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Datasheet for the decision of 9 January 2014

Case Number: T 1866/10 - 3.3.08

Application Number: 01961632.5

Publication Number: 1368460

IPC: C12Q1/68

Language of the proceedings: EN

Title of invention:
REAL-TIME SEQUENCE DETERMINATION

Patent Proprietor:
Life Technologies Corporation

Opponent:
Pacific Biosciences of California, Inc.

Headword:
Fluorescent PCR sequencing/LIFE TECHNOLOGIES

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
Main Request
Amendments - extension beyond the content of the application as filed (yes)
Admissibility of Auxiliary Request 1 (no)

Decisions cited:
G 0009/92, T 0296/96, T 0686/99, T 1610/07, T 2276/09, T 0606/10

Catchword:

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Office européen des brevets

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Case Number: T 1866/10 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 9 January 2014

Appellant: (Opponent)	Pacific Biosciences of California, Inc. 1505 Adams Drive Menlo Park CA 94025 (US)
Representative:	Bizley, Richard Edward avidity IP Kestrel House Falconry Court Baker's Lane Epping, Essex CM16 5DQ (GB)
Respondent: (Patent Proprietor)	Life Technologies Corporation 5791 Van Allen Way Carlsbad, CA 92008 (US)
Representative:	Hallybone, Huw George Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 28 April 2010 concerning maintenance of the European Patent No. 1368460 in amended form.**

Composition of the Board:

Chairman: M. Wieser
Members: P. Julià
D. S. Rogers

Summary of Facts and Submissions

I. An opposition was filed against European patent 1 368 460 based on European patent application No. 01 961 632.5 (published as International patent application WO 02/04680, hereinafter "*the application as filed*"). The grounds for opposition were based on Articles 100(a),(b) and (c) EPC. The opposition division considered the Main Request filed on 18 September 2009 and Auxiliary Request 1 filed on 13 November 2009 not to fulfil the requirements of Article 123(2) EPC. Auxiliary Request 2 filed on 20 November 2009 at the oral proceedings before the opposition division was considered to fulfil all the requirements of the EPC.

II. Auxiliary Request 2 on which the opposition division decided to maintain the contested patent contained three claims. Claim 1 read as follows:

"1. Use of a DNA polymerase including a molecular tag covalently bonded to a site on the polymerase, a monomer including a molecular tag covalently bonded to a γ phosphate group of the monomer, a primer and a template, where at least one of the tags has a fluorescence property that undergoes a change before, during and/or after each of a sequence of monomer incorporations due to an interaction between the polymerase tag and the monomer tag, where the sequence of monomer incorporations corresponds to a complement of a corresponding sequence of monomers in the template, wherein each of the monomers comprises a deoxynucleotide triphosphate (dNTP) and the monomer tag is covalently bonded to the γ phosphate group of each dNTP, and further wherein the tags comprise fluorescent tags and the fluorescence property comprises an

intensity and/or frequency of emitted fluorescent light for single-molecule sequencing."

Claims 2 and 3 were directed to preferred embodiments of claim 1.

III. An appeal was lodged by the opponent (appellant) against the decision of the opposition division. With its statement of Grounds of Appeal, the appellant requested the board to set aside the decision under appeal and to revoke the patent.

IV. In reply to the appellant's Grounds of Appeal, the patentee (respondent) requested the board to dismiss the appeal and to maintain the patent on the basis of the claim request upheld by the opposition division (Main Request) or, in the alternative, on the basis of an Auxiliary Request 1 containing three claims, which was filed with its reply. Claim 1 of Auxiliary Request 1 read as follows:

"1. A composition comprising a DNA polymerase including a molecular tag covalently bonded to a site on the polymerase, a monomer including a molecular tag covalently bonded to a γ phosphate group of the monomer, a primer and a template, where at least one of the tags has a fluorescence property that undergoes a change before, during and/or after each of a sequence of monomer incorporations due to an interaction between the polymerase tag and the monomer tag, where the sequence of monomer incorporations corresponds to a complement of a corresponding sequence of monomers in the template, wherein each of the monomers comprises a deoxynucleotide triphosphate (dNTP) and the monomer tag is covalently bonded to the γ phosphate group of each dNTP, and further wherein the tags comprise fluorescent

tags and the fluorescence property comprises an intensity and/or frequency of emitted fluorescent light."

