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Datasheet for the decision of 18 January 2023

Case Number: T 1219/19 - 3.3.08

Application Number: 15191903.2

Publication Number: 3045542

IPC: C12Q1/68

Language of the proceedings: EN

Title of invention:
Methods for nucleic acid sequencing

Patent Proprietor:
Pacific Biosciences of California, Inc.

Opponents:
Oxford Nanopore Technologies PLC
Regimbeau

Headword:
Methods for nucleic acid sequencing I/PACIFIC BIOSCIENCES

Relevant legal provisions:
EPC Art. 123(2), 76(1)
EPC R. 116
RPBA Art. 12(4)
RPBA 2020 Art. 13(2)
Guidelines for examination E-VI, 2.2.2 and 2.2.3

Keyword:

Amendments - added subject-matter (yes)
Discretion of the opposition division not to admit amended claims filed at the oral proceedings (yes)
Late-filed request - admitted (no)
Amendment after summons - exceptional circumstances (no)

Decisions cited:

G 0007/93, G 0001/05, G 0002/10, R 0006/19, T 0966/17, T 1213/19

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Case Number: T 1219/19 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 18 January 2023

Appellant: (Patent Proprietor)	Pacific Biosciences of California, Inc. 1380 Willow Road Menlo Park, CA 94025 (US)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Respondent I: (Opponent 1)	Oxford Nanopore Technologies PLC Gosling Building Edmund Halley Road Oxford Science Park Oxford OX4 4DQ (GB)
Representative:	Patent Boutique LLP 10A Printing House Yard Hackney Road London E2 7PR (GB)
Respondent II: (Opponent 2)	Regimbeau 20, rue de Chazelles 75847 Paris Cedex 17 (FR)
Representative:	Regimbeau 20, rue de Chazelles 75847 Paris Cedex 17 (FR)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 13 February 2019 revoking European patent No. 3045542 pursuant to Article 101(3)(b) EPC**

Composition of the Board:

Chairwoman	T. Sommerfeld
Members:	R. Morawetz
	A. Bacchin

Summary of Facts and Submissions

I. European patent EP 3 045 542 ("the patent") is based on European patent application No. 15 191 903.2 ("the application"), which was filed as a divisional application of earlier European patent application No. 09 724 672.2, published as WO 2009/120372 ("the earlier application"). The patent is entitled "Methods for nucleic acid sequencing".

II. Two oppositions to the granted patent were filed. The patent was opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), and under Article 100(b) and (c) EPC.

III. The opposition division revoked the patent. It held that the subject-matter of claim 1 of the main request and auxiliary requests 1 to 5, all submitted by letter dated 22 November 2018, did not meet the requirements of Articles 123(2) and 76(1) EPC. Auxiliary request 6, which was filed at the oral proceedings before the opposition division, was not admitted into the proceedings.

IV. The patent proprietor (appellant) filed notice of appeal against the opposition division's decision. Opponent 1 and opponent 2 are respondents I and II or "respondents" in these appeal proceedings.

V. With the statement setting out the grounds of appeal, the appellant maintained the sets of claims of the main request and auxiliary requests 1 to 5 considered in the decision under appeal and submitted sets of claims of auxiliary requests 6 and 7. Auxiliary request 6 was

identical to auxiliary request 6 filed at the oral proceedings before the opposition division, and auxiliary request 7 was newly filed.

VI. Claim 1 of the main request reads as follows:

"1. A method of generating nucleotide sequence data for a nucleic acid sequencing template, comprising:

providing a nucleic acid sequencing template comprising a double-stranded portion, the double stranded portion comprising two nucleic acid strands that are complementary to each other and are linked at one end by a connecting nucleic acid that links a 3' end of one strand of the two nucleic acid strands to a 5' end of another strand of the two nucleic acid strands;

performing a single-molecule sequencing process on said nucleic acid sequencing template, thereby generating nucleotide sequence data for both of said two nucleic acid strands of said nucleic acid sequencing template; and

comparing the nucleotide sequence data from the two nucleic acid strands to determine a consensus sequence for the double stranded portion of the nucleic acid sequencing template."

Claim 1 of each of auxiliary requests 1, 2, 3, 4 and 5 is directed to methods for generating nucleotide sequence data for a nucleic acid sequencing template and comprises the step of "*performing a single-molecule sequencing process*".

Claim 1 of auxiliary request 6 differs from claim 1 of the main request in that it specifies that the single-

molecule sequencing process is a "*template-directed real-time*" single-molecule sequencing process.

Claim 1 of auxiliary request 7 differs from claim 1 of the main request in that it specifies that the single-molecule sequencing process is a "*real-time*" single-molecule sequencing process.

VII. Both respondents filed replies to the appeal.

VIII. The board scheduled oral proceedings in accordance with the parties' requests and subsequently issued a communication under Article 15(1) RPBA, in which it indicated its preliminary opinion with respect to, *inter alia*, the construction of claim 1 of the main request, added subject-matter in claim 1 of the main request and auxiliary requests 1, 2, 3, 4 and 5 (Articles 123(2) and 76(1) EPC), and the admittance of auxiliary requests 6 and 7.

IX. In response, the appellant submitted sets of claims of auxiliary requests 8, 9 and 10 by letter dated 9 December 2022.

Claim 1 of auxiliary requests 8, 9 and 10 is identical to claim 1 of the main request, auxiliary request 6 and auxiliary request 7, respectively (see section VI. above).

X. Oral proceedings before the board took place as scheduled. At the end of the oral proceedings the Chairwoman announced the board's decision.

