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Datasheet for the decision of 27 February 2020

Case Number: T 1715/15 - 3.3.08

Application Number: 09774581.4

Publication Number: 2291533

C12P19/34, C12Q1/68 IPC:

Language of the proceedings: EN

Title of invention:

USING POPULATIONS OF BEADS FOR THE FABRICATION OF ARRAYS ON SURFACES

Patent Proprietor:

Illumina Cambridge Limited

Opponent:

Kilger, Christian

Headword:

Arrays on surfaces/ILLUMINA

Relevant legal provisions:

EPC Art. 54, 56, 83, 113(1) RPBA Art. 15(1)

RPBA 2020 Art. 15(3)

Keyword:

Main request - requirements of the EPC met (yes) Request for reimbursement of appeal fee (refused)

Decisions cited:

T 0688/14

Catchword:



Beschwerdekammern Boards of Appeal Chambres de recours

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Case Number: T 1715/15 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 27 February 2020

Appellant: Kilger, Christian Wachtelstr. 4 14195 Berlin (DE)

Representative: CH Kilger Anwaltspartnerschaft mbB

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Respondent:

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Decision under appeal: Interlocutory decision of the Opposition

Division of the European Patent Office posted on

20 July 2015 concerning maintenance of the European Patent No. 2291533 in amended form.

Composition of the Board:

Chairman B. Stolz
Members: P. Julià

R. Winkelhofer

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Summary of Facts and Submissions

- I. European patent no. 2 291 533 is based on European patent application no. 09 774 581.4 which was published under the PCT as International patent application WO 2010/003132 (hereinafter "the patent application"). The patent was granted with 14 claims.
- II. An opposition was filed on the grounds set out in Articles 100(a), (b) and (c) EPC. The opposition division considered the main request (claims as granted) to lack novelty (Article 100(a) EPC, Article 54(2) EPC) and auxiliary request 1 to fulfil the requirements of the EPC. Accordingly, the patent was maintained in amended form on the basis of auxiliary request 1.
- III. The opponent (appellant) lodged an appeal, requested the reimbursement of the appeal fee and maintained the objections raised under Articles 54, 56 and 83 EPC at first instance.
- IV. The patent proprietor (respondent), inter alia, filed auxiliary requests 1 to 4.
- V. As an auxiliary measure, both parties requested oral proceedings.
- VI. The parties were summoned to oral proceedings and were informed of the board's provisional, non-binding opinion on the issues of the case.
- VII. None of the parties filed substantive submissions in reply to the board's communication. The appellant

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informed the board that it intended not to attend the oral proceedings.

- VIII. Oral proceedings took place on 27 February 2020 in the absence of the appellant.
- IX. Claim 1 of the <u>main request</u> (claims upheld by the opposition division) reads:
 - "1. A method for fabricating an array of nucleic acids on a surface comprising:
 - (a) providing a surface comprising one or more primer oligonucleotides attached to the surface;
 - (b) providing a pool of beads, wherein beads in the pool have a plurality of templates attached thereto, the plurality comprising multiple copies of a single nucleic acid template sequence;
 - (c) arraying the beads onto the surface by hybridizing the templates to the primer oligonucleotides; and
 - (d) extending the primers to produce copies of the templates attached to the surface, wherein step (b) comprises forming the pool of beads by amplifying the nucleic acid template sequence on the beads, thereby producing the plurality of templates."

Dependent claims 3, 4 and 7 of the main request read as follows:

"3. The method according to claim 1, wherein the amplifying is performed by bridge amplification using two or more primer oligonucleotides immobilized on the beads and/or optionally wherein the templates amplified on the beads originate from a pool of chemically synthesized oligonucleotides.