V. On 2 February 2012, the appellant filed further submissions in reply to the respondent's letter. "As a precaution", it requested the board to refer questions to the Enlarged Board of Appeal (EBA).

VI. With a letter dated 16 May 2013, the respondent stated that the renewal fees for the patent had not been paid and that "the patent is no longer in force in the countries in which it has been validated". Thus, the respondent considered that the appeal proceedings could be terminated.

VII. On 27 May 2013, the board in a communication pursuant to Rule 100(2) EPC drew the parties' attention to Rule 84(1) EPC and invited the appellant to inform the board whether a continuation of the appeal proceedings was requested. The board also invited the respondent to state its intentions as to the granted patent. A time limit of two months was given to the parties for replying to the board's communication.

VIII. Whereas the respondent did not reply to the board's communication, the appellant, with letter dated 17 June 2013, requested the board to continue the appeal proceedings.

IX. On 16 September 2013, the board summoned the parties to oral proceedings. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) annexed to the Summons to oral proceedings, the board informed the parties of its preliminary opinion on the issues of the case. In

particular, the board mentioned that it considered Auxiliary Request 1 not to be admissible and it therefore saw no reason to consider appellant's questions to the EBA. The board also took the view that both requests did not comply with the requirements of Articles 123(2),(3) EPC. In view thereof, the board refrained from an analysis of the appellant's arguments put forward under Articles 84, 83, 54 and 56 EPC. Moreover, with reference to the case law established by the Boards of Appeal (decisions T 1610/07 of 14 April 2011, T 606/10 of 12 May 2011 and T 2276/09 of 7 February 2013), the board requested the respondent to clarify its requests.

X. With a letter dated 10 October 2013, the appellant informed the board that, if the respondent did not maintain its request for oral proceedings, it would, in principle, be prepared - on the basis of the board's comments made in the communication under Article 15(1) RPBA - to request the matter to be determined in writing without the need for oral proceedings.

XI. With a letter dated 4 November 2013, the respondent referred again to the fact that the renewal fees for the patent had not been paid and that the patent was no longer in force in the countries in which it had been validated. The respondent also informed the board that it no longer wished to take part in the appeal proceedings and that it had no intention to be represented at the scheduled oral proceedings.

XII. On 11 November 2013, the board cancelled the scheduled oral proceedings.

XIII. Appellant's submissions, insofar as relevant to the present decision, may be summarised as follows:

Main Request - Article 123(2) EPC

Several sequencing strategies were disclosed in the application as filed. Accordingly, the summary of the invention was divided into distinct sections relating to, for example, i) single tagged polymerases, ii) multiple tagged polymerases, and iii) cooperatively tagged monomers and tagged polymerases. Subject-matter disclosed in a section related only to that section and the specific tagging strategy described therein. There was no teaching that any ideas discussed with respect to one specific tagging method were more generally applicable, or that a disclosure in one section could relate to subject-matter of another section. The granted and upheld claims related to these sections describing cooperatively tagged monomers and tagged polymerases. However, there was no teaching in these sections of a use according to the specific combination of features of claim 1 of the Main Request.