XI. The appellant's arguments, in so far as they are relevant to the decision, are summarised below.

Main request
Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

The processes for sequencing in terms of concrete steps to be taken to reproduce the template sequence described in the earlier application were polymerase-mediated sequencing-by-synthesis processes.

In addition, though, the earlier application disclosed template constructs and their utility (see paragraphs [0053] and [0054]). These paragraphs, when read together, provided a stand-alone direct and unambiguous disclosure of the utility of the template configurations according to the invention in any single-molecule sequencing process, without further qualification, and not just in the more limited context of the polymerase-dependent SMRT™ sequencing technology.

Thus, paragraph [0053] of the earlier application disclosed that one of the advantages of the invention, in so far as it related to the templates of the invention, was that it enabled "*single molecular consensus sequence determination*" because the template included both sense and antisense strands and these were sequenced in the same single-molecule sequencing process. This was further explained in paragraph [0053] (see page 13, lines 5 to 7).

The understanding that "*single molecular consensus sequence determination*" meant single-molecule sequencing was confirmed by Example 2 of the earlier

application (see paragraph [0142]), which provided an example of single molecular consensus sequence determination, namely single-molecule sequencing at the same level of generality as paragraph [0053] of the earlier application.

Paragraph [0054] of the earlier application gave an example of how the template configurations of the invention could be used in the context of a single-molecule sequencing process (see page 13, lines 16 to 20).

In summary, paragraph [0053] of the earlier application described the utility of the template of the invention, namely that it could be used to achieve consensus sequence determination in a single-molecule sequencing process, and paragraph [0054] of the earlier application extended this utility to any single-molecule sequencing process by describing a process that took advantage of the template.

Therefore, what was disclosed when paragraphs [0053] and [0054] of the earlier application were read together was that the template of the invention could be used to generate a consensus sequence in a single-molecule sequencing process. This disclosure provided the basis for a claim drafted to the use of a template construct of the invention for determining the consensus sequence using a single-molecule sequencing process by the method described at the end of paragraph [0053] of the earlier application. Claim 1, a method claim, was merely a re-drafted version of such a use claim.

Contrary to respondent I's submissions, the processes mentioned in paragraph [0054] of the earlier

application in relation to a registration sequence ("*e.g. the same molecule, or identical molecules in a template population*") were single-molecule sequencing processes because a registration sequence had no use in ensemble sequencing. In so far as paragraph [0054] referred to a "*template population*", it referred to parallel single-molecule sequencing. The argument that everything from paragraph [0052] of the earlier application onwards related to bioinformatics and not to sequencing processes was contradicted by paragraph [0054], which described a sequencing process.

It was irrelevant that paragraph [0054] of the earlier application did not provide any technical information regarding which single-molecule sequencing processes could be used because it was stated that the templates of the invention could be used in any single-molecule sequencing process. What was disclosed was a genus of single-molecule sequencing processes, not a species.

Paragraph [0054] of the earlier application made it clear (see "*e.g., is primed*" on page 13, line 23) that it was optional, not essential, to use a sequencing process that involved priming, i.e. a polymerase-mediated sequencing-by-synthesis process. Therefore, paragraph [0054] of the earlier application contradicted respondent II's submission that the technical teaching of the application as filed was limited to polymerase-mediated sequencing-by-synthesis methods.

The use of the term "single-molecule sequencing" in claim 1 of the main request therefore did not contravene Article 76(1) or Article 123(2) EPC.

Auxiliary requests 1 to 5
Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

The subject-matter of claim 1 of auxiliary requests 1 to 5 did not add matter for the same reasons as given for claim 1 of the main request.

Auxiliary request 6
Admittance (Article 12(4) RPBA 2007)

In its preliminary opinion, the opposition division had agreed with the appellant's position on the meaning of the term "*template*". The appellant could not have foreseen that the opposition division would change its position on this particular point on the day of the oral proceedings. The conclusion that claim 1 of the main request did add matter was a change of mind by the opposition division.

The opposition division did have discretion, but pursuant to the EPO Guidelines, which the opposition division was obliged to apply, claim requests which were submitted in due course in relation to objections raised by the opposition division may not be rejected (see EPO Guidelines E-VI, 2.2.2, third paragraph).

In contrast, EPO Guidelines E-VI, 2.2.3 applied to a situation where the opposition division had already indicated objections which may prejudice the maintenance of the patent in the preliminary opinion. Only then could the opposition division apply the "clearly allowable" criterion to claim requests filed after the final date set under Rule 116(1) EPC.

Auxiliary request 7
Admittance (Article 12(3) RPBA 2020 and Article 12(4) RPBA 2007)

The amendment had a basis in paragraph [0048] of the earlier application. The amendment addressed the clarity concerns related to the term "*template-directed*" raised by the opposition division in relation to auxiliary request 6.

Auxiliary requests 8, 9 and 10
Admittance (Article 13(2) RPBA 2020)

Deleting claims 4 to 7 in these claim requests addressed the objections raised by respondent I against the main request: under Articles 76(1) and 123(2) EPC for claims 5 and 6, under Article 84 EPC for claims 4 and 6, and under Rule 80 for claim 7.

XII. Respondent I's arguments, in so far as they are relevant to the decision, are summarised below.

Main request
Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

There was no teaching anywhere in the earlier application of a generic group of sequencing processes that might be used and which could be equated with the expression "a single-molecule sequencing process" as used in claim 1. Every single method described in the earlier application related to sequencing-by-synthesis processes (see paragraphs [0037] to [0047]).