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- 4. The method according to claim 3, wherein one or more of the primer oligonucleotides is cleaved after the amplification to leave single stranded templates on the beads.
- 7. The method according to claim 1, wherein the copies of the templates attached to the surface that are produced in step (d) comprise a plurality of nucleic acid features on the surface, wherein each of the features covers less area of the surface than the area covered by each of the beads."
- X. The following documents are cited in this decision:

 - (4): WO 2007/010251
 (publication date: 25 January 2007);
 - (5): US 2004/0171053
 (publication date: 2 September 2004);
 - (7): US 2008/0242560
 (publication date: 2 October 2008);
- XI. The appellant's submissions in writing, insofar as relevant to the present decision, may be summarised as follows:

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<u>Main request</u> Article 83 EPC

According to the appellant, the methods of claims 4 and 7 did not fulfil the requirements of Article 83 EPC.

As regards claim 4, the submissions made in the notice of opposition and in the appellant's submissions of 9 October 2014, were repeated *verbatim* in the statement of grounds of appeal. With reference to Article 69 EPC, the appellant further argued that, although the claims were not limited to a literal interpretation, such interpretation was part of the scope of protection and thus, the claimed method had to be enabled. Whilst the patent application disclosed several methods for removing the second amplified strand, such as denaturation, cleaving the strand was not included. A skilled person would have understood the term "cleavage" as indicating the breaking of a chemical bond. However, such a cleavage/breaking did not result in single-stranded templates and hence, the claim was not enabled.

As regards claim 7, the submissions made on 9 October 2014 were also repeated *verbatim* in the statement of grounds of appeal, and it was argued that these submissions had not been addressed by the opposition division in the decision under appeal.

Article 54 EPC

According to the appellant, the method of claim 1 was anticipated by documents (1), (5) and (8). As regards documents (1) and (8), the submissions made in the notice of opposition and on 9 October 2014, were

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repeated *verbatim* in the statement of grounds of appeal.

As regards document (5), the appellant further argued that the opposition division had acknowledged that this document disclosed a method for fabricating an array of nucleic acids on a surface comprising steps (a), (b), (c) and (d) of claim 1. Claim 1 further required that the pool of beads in step (b) be formed by amplifying the nucleic acid template sequence on the beads; i.e. the last feature (in the last paragraph) of claim 1. Document (5) described in paragraph [0071] methods of attaching a molecule to a microparticle (bead) and referred to nucleic acid polymerisation technologies. A skilled person knew that nucleic acid amplification belonged to polymerisation technologies. Reference was also made in this paragraph to a polymerase and a polymerisation process. Paragraph [0071] referred thus to a process of copying nucleic acids, i.e. amplifying nucleic acids. The first sentence in paragraph [0072] indicated that the polymerisation referred to in paragraph [0071] was understood as a nucleic acid amplification. The use of nucleic acid amplification for generating nucleic acids on beads was part of a skilled person's common general knowledge and thus, the references to nucleic acid polymerisation/amplification in document (5) also anticipated the last feature (in the last paragraph) of claim 1. The fact that there were no examples of nucleic acid polymerisation/ amplification in document (5) was irrelevant because these technologies belonged to the common general knowledge and thus, no examples were needed.

Article 56 EPC

The method of claim 1 differed from the method disclosed in the closest prior art document (5) by requiring that the pools of beads in step (b) be formed by amplifying the nucleic acid template sequence on the beads, i.e. the last feature (in the last paragraph) of claim 1. This distinguishing feature provided no technical effect and thus, starting from document (5), the objective technical problem was the provision of an alternative method for fabricating an array of nucleic acids on a surface. The opposition division applied a wrong "could-would approach" and acknowledged inventive step merely based on a problem-invention argument (since no alternative was needed, it was not obvious to look for such alternative). However, according to the established case law, the skilled person was constantly occupied with furthering the prior art and thus, the appreciation of conventional technical problems - even though there was no hint in the prior art - did not involve an inventive step. Thus, the only relevant question was whether a method comprising the distinguishing feature was an obvious alternative to the methods described in document (5). The reference to nucleic acid polymerisation technologies in paragraph [0071] of document (5) clearly suggested (if not disclosed) the amplification of the template nucleic acids on the beads by methods known in the art, such as shown by the prior art cited in paragraph [0050] of the patent, the emulsion PCR amplification of nucleic acids on beads disclosed in document (7), a method cited also on page 31, lines 8 to 24 of document (1) and the literature referred to therein. Thus, the method of claim 1 was not inventive in view of document (5) in combination with either the

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common general knowledge of the skilled person or, in the alternative, with document (7).