Claim 1 required the use of a DNA polymerase, a monomer, a primer and a template. The method disclosed in the section spanning pages 37-38 of the application as filed had been indicated as a basis for this claim. However, there was no explicit reference to a primer and template in this section. The selection of only a primer and template from a list of implicitly disclosed reagents (such as the reaction buffer) and equipment requirements was an arbitrary selection (intermediate generalisation) which had no basis in the application as filed. The use of a primer was not necessarily disclosed in an implicit manner by the application as filed. There were structures in general (such as nucleic acids having a shepherd's crook structure, nicked DNA sequence, etc.) for which the use of a

separate primer was not strictly necessary. Moreover, the section on pages 37-38 was restricted to situations in which there was a unique tag on each monomer, which was not a feature of claim 1. In the absence of this feature, the subject-matter of claim 1 related to an intermediate generalisation with no basis in the application as filed. Furthermore, there was no basis in this section for the change in fluorescence property occurring "before, during and/or after each of a sequence of monomer incorporations" as required by claim 1.

Admissibility of Auxiliary Request 1

The patentee did not file any appeal against the decision of the opposition division. Therefore, according to case law established by the EBA, the patentee was primarily restricted to defending the patent in the form in which it was maintained by the opposition division. The reversion from use claims (Main Request) to product/composition claims (Auxiliary Request 1) was an improper attempt by the patentee to "cross-appeal" and therefore not admissible. If Auxiliary Request 1 would be admitted this would have the consequence that the appellant was put in a worse situation than if it had not appealed. The reversion to claims in composition format would have the effect that Auxiliary Request 1 encompassed product protection, in contrast to protection of the particular use for single-molecule sequencing as specified in the Main Request.

XIV. Respondent's submissions, insofar as relevant to the present decision, may be summarised as follows:

Main Request - Article 123(2) EPC

The subject-matter of claim 1 could be directly and unambiguously derived *inter alia* from the paragraph bridging pages 37-38 in the application as filed. According to this passage, tagged dNTP were incorporated into a growing DNA polymer, i.e. an explicit reference to a primer. The skilled person reading the application as filed would have understood that, for a DNA polymerase to synthesize a DNA polymer, a primer and a template were necessary. Appellant's references to other ways of priming a DNA sequencing reaction were irrelevant since this was not in line with the whole disclosure and the teachings of the application as filed. Although the passage on pages 37-38 did not explicitly mention that the change in fluorescent property took place "before, during and/or after monomer incorporation", this was not necessary because it was clear from the disclosure as a whole that this feature was part of the described method. The application as filed contained several general (umbrella) statements concerning single-molecule sequencing which clearly taught the skilled person that this feature was directly applicable to the specific method of single-molecule sequencing as described on page 37.

Admissibility of Auxiliary Request 1

No submissions were filed by the respondent in reply to the appellant's objections on the admissibility of Auxiliary Request 1 and to the board's communication pursuant to Article 15(1) RPBA in which the parties were informed of the board's preliminary opinion that Auxiliary Request 1 could not be admitted into the appeal proceedings (cf. point IX *supra*).

XV. The opponent (appellant) requested to set aside the decision under appeal and to revoke the patent.

XVI. Since the patentee (respondent) has neither requested the revocation of the patent nor disapproved the text of the patent on which the opposition division intended to maintain the patent, the board considers respondent's request to be the maintenance of the patent on the basis of the claim request upheld by the opposition division (Main Request) or, in the alternative, on the basis of the Auxiliary Request 1 filed on 28 March 2011 in its reply to the appellant's Grounds of Appeal.

Reasons for the Decision

1. The appeal is admissible.

Main Request (claims upheld by the opposition division)
Article 100(c) EPC, Article 123(2) EPC

2. According to the established case law, the content of the application as filed cannot be considered as a reservoir from which individual features pertaining to separate sections or embodiments can be combined in order to artificially create a particular embodiment. In the absence of any pointer to that particular combination, this combined selection of features cannot be considered as being clearly and unambiguously derived from the application as filed (cf. "Case Law of the Boards of Appeal of the EPO", 6th edition 2010, III.A.1, page 315 and III.A.7.1, page 347, with reference in particular to decisions T 296/96 of 12 January 2000, point 3.1 of the Reasons, and T 686/99 of 22 January 2003, point 4.3.3 of the Reasons).