In discussing paragraph [0053] of the earlier application, the appellant had ignored its context, in

particular paragraph [0052], which was important in understanding paragraph [0053]. Paragraph [0053] related to handling data, not to how those data were obtained.

The term "*single molecular consensus sequence determination*" described an alleged technical benefit of the constructs of the disclosure, not a sequencing process. Paragraph [0053] of the earlier application did not equate the term "*single molecular consensus sequence determination*" with sequencing both the sense and antisense strands "in the same single-molecule sequencing process". Paragraph [0053] taught nothing about the sequencing process – it merely discussed a feature provided by the structure of the templates.

There was nothing in the earlier application as filed that encouraged the skilled person to infer from the term "*single molecular consensus sequence determination*" that this feature of the template configurations of obtaining duplicative or replicate data was applicable only to the field of single-molecule sequencing and not to the ensemble sequencing processes that were also discussed in the earlier application as filed. There was no reason, therefore, to interpret paragraph [0053] as providing a disclosure of a broad concept of single-molecule sequencing.

From paragraph [0142] of the earlier application it did not follow that "*single molecular consensus sequence determination*" as referred to in paragraph [0053] was "single-molecule sequencing" by definition. Example 2 used a sequencing-by-synthesis process, i.e. SMRT™, to assess how accurate the consensus determination was. It therefore confirmed that paragraph [0053] was about data handling, not single-molecule sequencing.

The sentence in paragraph [0054] of the earlier application relied on by the appellant (see page 13, lines 16 to 20) referred to "*a single template molecule*", not to a single molecule; it did not describe the sequencing process and was not limited to single-molecule sequencing processes. Reference to "*a single template molecule*" in this sentence meant that a single species of template molecule was used in one integrated process to obtain sense and antisense sequence reads. It was immediately apparent to the skilled reader that the teaching of paragraph [0054] related to both ensemble methods and the single-molecule sequencing methods disclosed in the application. Therefore, it did not make sense to interpret "*a single template molecule*" in this sentence as referring to just one molecule and thus to single-molecule sequencing. The purpose of the registration sequence was spelled out in paragraph [0054] and was not that alleged by the appellant, namely aligning multiple copies in parallel single-molecule sequencing, which was not mentioned in the application at all. There was no disclosure in the earlier application that Figure 3A related exclusively to single-molecule sequencing.

Even if the skilled person understood paragraph [0054] of the earlier application as referring to single-molecule sequencing, the paragraph taught nothing about how that sequencing should be carried out, i.e. the steps to be taken. How the process was to be carried out was described in paragraphs [0037] to [0047] of the earlier application as filed. These were all sequencing-by-synthesis processes, whether they were single-molecule sequencing processes or ensemble sequencing processes. The only single-molecule sequencing processes that were described in the

application were sequencing-by-synthesis methods, and there was nothing in paragraph [0054] that changed that.

Paragraph [0054] of the earlier application (see page 13, line 23) was not enough to change the impression that the skilled person got from reading the whole application. Therefore, asserting that "*e.g., is primed*" should be construed as disclosing any single-molecule sequencing process was not credible.

Since all single-molecule sequencing methods disclosed in the earlier application as filed were sequencing-by-synthesis methods, the lack of reference to sequencing-by-synthesis in claim 1 added matter.

Auxiliary requests 1 to 5
Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

These claim requests should be rejected for the same reasons as the main request.

Auxiliary request 6
Admittance (Article 12(4) RPBA 2007)

In view of the opposition division's preliminary opinion (see point 1.3), the appellant could not have been surprised by the division's finding at the oral proceedings that claim 1 of the main request added matter.

Even if the opposition division had changed its mind from the preliminary opinion, this did not mean that the appellant had an absolute right to have auxiliary request 6 admitted into the proceedings (see decision

T 966/17). The opposition division's discretion was not conditional on having notified the patent proprietor of a problem, and the opposition division's change of mind did not amount to a change of the subject of the proceedings.

The opposition division had discretion to admit or not admit claim requests (see R 6/19), and a change of mind by the opposition division was not enough to remove this discretion. The opposition division had therefore had discretion to refuse to admit auxiliary request 6.

The only issue was therefore whether it had exercised its discretion correctly. It was apparent from the decision under appeal (see paragraph 3.5) that it had.

Moreover, there was no reason for the board to exercise its own discretion and admit auxiliary request 6 into the appeal proceedings (Article 12(4) RPBA 2007). The amendments did not constitute a serious attempt to overcome the added-matter objection and also raised new issues.

Auxiliary request 7
Admittance (Article 12(3) RPBA 2020 and Article 12(4) RPBA 2007)

The appellant had not provided any arguments in the statement of grounds of appeal as to why the amendments made in claim 1 overcame the added-matter problem identified in the decision under appeal.

Some of the words disclosed in paragraph [0048] of the application as filed had been introduced into the claim, but not all of them. The amendment did not solve the added-matter problem because the whole application

as filed was concerned with sequencing-by-synthesis processes.

Auxiliary requests 8, 9 and 10
Admittance (Article 13(2) RPBA 2020)

Auxiliary requests 8, 9 and 10 should not be admitted into the proceedings.

XIII. Respondent II's arguments, in so far as they are relevant to the decision, are summarised below.

Main request
Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

The technical teaching of the application as filed was limited to polymerase-mediated sequencing-by-synthesis methods (see paragraphs [0009] to [0019], [0042] to [0047], [0051], [0056], [0063], [0067], [0069], [0075], [0080], [0083] to [0091], [0093] to [0096] and [0130] to [0135]; Figures 3 to 6). The sole single-molecule sequencing method disclosed in the application as filed was single-molecule real-time sequencing, i.e. the SMRT^{TM} method, which was also a sequencing-by-synthesis method. The SMRT^{TM} method was clearly defined as the method of choice for putting the invention into practice (see [0042] to [0045], and Figures 1A and B and the examples).