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

<u>Main request</u> Article 83 EPC

As regards claim 4, the respondent argued that a skilled person would have understood the wording "cleaved after the amplification" to mean that, at the end of the amplification, the hybridised primertemplate pairs were separated (so as to leave singlestranded templates on the beads); this was the only logical interpretation because separation had always been the standard next step in the procedure. Paragraphs [0050] and [0051] of the patent disclosed several methods of (cleaving and) separating the hybridised strands, such as by denaturation. According to the case law, when considering a claim, interpretations which were illogical or did not make technical sense had to be ruled out. Article 69 EPC related to the extent of protection, not to sufficiency of disclosure.

Article 54 EPC

As regards documents (1) and (8), the submissions made by the respondent in reply to the notice of opposition and to the summons to the oral proceedings at first instance, were likewise repeated almost *verbatim* in reply to the appellant's appeal. Claim 1 was a method-claim which defined a multi-step method comprising consecutive steps (a) to (d). The last feature (in the last paragraph) of claim 1 defined a physical activity that had to be performed in step (b), namely to form a pool of beads by amplifying a nucleic acid template sequence on the beads. This was an active process-step of the claimed method, an essential feature that was not disclosed in document (5). Whilst this document mentioned some features of the claimed method, they were disclosed in different lists, and there was no teaching to select the specific features from each list so as to arrive at the claimed method. Document (5) disclosed a plurality of different nucleic acid sequences optionally coupled to microparticles as well as microparticles with a single nucleic acid attached thereto (paragraphs [0050], [0058] and [0072]), but there was no disclosure of beads having attached multiple copies of a single nucleic acid sequence, in particular not in paragraphs [0017], [0094] to [0097] and [0115] to [0120]. Although nucleic acid polymerisation technologies were mentioned in paragraph [0071], polymerisation was the process to join nucleotides together for forming polynucleotides; it encompassed not only replication of nucleic acids, but also their ab initio synthesis. Polymerisation was not limited to nucleic acid copying, other methods were also known in the art, such as gap filling. Thus, an amplification in the sense of claim 1 was not directly and unambiguously derivable from the polymerisation process referred to in document (5).

Article 56 EPC

Several features distinguished the method of claim 1 from the methods disclosed in the closest prior art

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document (5). In particular, the use of beads was only optional in these methods, not an essential feature. Moreover, document (5) suggested neither the use of a pool of beads, the beads having a plurality of templates attached thereto and said plurality comprising multiple copies of a single nucleic acid template sequence (step (b) of claim 1), nor to form a pool of beads by amplifying the nucleic acid template sequence on the beads (last feature of claim 1). This latter feature allowed to have multiple copies of a single template sequence across all beads, a more controllable and uniform loading of template sequences on the beads, enabling thereby a better design of the array pattern. Starting from document (5), the objective technical problem was the provision of an improved method for fabricating an array of nucleic acids on a surface. This problem was solved by the method of claim 1. A large number of possible methods for coupling - not amplifying - a nucleic acid to microparticles were mentioned in document (5), including polymerisation technologies. However, there was no suggestion, let alone an indication, to amplify the nucleic acid on the microparticles/beads, neither in paragraph [0072], wherein all references to a nucleic acid were always in singular, nor in paragraphs [0115] to [0120] of Example 3, where only a unique copy of a (template) nucleic acid sequence was present on the microparticle. Although an amplification could have been carried out by a skilled person, there was nothing in document (5) that would have motivated him/her to perform it; the less so because the pattern on the array in document (5) was not obtained by bead transfer as in the patent, but by rubber-stamping the (pattern of the) template microarray onto the (new) array surface. It was only with the benefit of hindsight that a skilled person would have considered

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the combination of documents (5) and (4) (a prior art document cited in paragraph [0051] of the patent), the more so because the nucleic acid amplification described in document (4) was preferably carried out on planar surfaces leading thus away from using beads.