3. The subject-matter of claim 1 is directed to embodiments relating only to "*Cooperatively tagged systems*", more particularly to "*Cooperatively tagged systems using a polymerase*" and to "*Cooperatively tagged monomers and tagged polymerase*" (cf. point II *supra*). These embodiments are disclosed in the application as filed under the Heading "*Summary of the invention*" on page 19, line 9 to page 22, line 18 and on page 29, line 29 to page 33, line 4 of the application as filed. Reference is made therein only to a cooperatively tagged polymerase and tagged monomers as well as to compositions which are defined by the presence of these two components (cf. in particular, page 30, lines 5-23 of the application as filed). There is no mention of a primer and/or a template in any of these references. The disclosure in "*Brief overview of single-molecule DNA sequencing*" on pages 37 and 38 of the application as filed, referred to in the decision under appeal and by both parties in their submissions (cf. points XIII and XIV *supra*), is also clearly limited to these embodiments, in particular to a cooperatively single-tagged polymerase and tagged monomers. However, there is no explicit mention of a primer and/or a template in this disclosure.

4. In view of the specific use of the above embodiments, which is explicitly designated in the application as being single-molecule DNA sequencing, the presence of a template may be seen as disclosed in an implicit manner in all references cited above. However, this is not the case for a primer, since its presence, as argued by the appellant, may not always be necessary (cf. page 43, lines 7-10 of the application as filed). Moreover, contrary to the respondent's opinion, the board does not consider that the term "*a growing DNA polymer*", present on page 37, line 29 of the application as

filed, can always and inevitably be equated to a primer.

5. Claim 1 requires that "*... at lest one of the tags has a fluorescence property that undergoes a change,* ***before, during*** *and/or after each of a sequence of monomer incorporations ...*", wherein the molecular tag of the monomer is "*... covalently bonded to a* ***γ*** *phosphate group of the monomer ...*" (emphasis added by the board). In all passages of the application referring to this particular covalently bonded tag in a cooperatively tagged system, the fluorescence property changes only **after** a monomer incorporation (cf. page 19, lines 14-23 and page 21, lines 4-13 of the application as filed). This is also in line with the disclosure on page 37, lines 26-30 ("*a unique emission signature ... is directly detected* ***upon incorporation****. As a tagged dNTP is incorporated into a growing DNA polymer, a characteristic fluorescent signal or base emission signature is emitted ...*"; emphasis added by the board).

6. Furthermore, there is no direct and unambiguous disclosure in the application as filed of a single-molecule DNA sequencing method comprising the specific cooperatively fluorescent tagged system described in claim 1 which does not rely on the fact that a unique tag is attached to each of the four nucleotides for the determination of the DNA base sequence of the template (cf. page 37, lines 25-28; see in this context "Case Law of the Boards of Appeal of the EPO", 6th edition 2010, III.3, page 327, in particular decisions concerned with deletion of an essential feature).

7. In view of these considerations, the Main Request does not fulfil the requirements of Article 123(2) EPC.

Admissibility of Auxiliary Request 1

8. The patentee/respondent did not file an appeal against the decision of the opposition division which considered Auxiliary Request 2 (the present Main Request) to fulfil the requirements of the EPC (cf. point I *supra*). This request contained only claims referring to the specific use of a DNA polymerase (cf. points II and IV *supra*). Contrary to this, Auxiliary Request 1, introduced by the respondent in the appeal proceedings contains claims referring to a composition comprising a DNA polymerase (cf. section IV *supra*). This is in clear contradiction to the established case law of the Boards of Appeal (cf. G 9/92, OJ EPO 1994, page 875).

9. Thus, Auxiliary Request 1 is not admitted into the appeal proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

A. Wolinski M. Wieser

Decision electronically authenticated