Paragraph [0053] of the application as filed did not disclose single-molecule sequencing in general.

Paragraph [0054] of the application as filed (see "*e.g., is primed*" on page 13, line 23) did not provide any technical information relating to single-molecule

sequencing that was not by sequencing-by-synthesis. A single-molecule sequencing process that was not sequencing-by-synthesis could therefore not be directly and unambiguously derived from paragraph [0054] of the application.

As claim 1 concerned any and all "single-molecule sequencing" methods, it gave the skilled person new technical information that could not be directly and unambiguously derived from the application as filed.

Auxiliary requests 1 to 5
Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

The subject-matter of auxiliary requests 1 to 5 extended beyond the content of the application as filed for the same reasons as claim 1 of the main request.

Auxiliary request 6
Admittance (Article 12(4) RPBA 2007)

Contrary to the appellant's arguments, it had been clearly predictable that added-matter concerns relating to the term "single-molecule sequencing" were to be discussed at the oral proceedings (see point 1.3 of the opposition division's preliminary opinion).

The opposition division correctly exercised its discretion in refusing to admit auxiliary request 6 into the proceedings because it followed the right principles.

Auxiliary request 7
Admittance (Article 12(3) RPBA 2020 and Article 12(4) RPBA 2007)

As claim 1 did not specify that the single-molecule sequencing process was a template-dependent synthesis process, it did not overcome the Article 123(2) and Article 76(1) EPC objections.

Auxiliary requests 8, 9 and 10
Admittance (Article 13(2) RPBA 2020)

The appellant had not provided any justification for filing these claim requests so late in the proceedings. No exceptional circumstances were apparent.

XIV. The appellant (patent proprietor) requested that the decision under appeal be set aside and the patent be maintained as amended on the basis of the main request or, alternatively, on the basis of one of auxiliary requests 1 to 5, all claim requests filed by letter dated 22 November 2018. As a further alternative, it requested that auxiliary request 6, filed during oral proceedings on 22 January 2019 and re-submitted with the statement of grounds of appeal, be admitted into the proceedings and the patent be maintained as amended on that basis. As a further alternative, it requested that auxiliary request 7, filed with the statement of grounds of appeal, be admitted into the proceedings and the patent be maintained as amended on that basis. As a further alternative, it requested that auxiliary requests 8, 9 and 10, filed by letter dated 9 December 2022, be admitted into the proceedings and the patent be maintained as amended on that basis. In the context of all of the above claim requests, it requested that the case be remitted to the opposition

division for consideration of the grounds under Article 100(a) EPC, as to lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), and under Article 100(b) EPC if the requirements of Articles 76(1) and 123(2) EPC are held to be satisfied in respect of any claim request.

Respondents I and II (opponents 1 and 2) requested that the appeal be dismissed and that auxiliary requests 6 to 10 not be admitted into the appeal proceedings. Respondent I additionally requested that the case be remitted to the opposition division for further prosecution in the event that the appeal be allowed in relation to any claim request.

Reasons for the Decision

Main request

The claimed invention - claim construction

1. Claim 1 is directed to a method of generating nucleotide sequence data for a nucleic acid sequencing template comprising a double-stranded portion, the method comprising providing said template, "*performing a single-molecule sequencing process on said nucleic acid sequencing template*", thereby generating nucleotide sequence data for both strands of the template, and comparing the nucleotide sequence data from the two nucleic acid strands to determine a consensus sequence for the double-stranded portion of the template.

2. It was common ground that the expression "*performing a single-molecule sequencing process on said nucleic acid sequencing template*" did not limit the claimed subject-

matter to sequencing-by-synthesis processes. The board sees no reason to deviate from this understanding.

Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

3. The opposition division held that the disclosure of single-molecule sequencing in both the earlier application as filed and the application as filed was limited to sequencing-by-synthesis processes, which are termed "*template directed*" and "*single molecule, real-time sequencing processes*" (see decision under appeal, point 1.13). Since claim 1 was not limited to sequencing-by-synthesis processes but simply referred to "*performing a single-molecule sequencing process*", claim 1 was held to contravene Articles 123(2) and 76(1) EPC.

4. If a divisional application is amended, it must meet the requirements of both Article 123(2) EPC and Article 76(1) EPC. It is established jurisprudence that the standard for assessing compliance with the requirements of Articles 123(2) EPC and 76(1) EPC is the same (see G 1/05, OJ EPO 2008, 271, Reasons 5.1), namely the standard set out in decision G 2/10 (OJ EPO 2012, 376, Reasons 4.3), also known as the "gold standard". Amendments are only permitted within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the (earlier) application as filed. After the amendment, the skilled person may not be presented with new technical information (ibid., Reasons 4.5.1).

5. It is common ground that the descriptions of the divisional application as filed and the earlier

application as published are identical (including the paragraph numbering), with the exception that the former also includes, in paragraph [0152], the claims of the earlier application. Since in the case in hand the test for whether the claimed subject-matter extends beyond the content of the divisional application as filed (Article 123(2) EPC) and the test for whether the claimed subject-matter extends beyond the content of the earlier application as filed (Article 76(1) EPC) are based on the consideration of identical passages in both applications, the tests can be combined. For ease of reference, the divisional application as filed and the earlier application as filed are referred to in the following simply as "the application" and, unless indicated otherwise, reference is made in this decision to the page and paragraph numbering of the earlier application (published as WO 2009/120372).