- XIII. The appellant (opponent) requests (in writing) that the appeal fee be reimbursed, the decision under appeal be set aside and that the patent be revoked.
- XIV. The respondent (patent proprietor) requests that the appeal be dismissed or, in the alternative, that the decision under appeal be set aside and that the patent be maintained on the basis of any one of auxiliary requests 1 to 4.

Reasons for the Decision

Right to be heard (Article 113(1) EPC)

- 1. By its decision not to attend the oral proceedings and not to file substantive arguments in reply to the issues raised in the board's communication pursuant to Article 15(1) RPBA 2007, the appellant chose not to make use of the opportunity to comment on the board's provisional opinion.
- 2. Although the board's initial opinion as regards
 Articles 54 and 56 EPC was in the appellant's favour,
 this opinion was, as clearly stated in the board's
 communication, only provisional. In the present case,
 the board has changed its opinion as regards
 Articles 54 and 56 EPC, on the basis of the discussion
 in the oral proceedings.

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3. It is recalled that according to
Article 15(3) RPBA 2020, the board is not obliged to
delay any step in the proceedings, including its
decision, by reason only of the absence at the oral
proceedings of any party duly summoned who may then be
treated as relying on their written case.

Main request

4. The main request is identical to the auxiliary request 1 underlying the decision under appeal and thus, it already forms part of the appeal proceedings.

Article 83 EPC

- 5. The requirements of Article 83 EPC are fulfilled by the main request, in particular by claims 4 and 7. In its communication pursuant to Article 15(1) RPBA 2007 the board already stated that:
- 5.1 "As regards claim 4, the disclosure on page 21, line 14 to page 22, line 24 of the patent application concerns two embodiments of the method of claim 1 which relate to step (b), in particular, to the formation of the pool of beads and the production of the plurality of template sequences as described in the last paragraph of claim 1 (page 21, lines 1 to 13 of the patent application). Whilst page 21, lines 14 to 25 describes emulsion-based amplification techniques (claim 2 of the main request), page 21, line 26 to page 22, line 24 describes bridge-amplification on the beads (claim 3 of the main request). Claim 4 is dependent on claim 3 and relates to a particular embodiment of the bridgeamplification. This embodiment is described on page 22, lines 2 to 24 as an alternative bridge-amplification technique which results in a double-stranded template

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where both ends are immobilised (Figure 1). Therefore, "[i]n order to obtain a single stranded template suitable for hybridization, one of the strands can be cleaved from the [bead] surface" (underlined by the board) (page 22, lines 6 and 7 of the patent application). In this context, reference is made to the methods of "bridge amplification" disclosed in document WO 2007/010251 (document (4) in these proceedings) (see also references to other prior art related to "beadbased bridge amplification" on page 26, lines 5 to 7 of the patent application). In the board's view, this document discloses in detail the particular embodiment of claim 4 and allows a skilled person to put it into practice without undue burden (cf. inter alia, page 16 of document (4) under the heading "Cleavage methods").

