paragraph) of document (1) is correct, the board observes that the subpopulations described in this document appear to consist solely of tumour cells and to differ from each other only in the level of oncogene amplification. In contrast, it is implicit in the wording of claim 1 that the biological sample analyzed applying the claimed method does not consist solely of transformed cells – otherwise it would not be necessary to "detect" their presence –, but contains also - possibly even only - normal, i.e. non-cancerous cells. Thus, the subpopulations described in document (1) cannot be considered as "*a subpopulation of transformed cells in a biological sample*" as specified in claim 1.

25. Similar considerations apply to document (2) which describes a FISH method applied to the analysis of the allelic loss of the chromosome 8 in human prostate tumour cells. The purpose of the study reported in this document was to determine the status of chromosome 8 in prostate tumours which have undergone deletion of sequences at a certain region (8p22) of the chromosome. For this purpose, cell populations obtained from prostate tumours were evaluated for allelic dosage. As stated above for document (1), at least the feature "*... detecting the presence of a subpopulation of transformed cells in a biological sample ...*" specified in claim 1 cannot be directly and unambiguously derived from document (2). Thus, the content of document (2) is not prejudicial to the novelty of the method of claim 1.

26. The same applies, *mutatis mutandis*, to document (3). This document describes a method for localizing precise regions of loss of heterozygosity on chromosome 16q in breast tumour cells, and identifying putative tumour suppressor gene(s) encoded by this region (see page 1, lines 9 to 14). In the passage indicated by appellant II (see page 15, lines 17 to 30) it is stated that different kinds of samples can be used for detecting chromosomal amplifications and deletions associated with cancer. Among others, cells in bodily fluids are mentioned. However, there is no indication that the purpose of the analysis is to determine whether or not cancer cells are present. Rather, the presence of cancer cells is a prerequisite because the aim of the described method is to determine the occurrence of amplifications and deletions of certain chromosomal regions in such cells.

27. In summary, the board is convinced that a method with all the features specified in claim 1 is not disclosed in any of documents (1), (2) or (3). Thus, appellant II's objection of lack of novelty based on these documents is not justified.

Article 56 EPC

28. In the decision under appeal, the opposition division found that documents (1) to (3) addressed a problem which was entirely different from the problem underlying the claimed invention. While the prior art documents concerned the study of genomic alterations in cancer cells, the claimed invention aimed at screening for the presence of a mutation in a sample obtained from an organism. Additionally, a distinguishing feature of the claimed method, namely the determination of a statistically significant difference between numbers X and Y was, in the view of the opposition division, neither disclosed nor suggested in any of the prior art documents on file, in particular not in documents (1) to (3). Consequently, the opposition division concluded that the subject-matter of the claims of the auxiliary request I then on file involved an inventive step.

29. In the board's view, the opposition division's conclusion is correct. According to the jurisprudence of the Boards of Appeal (see, e.g., decision T 606/89 of 18 September 1990), the closest prior art serving as starting point for objectively assessing inventive step should generally be a document describing a method - or product - used for the **same purpose** as the claimed

method - or product -, or related to the same or similar technical problem.

30. In the present case, the purpose of the method of claim 1 is to detect the presence of a subpopulation of transformed cells in a biological sample in order to find out whether or not the biological sample, e.g. a stool sample or biopsy tissue, contains transformed cells, i.e. tumour cells. As the opposition division stated in the decision under appeal, documents (1) to (3) do not describe a method serving the same purpose as the claimed method. In fact, the methods described in these documents are aimed at analyzing the level of amplification of a particular oncogene in tumour cells. Thus, if any of these documents were chosen as a starting point for the problem-solution approach, it would be difficult to formulate a relevant technical problem to be solved without inappropriate hindsight. In the absence of a relevant goal to be achieved, hindsight would be required also in order to establish a logical chain of considerations which could have led a person skilled in the art towards the claimed invention. Consequently, under the circumstances of the present case, in which the relevant technical problem cannot be derived from any of the alleged closest prior art documents (1) to (3) or any other prior art document on file, the measures taken for its solution cannot be considered to be derivable either (see decision T 548/03 of 28 March 2006).

31. The present patent proposes a method comprising steps (a) to (c) as specified in claim 1 (see paragraph XIII above). In view of the examples provided

in the patent starting at paragraph [0039] which describe a method based on the two-colour FISH method, the board is convinced that the method allows the skilled person to successfully achieve the aim of the patent in suit, namely to detect whether or not a subpopulation of transformed cells is present in a biological sample obtained from an organism.

32. Even if, as argued by appellant II, the skilled person would consider the disclosure in prior art documents (1) to (3) as starting point, the board is convinced that a method according to claim 1 could not be derived therefrom in an obvious manner. Neither in document (1) nor in any of the further documents on file is there any suggestion or hint to use FISH as a tool for **detecting the presence** of cancer cells in a sample. In the experiments reported in documents (1) and (2) the biological sample analyzed consisted of a "pure" population of transformed cells obtained from either cell cultures or tumour tissue. In document (3) blood is suggested as biological sample, but there is no indication that a FISH method may serve to discriminate between transformed and normal blood cells.

33. Since appellant II has not provided any arguments as to why the skilled person, without any specific hint in the prior art, would have tried to apply the method described in documents (1) to (3) for detecting the presence of a subpopulation of transformed cells in a biological sample, the board is not persuaded that the subject-matter of claim 1 lacks an inventive step.

Conclusion

34. Claims 1 to 4 according to the main request and the invention to which they relate, meet the requirements of the EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to maintain the patent on the basis of claims 1 to 4 of the Main Request filed during the oral proceedings and a description to be adapted thereto.

The Registrar: The Chairman:

A. Wolinski M. Wieser