6. Under the heading "DETAILED DESCRIPTION OF THE INVENTION", Chapter I of the application describes what are known in the art as sequencing-by-synthesis methods: To identify the nucleotide sequence of the template, a polymerase or ligase is used to generate a complementary strand, and individual bases, or groups of bases, are identified as they are incorporated into an elongating strand that is complementary to the template (see paragraph [0037]). These methods are further illustrated by reference to Sanger sequencing methods, which use populations of template molecules (see paragraph [0038]; also referred to as ensemble sequencing processes in this decision, in line with respondent I's submissions). The methods are further illustrated by reference to single-molecule real-time sequencing methods, such as the SMRT™ sequencing method and the like, which are sequencing-by-synthesis methods in which the incorporation of differently

labelled nucleotides is observed in real time as they are added in a polymerase-mediated primer extension reaction (see paragraphs [0042] to [0045]). In agreement with respondent I's submissions, the board considers that Chapter I of the application describes the processes that are intended to be used to implement the sequencing methods of the invention.

7. In Chapter II, entitled "Contiguous Double Stranded Templates", the application sets out the structure of partially and completely contiguous templates with double-stranded segments, their general construction, preparation and advantages in terms of sequence data handling "[f]*ollowing sequence determination*" (see in particular paragraphs [0052], [0053] and [0054]).

8. The appellant did not dispute that the application describes processes for single-molecule sequencing in terms of concrete steps to be taken to reproduce the template sequences, which involve a polymerase-mediated sequencing-by-synthesis process, or that the application did not verbatim disclose performing "*a single-molecule sequencing process*" on a nucleic acid sequencing template.

9. However, it submitted that in paragraphs [0053] and [0054] the application provided a stand-alone disclosure of the utility of the template configurations of the invention in any single-molecule sequencing process, in terms which were not limited to sequencing-by-synthesis processes, thus providing a basis for claim 1.

10. The appellant's line of reasoning hinges on the propositions that (i) paragraph [0053] of the application discloses that one of the advantages of the

invention, in so far as it relates to the templates of the invention, is that it enables "*single molecular consensus sequence determination*" because the template includes both sense and antisense strands and these are sequenced in the same single-molecule sequencing process, and that (ii) paragraph [0054] of the earlier application extends this teaching to any single-molecule sequencing process (see section XI. above).

11. The passage in paragraph [0053] of the application relied on by the appellant as disclosing single-molecule sequencing reads as follows:

"*The templates of the invention provide numerous advantages over simple linear template sequences, and even other circular template sequences (...). In particular, as with circular templates, the template configurations of the invention allow for single molecular consensus sequence determination, where sequencing a given template provides duplicative or replicate data of the sequence information obtained, and thereby improves accuracy over linear templates by providing multiple reads for a given template sequence or sequence portion, that can be used to derive consensus sequence data from a given template sequence and/or for specific base locations within such sequence*" (emphasis added by the board).

12. It is apparent that this passage neither specifically mentions single-molecule sequencing nor equates the expression "*single molecular consensus sequence determination*" with sequencing a template in a single-molecule sequencing process. Indeed, paragraph [0053] of the application is silent on the process used for "*sequencing a given template*" and provides no technical information regarding any of the steps involved in

sequencing the template, i.e. it does not explicitly disclose a single-molecule sequencing process.

13. The appellant's argument that paragraph [0053] of the application discloses that one of the advantages of the invention, in so far as it relates to the templates of the invention, is that it enables "*single molecular consensus sequence determination*" because the template includes both sense and antisense strands and these are sequenced in the same single-molecule sequencing process is thus understood by the board to mean that paragraph [0053] implicitly discloses a single-molecule sequencing process.

14. It is established jurisprudence that the term "implicit disclosure" relates solely to matter that any person skilled in the art, using common general knowledge, would consider as necessarily implied by the application as a whole, as a clear and unambiguous consequence of what is explicitly mentioned (see also the Case Law of the Boards of Appeal, 10th edition 2022 ("CLBA"), section II.E.1.3.3).

15. Paragraph [0053] of the application defines "*single molecular consensus sequence determination*" as "*where sequencing a given template provides duplicative or replicate data (...) by providing multiple reads for a given template sequence or sequence portion, that can be used to derive consensus sequence data from a given template sequence ...*" (see page 12, fifth line from the bottom to the last line).

16. The skilled person reading paragraph [0053] of the application understands that obtaining duplicative data is a feature of the template configuration, not the mode of sequencing, since the template's partially

contiguous structure allows both strands of the template to be sequenced, providing "*duplicative or replicate data*". This understanding is further supported by paragraph [0053], which sets out that "*the templates of the invention, by virtue of their inclusion of double stranded segments, provide consensus sequence determination through the sequencing of both the sense and antisense strand of such sequences (in both the partially and completely contiguous configurations)*" (see page 13, lines 4 to 7).

17. The board concludes from the above that the skilled person reading paragraph [0053] would understand that the expression "*single molecular consensus sequence determination*" describes a benefit of the templates for deriving a consensus sequence but not a sequencing process. The skilled person would furthermore understand this benefit to be the result of the templates' structure, not of the particular process for sequencing the template. Moreover, there is nothing in paragraph [0053] to indicate that the feature of obtaining "*duplicative or replicate data*" is only achieved in a single-molecule sequencing process and would not also be achieved in any other sequencing process, e.g. ensemble sequencing processes that use populations of identical template molecules.