- 5.2 As regards claim 7, the reasons given by the opposition division in the decision under appeal correspond verbatim to those given in their communication (annex to the summons to attend the oral proceedings pursuant to Rule 115(1) EPC). In the decision under appeal, the opposition division did not address the opponent's arguments submitted in reply to said communication. However, the opponent did not put forward any arguments at the oral proceedings before the opposition division but, as far as Article 83 EPC is concerned, relied upon its written submissions. The opponent chose not to seize the opportunity to argue its case, to contest the reasons given by the opposition division in the communication and to explain the relevance of the arguments put forward in reply to that communication and why these arguments should convince the opposition division."
- 5.3 In view of this course of events, the parties were informed in the communication pursuant to

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Article 15(1) RPBA 2007 that the board considered it inappropriate to enter into a detailed discussion on the merits of the appellant's arguments at this late stage of the proceedings. It further stated that, in view of the parties' submissions, the disclosure of the patent application (in particular on page 19, lines 8 to 31) and the prior art on file, the board saw no reason to deviate from the findings of the opposition division.

6. There is no reason to deviate from what was said there.
Thus, the main request fulfils the requirements of
Article 83 EPC.

Article 54 EPC

7. Claim 1 is a method-claim comprising steps (a) to (d), wherein step (a) and (b) require the provision of a surface comprising one or more primer oligonucleotides attached thereto and the provision of a pool of beads having a plurality of templates attached thereto, wherein the plurality comprises multiple copies of a single nucleic acid template sequence, respectively. There is no specific requirement or limitation in these steps as regards the methods used for attaching the primer oligonucleotides to the surface in step (a) or the multiple copies of a single nucleic acid template sequence to the pool of beads in step (b). However, the last feature (in the last paragraph) of claim 1 defines the method used for forming the pool of beads, namely by amplifying the nucleic acid template sequence on the beads. Therefore, the method of claim 1 does not merely comprise the provision of a pool of beads as defined in step (b), but it further comprises, as an active step of said method, the specific process for producing the pool of beads.

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- 8. Indeed, as correctly laid out by the respondent, it is the combination of both features, namely the provision of the pool of beads with the specific technical features as defined in step (b) and the specific process for obtaining this pool of beads as defined in the last paragraph of claim 1, which distinguishes the method of claim 1 from all methods disclosed in document (5). Whilst novelty was acknowledged by the opposition division solely on the basis of the last feature, the appellant argues that both features are present in the methods described in document (5). This is not convincing, though.
- 9. Paragraph [0023] of document (5) defines a "population of at least one entity of interest" as "one or more entities of interest", wherein an "entity of interest" is defined in paragraph [0024] as "a population of molecules ... of a single type, e.g. a polynucleotide or a polypeptide". This definition does not require the "population of molecules" (such as oligonucleotides or polynucleotides forming the "entity of interest") to be all identical. This might well be so, but it is not necessarily the case. The "entities of interest" are further defined in more detail in paragraphs [0055] to [0062], wherein nucleic acid polymers and nucleic acids are identified as preferred embodiments (cf. paragraphs [0057] and [0058]). However, there is no reference in these paragraphs to the nucleic acid polymers or nucleic acids (forming the "entity of interest") all being identical. On the contrary, there is a reference to a "collection of molecules" which, due to their method of production (combinatorial chemistry, library of compounds), are different but not identical (cf. paragraph [0061]).

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- 10. Paragraphs [0048] to [0054] are concerned with the microparticles, with paragraph [0050] referring to spherical microparticles as being most commonly available and an embodiment of the invention. Paragraphs [0068] to [0072] disclose the coupling of the molecular entities to microparticles, with paragraph [0069] referring to a "populationwise" coupling in that "each population of microparticles contains at least one entity of interest coupled thereto". In view of the definition of "entity of interest", the presence of more than one "entity of interest" is understood as in line with the disclosure in paragraph [0059], i.e. "oligonucleotides, polypeptides and small molecules", such as comprising "at least one polypeptide and at least one nucleic acid" (see also paragraph [0054]). Again, it is not derivable from these paragraphs that the molecules (forming each "entity of interest") must necessarily be all identical.
- 11. The "association between [the] microparticles and the substrate" is disclosed in paragraphs [0073] to [0099], and the "methods of making microarrays" in paragraphs [0063] to [0067]. The method disclosed in paragraph [0066] (which is identical to that described in paragraph [0017]; see also claim 42 of document (5)) refers to the hybridisation between a first population of nucleic acid sequence(s) optionally coupled to microparticle(s) (and associated with first substrate) and a second population of complementary sequence(s) optionally coupled to microparticle(s) (and associated with second substrate). However, there is no information on whether, when microparticles are used, the first population of (template) nucleic acid sequence(s) are all identical or, if this is not the case, whether multiple copies of a single (template)

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nucleic acid sequence are coupled to the microparticles.