18. Contrary to the appellant's submission, the expression "*single molecular consensus sequence determination*" in the context of paragraph [0053] therefore does not necessarily imply to the skilled reader that the sense and antisense strands of the template are sequenced in the same single-molecule sequencing process.

19. Nor does consideration of Example 2 support the appellant's assertion that "single molecular consensus sequence determination" means single-molecule sequencing. The reasons are as follows. Example 2 does not equate the term "*single molecular consensus sequencing*" with single-molecule sequencing, and while Example 2 uses SMRT™ sequencing, which is a single-molecule sequencing process, it is evident that the expression "*single molecular consensus sequencing*" as used in Example 2 relates not to the sequencing process itself but to the subsequent determination of a consensus sequence from multiple sequence reads (see paragraphs [0142] and [0143] of the application). Contrary to the appellant's submission, Example 2 therefore also fails to provide an example of single molecular consensus sequence determination which is single-molecule sequencing. Instead it supports the understanding that the expression "*single molecular consensus sequencing*" relates not to the sequencing process as such but to the sequence data analysis, following sequence determination.

20. The passage in paragraph [0054] relied on by the appellant as providing a basis for single-molecule sequencing processes in general reads as follows:

"*By way of example, with respect to a partially contiguous template shown in Figure 2A, obtaining the entire sequence, e.g., that of segments 202, 204 and 206 provides a measure of consensus sequence determination by virtue of having sequenced both the sense strand, e.g., segment 202, and the antisense strand, e.g., segment 204. In addition to providing sense and antisense sequence reads from a single template molecule that can be sequenced in one integrated process, the presence of linking segment 206*

also provides an opportunity to provide a registration sequence that permits the identification of when one segment, e.g., 202, is completed and the other begins, e.g., 204. Such registration sequences provide a basis for alignment sequence data from multiple sequence reads from the same template sequences, e.g., the same molecule, or identical molecules in a template population. The progress of sequencing processes is schematically illustrated in Figure 3A. In particular, as shown, a sequencing process that begins, e.g., is primed, at the open end of the partially contiguous template, proceeds along the first or sense strand, providing the nucleotide sequence (A) of that strand, as represented in the schematic sequence readout provided." (emphasis added by the board; see paragraph [0054], page 13, lines 13 to 26).

21. While this passage mentions that "*a single template molecule ... can be sequenced in one integrated process*", it is silent about the steps of the "*integrated process*" and does not explicitly disclose that this process is a single-molecule sequencing process.

22. It is evident that the skilled person would not necessarily interpret the reference to "*from a single template molecule*" (see point 20. above) as referring to just one molecule in view of the following sentence in paragraph [0054], which discloses that the "*same template sequences*" can be "*the same molecule, or identical molecules in a template population*" (see point 20. above).

23. The skilled person would understand this reference to "*the same molecule, or identical molecules in a template population*" to relate to single-molecule

sequencing or ensemble sequencing processes that use populations of identical template molecules. In this context, the board notes that the reference to the "*registration sequence*" in paragraph [0054] does not alter this understanding. Paragraph [0054] explains that the purpose of the registration sequence is applicable to single-molecule sequencing and ensemble sequencing processes. On the other hand, the application does not disclose using the registration sequence when aligning multiple copies in parallel single-molecule sequencing, which was cited by the appellant to refute the disclosure of ensemble sequencing.

24. The reference to "*from a single template molecule*" therefore does not implicitly limit the "*integrated process*" disclosed in paragraph [0054] (see point 20. above) to single-molecule sequencing processes.

25. Furthermore, assuming that the skilled person understands paragraph [0054] of the application to be referring to single-molecule sequencing as one option, it remains a fact that paragraph [0054] is silent on the technical details of the sequencing process. However, contrary to the appellant's assertion, the consequence of this lack of teaching is not that paragraph [0054] discloses a genus of single-molecule sequencing processes.

26. Instead, the consequence is that the skilled person reading paragraph [0054] with the common general knowledge in mind and in the context of the application as a whole (see point 4. above) turns to the remainder of the application for guidance on how to perform the sequencing process mentioned in paragraph [0054]. As set out in point 6. above, the sequencing processes

that are described in the application are all sequencing-by-synthesis methods, be it ensemble or single-molecule sequencing processes. The appellant has not argued that the skilled person would arrive at a different conclusion on the basis of their common general knowledge.

27. Contrary to the appellant's submissions, therefore, paragraph [0054] of the application does not disclose that the templates of the invention can be used in single-molecule sequencing processes in general.

28. This conclusion is not changed by the appellant's further argument that paragraph [0054] of the application made it clear that it was optional to use a sequencing process that involved priming, i.e. a polymerase-mediated sequencing-by-synthesis process, meaning that the technical teaching of the application as filed was not limited to polymerase-mediated sequencing-by-synthesis methods.

29. This argument addresses respondent II's submission that the technical teaching of the application as filed was limited to sequencing-by-synthesis methods which were also polymerase-mediated. However, even if the skilled person were to interpret paragraph [0054] as disclosing that priming is optional, this does not mean that there is any disclosure of a single-molecule sequencing process that would not be a sequencing-by-synthesis process.

30. It remains a fact that paragraph [0054] is silent on the technical details of the sequencing process, and the mention of "*e.g., is primed*" does not change that. The skilled person reading paragraph [0054] would still turn to Chapter I for guidance, and as set out above

(see point 26.) the processes disclosed in that paragraph are all sequencing-by-synthesis processes.

31. In summary, the board concludes from the above considerations that paragraphs [0053] and [0054] when read together provide no generic disclosure of "single-molecule sequencing" processes to be performed on a nucleic acid sequencing template to obtain data from both strands of the template.

32. The board also concurs with respondent I that there is no teaching anywhere in the application of a generic group of sequencing processes that could be equated with the expression "a single-molecule sequencing process" as used in claim 1. The only single-molecule sequencing processes described in the earlier application are sequencing-by-synthesis processes (see point 6. above). Omission of the limitation to sequencing-by-synthesis processes therefore presents the skilled person with new technical information.

33. Claim 1 does not comply with Articles 123(2) and 76(1) EPC.

Auxiliary requests 1 to 5

Added subject-matter (Articles 123(2) and 76(1) EPC) - claim 1

34. Claim 1 of auxiliary requests 1 to 5 is directed to methods for generating nucleotide sequence data for a nucleic acid sequencing template, comprising the step of "*performing a single-molecule sequencing process*". Auxiliary requests 1 to 5 therefore do not meet the requirements of Articles 123(2) EPC and 76(1) EPC for the same reasons as set out above for claim 1 of the

main request, *mutatis mutandis*.

Auxiliary request 6

Admittance and consideration (Article 12(4) RPBA 2007)

35. Auxiliary request 6 was filed during the oral proceedings before the opposition division. Claim 1 of this request differs from claim 1 of the main request in that it specifies that the single-molecule sequencing process is a "*template-directed real-time*" single-molecule sequencing process.

36. The opposition division did not admit auxiliary request 6 into the proceedings, on account of the criteria set out in the Guidelines for Examination with regard to the admissibility of late-filed requests (see E-III, 8.6, in the version applicable from November 2018). It held that auxiliary request 6 had been filed late (after the time limit prescribed by Rule 116 EPC), was an attempt to address an issue already raised in the notices of opposition, was *prima facie* unsuitable to solve the issue of added subject-matter (Article 123(2) EPC) and appeared to lack clarity (Article 84 EPC).

37. The appellant disputed the correctness of the opposition division's decision not to admit auxiliary request 6, both as to whether the opposition division had indeed had discretion not to admit this request and, in the event that it had, whether it had exercised its discretion in accordance with the proper criteria.

37.1 The appellant invoked Rule 116(2) EPC to argue that the opposition division had no discretion to disregard this auxiliary request or to apply the criterion of *prima*

facie allowability. Since at oral proceedings the opposition division changed its view, expressed in the preliminary opinion sent with the summons, that omitting the feature "template-directed" did not result in added subject-matter, auxiliary request 6, although filed after the time limit under Rule 116 EPC, could not be regarded as late-filed and should have been admitted.

37.2 Under Rule 116(2) EPC, requests filed after the final date set for making written submissions in preparation for oral proceedings can only then not be admitted if the patent proprietor had been notified of the grounds prejudicing the maintenance of the patent.

38. In this respect the board concurs with the established jurisprudence, which was also cited by respondent I in the reply to the statement of grounds of appeal and which states that when the exercise of discretion of a first-instance department is disputed, it is not the function of a board of appeal to review all the facts and circumstances of the case as if it were in the place of the first-instance department, in order to decide whether or not it would have exercised such discretion in the same way. A board of appeal in principle only overrules the way in which a first-instance department has exercised its discretion if it comes to the conclusion either that the first-instance department has not exercised its discretion in accordance with the right principles or that it has exercised its discretion in an unreasonable way and has thus exceeded the proper limits of its discretion (see G 7/93, OJ EPO 1994, 775, Reasons 2.6).

39. For the following reasons, the board found that under the circumstances in hand the opposition division was

entitled to exercise its discretion accorded by Article 123(1) in conjunction with Rule 81(3) EPC to disregard the auxiliary request at issue (see R 6/19, Reasons 6 to 11; T 966/17, Reasons 2.2.1; T 1213/19, Reasons 19). It further found that the opposition division had exercised its discretion in accordance with the right principles, primarily the clear allowability criterion. The opposition division could not have been deprived of that discretion merely because it expressed a different opinion at the oral proceedings from that provisionally set out in the communication accompanying the summons (see also T 966/17, Reasons 2.4).

40. The opposition division's preliminary opinion discussed the added-matter objections raised by the opponents and clearly indicated that those objections were to be the subject of further discussion at the oral proceedings: "*It will have to be discussed in oral proceedings whether a 'single molecule sequencing process' can also be non-template directed. It further will have to be discussed whether the original disclosure of single molecule sequencing is limited to 'real-time' processes*" (point 1.3 of the annex to the summons). In doing so, the opposition division set the boundaries of the discussion expected at the oral proceedings on added subject-matter concerning the feature "*single molecule sequencing process*".

40.1 The preliminary conclusion that claim 1 does not add subject-matter (see points 1.3 and 1.5) is expressed in a careful manner ("*Currently the opposition division is of the opinion that ...*" and "*... the opposition division is of the preliminary opinion that ...*") and cannot be understood as if the opposition division

thereby gave up its discretionary power to disregard submissions filed later.

40.2 A different conclusion would penalise the useful practice by opposition divisions of providing a detailed discussion of the relevant issues in preparation for oral proceedings, versus preliminary opinions with barely any content, which is not in the interest of any of the parties involved.

41. At the oral proceedings before the board, the appellant referred to the Guidelines for Examination (E-VI, 2.2.2 and 2.2.3, in the version of March 2022) to argue that the opposition division's change of opinion at the oral proceedings constituted a change of subject of the proceedings, justifying the later filing of auxiliary request. That passage of the Guidelines reads:

"The following are examples of what would normally constitute a change of subject of the proceedings:
(...)
- the examining or opposition division departs from a previously notified opinion: for example, contrary to its preliminary opinion set out in the annex to the summons, the opposition division concludes during oral proceedings that an objection prejudices the maintenance of the patent."