- Paragraphs [0094] to [0097] refer to "a template 12. microarray bearing a plurality of different single stranded nucleic acid sequences (optionally coupled to microparticles) ... associated at distinct addresses", wherein at "the distal end of each sequence ..., a short common sequence is present"; and to a "second array [which] is constructed to contain a sequence complementary to the common sequence" (underlined by the board) (cf. paragraph [0094]). This method is described in Example 3, wherein in the template microarray a "plurality of unique nucleic acid sequences are bound to microparticles, and the microparticles are bound to a substrate such that each unique nucleic acid sequence occupies a unique address on the substrate" and at "the distal end of each nucleic acid sequence ..., a short common single stranded nucleic acid sequence is present" (cf. paragraph [0116]) (underlined by the board). In the second (new) microarray, a "nucleic acid sequence complementary to the common sequence is bound to microparticles ... [wherein] ... the microparticles are bound to a second substrate" (cf. paragraph [0117]).
- 13. In the board's view, in order to achieve that "each unique nucleic acid sequence occupies a unique address on the substrate", it is necessary that "each unique nucleic acid" is coupled to a microparticle so that, by using the association methods described in paragraphs [0073] et seq., it may be possible to direct (localise) the (each of the) different/unique template nucleic acids to a distinct/unique address (localisation) on the (first) substrate. However, there is no indication in any of these paragraphs regarding

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the number of copies of the (single) nucleic acid template sequence attached to the microparticle. There may well be multiple copies but there may also be only one copy, a single one, of a nucleic acid template sequence. The actual number of copies attached to a microparticle depends not only on the size of the microparticle - a broad size range is disclosed in paragraph [0050] of document (5) - but also on the concentration of (template) nucleic acids and microparticles as well as on the coupling conditions used. Thus, the presence of multiple copies of a single nucleic acid template sequence on each microparticle is not directly and unambiguously derivable from the information provided in Example 3 of document (5). Nor does this example provide any information on the method actually used (i.e. the active method-step) for attaching or coupling the nucleic acid template sequence - regardless of whether one or multiple copies - to the microparticle.

14. Thus, the main request fulfils the requirements of Article 54 EPC.

Article 56 EPC

Document (5) is the closest prior art and the method described in paragraph [0094] and Example 3 is the method most closely related to the method of claim 1. As stated in connection with the assessment of Article 54 EPC, there are several technical features distinguishing the methods described in document (5) from the claimed method. Whilst the presence of microparticles and the selection of beads as suitable microparticles are only optional features in the methods described in document (5), they are essential features of the claimed method. More importantly, the

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presence of multiple copies of a single nucleic acid template sequence on the beads, achieved - by an active step of the method for fabricating the array - by amplifying the nucleic acid template sequences on the b eads, is not directly derivable from any of the methods described in document (5), in particular not from that disclosed in Example 3 of this document.

- 16. Whilst the respondent argues that these technical differences result in several advantageous effects which is disputed by the appellant the opposition division considered that the features distinguishing the claimed method from the methods disclosed in document (5) did not provide any technical effect.