41.1 Irrespective of the fact that the Guidelines applicable at the time the opposition division took its decision (version in force in November 2018) did not contain this particular example, the question of whether a change of opinion represents a change of subject of the proceedings remains crucial in the matter in hand. The board agrees that, in principle, it does change the subject of the proceedings, especially where the

opposition division introduces a new objection at a relatively late stage. However, the cited passage of the Guidelines refers to examples that would *normally* constitute a change of subject of the proceedings. It therefore does not exclude the possibility that, under particular circumstances, a change from the preliminary opinion does not necessarily involve a change of subject of the proceedings.

41.2 The board finds that in the case in hand, the content of the preliminary opinion, taken as a whole, is articulate and cannot be read in a manner limited to the conclusion in point 1.5 (that claim 1 does not add subject-matter), as the appellant has done. On the contrary, it should also be read in consideration of the discussion under point 1.3 (both referred to in points 40. and 40.1 above). The objection that the single-molecule sequencing process had no basis in the parent application had been raised by both opponents at the outset of the opposition proceedings – it was not introduced into the proceedings by the opposition division. The issue had been discussed at length in preparation for the oral proceedings, it had been considered an issue by the opposition division in the preliminary opinion (see point 1.3) and it was also sufficiently clear that it was a crucial one. The appellant therefore could not have been surprised by the decision taken at the oral proceedings. It appears that the appellant had indeed been notified of the grounds prejudicing the maintenance of the patent.

41.3 Under the circumstances of this particular case, the different conclusion reached at the oral proceedings by the opposition division with regard to the feature "single-molecule sequencing process" cannot be regarded as a change of subject of the proceedings.

41.4 As a consequence, auxiliary request 6 was not submitted in due time and the opposition division had discretion to disregard it, pursuant to the correct criterion of *prima facie* allowability (or non-allowability). The fact that auxiliary request 6 raised clarity issues was an additional criterion for non-admittance.

42. The board therefore saw no reason to revise the opposition division's decision.

43. As there were no additional circumstances in the appeal, and absent any submissions by the appellant, the board also saw no reason to exercise its own discretion in favour of admitting auxiliary request 6 into the appeal proceedings (Article 12(4) RPBA 2007) and decided to hold auxiliary request 6 inadmissible.

Auxiliary request 7

Admittance and consideration (Article 12(3) RPBA 2020 and Article 12(4) RPBA 2007)

44. Auxiliary request 7 was filed with the statement of grounds of appeal. Claim 1 of auxiliary request 7 differs from claim 1 of the main request in that it specifies that the single-molecule sequencing process is a "*real-time*" single-molecule sequencing process.

45. Admittance of this request is subject to the provisions of Article 12(3) RPBA 2020 (see Article 25(1) RPBA 2020), under which claim requests submitted in the appeal proceedings must be justified by reasons as to the extent to which the amendments made overcome the objections raised in the decision under appeal, unless this is self-explanatory (see CLBA, V.A.4.3.5(b)(i)).

46. Pursuant to Article 12(4) RPBA 2007, which applies in the case in hand (see Article 25(2) RPBA 2020), the board does not consider claim requests filed with the statement of grounds of appeal that do not meet the substantiation requirement of Article 12(2) RPBA 2007 (the wording of which has remained substantially unamended in Article 12(3) RPBA 2020). Any such requests, unless self-explanatory, are not considered submitted until the date they are substantiated.

47. The appellant submitted that the basis for the amendment was found in paragraph [0048] of the application as filed and that deleting the expression "*template-directed*" addressed the clarity concerns regarding that term raised by the opposition division in relation to auxiliary request 6. In the appellant's view, the arguments provided with regard to auxiliary request 6 could serve as justification for the auxiliary request at issue.

48. However, no explanation was ever provided, either in the statement of grounds of appeal or during the oral proceedings, as to how the amendment overcame the objections under Articles 123(2) and 76(1) EPC raised in the decision under appeal against claim 1 of the main request (see point 3. above). Moreover, it was not self-explanatory that this amendment would address the opposition division's finding that the application only disclosed sequencing-by-synthesis processes, nor has the appellant submitted that it was. It was therefore not immediately apparent to the board that the objection raised in the decision under appeal no longer applied to claim 1 of auxiliary request 7.

49. The board therefore decided not to admit auxiliary request 7 into the proceedings (Article 12(3) RPBA 2020

and Article 12(4) RPBA 2007).

Auxiliary requests 8, 9 and 10

Admittance and consideration (Article 13(2) RPBA 2020)

50. Auxiliary requests 8, 9 and 10 were submitted after notification of the summons to oral proceedings (see section IX. above). When submitting these claim requests, the appellant indicated that the amendments made addressed objections raised by respondent I in its reply to the appeal. However, the appellant did not provide any justification for not filing these claim requests until this late stage in the appeal proceedings.

51. Under Article 13(2) RPBA 2020, which applies in the case in hand (see Article 25(1) RPBA 2020), any amendment to a party's appeal case after notification of a summons to oral proceedings is, in principle, not to be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

52. When asked at the oral proceedings, the appellant stated that it had no cogent reasons as per Article 13(2) RPBA 2020 to submit. The board therefore decided not to admit auxiliary requests 8, 9 and 10 into the appeal proceedings.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairwoman:

L. Malécot-Grob T. Sommerfeld

Decision electronically authenticated