 Accordingly, when starting from the closest prior art document (5), the objective technical problem has been differently formulated by the respondent (provision of an improved method for fabricating an array of nucleic acids on a surface), and by the opposition division (provision of an alternative method for fabricating said array).
- 17. The board assumes, to the appellant's benefit, that the objective technical problem may be defined as the provision of a mere alternative method for fabricating an array of nucleic acids on a surface. Since, under such an assumption, the method of claim 1 is not rendered obvious by the prior art (cf. points 18 to 22 infra), it is not necessary to assess whether the claimed method provides any improvement which should then be taken into account when formulating the objective technical problem, as argued by the respondent.
- 18. The board agrees with the "could-would approach" followed by the opposition division in the assessment

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of Article 56 EPC (cf. "Case Law of the Boards of Appeal of the EPO", 9th edition 2019, I.D.5, 197), even though it also endorses appellant's definition of the person skilled in the art. Said person can be regarded as being cautious and of a conservative attitude (cf. "Case Law", supra, I.D.8.1.3, 205) but also tasked with the furthering of the prior art by routine adaptations or trials (cf. "Case Law", supra, I.D.9.11, 254; inter alia, T 688/14 of 24 July 2019, point 25.1 of the Reasons).

- 19. As stated above, there is no information in Example 3 of document (5) on the method used for coupling the nucleic acid to the microparticles. Example 3 provides only a factual information ("are bound to") without giving any further details on the actual coupling method used. This is far from the disclosure of an active step of the method described in Example 3. Indeed, nothing in Example 3 draws the skilled person's attention to the coupling method and, when looking for possible alternatives, away from other features, such as the type of association between the microparticles and the substrate used for forming the template array and the new array (cf. paragraphs [0073] to [0092]), the nature and properties of these substrates (cf. paragraphs [0036] to [0047]), etc. This is even more so, if the description of the microarray is considered. Whilst some of these other features are essential to the methods for fabricating the nucleic acid array described in document (5), the use of the microparticles is described as only optional (cf. paragraph [0094]).
- 20. Even if, for the sake of the argument, a skilled person would turn the attention to the coupling method described in Example 3, the chemical and biological

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methods known in the art and referred to in document (5) would provide the skilled person with a large number of possible alternatives (cf. paragraphs [0070] to [0072] of document (5)), as correctly found by the opposition division. Whilst all these methods provide the coupling of a nucleic acid to a microparticle, and although several nucleic acids or copies of a nucleic acid may be coupled to the microparticle, the method defined in claim 1 - by its very nature, namely on bead amplification - always and necessarily results in the coupling of several copies of a nucleic acid to the microparticle. In this sense, an amplification, such as that mentioned in claim 1, is not a mere alternative to the methods mentioned in document (5) but goes beyond all of them. The selection and inclusion of an on bead amplification reaction is thus not straightforward and obvious in the absence of any suggestion or indication, which cannot be seen in document (5).

- 21. It follows from these considerations that, although methods for amplifying a nucleic acid sequence on beads were known in the art and available to the skilled person, such as those described in document (4) or referred to in document (1) (cf. page 31, lines 8 to 24) and cited in the patent itself (cf. paragraphs [0050] and [0051] of the patent), the combination of any of these amplification methods with the method disclosed in Example 3 of document (5) is not obvious without hindsight knowledge of the patent.
- 22. Document (7), cited by the appellant under
 Article 56 EPC, was published on 2 October 2008, i.e.
 after the first priority date claimed (2 July 2008;
 US 61/077,844) and thus, it is not prior art in the

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sense of Article 54(2) EPC and cannot be used for the purpose of Article 56 EPC.

23. Thus, the main request fulfils also the requirements of Article 56 EPC.

Conclusion

24. The main request fulfils the requirements of the EPC.

Reimbursement of the appeal fee

25. Given that the appeal is to be dismissed, no reimbursement can take place. In addition, as stated in the board's communication pursuant to Article 15(1) RPBA 2007, the request for reimbursement has never been substantiated.

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Order

For these reasons it is decided that:

- 1. The appeal is dismissed.
- 2. The request for reimbursement of the appeal fee is refused.

The Registrar:

The Chairman:



L. Malécot-Grob

B. Stolz

Decision electronically authenticated