Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 18 July 2023

Case Number: T 1266/19 - 3.3.08

Application Number: 13164430.4

Publication Number: 2623613

IPC: C12Q1/68

Language of the proceedings: EN

Title of invention:
Increasing confidence of allele calls with molecular counting

Patent Proprietor:
Agilent Technologies, Inc.

Opponents:
Mathys & Squire LLP
Cellular Research, Inc.

Headword:
Increasing confidence of allele calls/AGILENT TECHNOLOGIES

Relevant legal provisions:
EPC Art. 54, 111(1)
RPBA 2020 Art. 11, 12(2), 12(4), 13(2)

Keyword:
Novelty - main request and auxiliary request 1 - (no)
Admittance of a late new line of argument - (no)
Admittance of auxiliary requests 1a, 2a, 3a, 4a, 5a and 6a - (no)
Remittal - (yes)

Decisions cited:
G 0002/91, G 0009/92, T 2084/11, T 1646/12, T 1666/14, T 1870/16, T 0169/20, T 1270/20, T 1360/21

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1266/19 - 3.3.08

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

Appellant: (Opponent 1)	Mathys & Squire LLP The Shard 32 London Bridge Street London SE1 9SG (GB)
Representative:	GRIFFIN, Philippa J Mathys & Squire The Shard 32 London Bridge Street London SE1 9SG (GB)
Respondent: (Patent Proprietor)	Agilent Technologies, Inc. 5301 Stevens Creek Boulevard Santa Clara CA 95051 (US)
Representative:	GRAMMEL, Markus Grünecker Patent- und Rechtsanwälte PartG mbB Leopoldstraße 4 80802 München (DE)
Party as of right: (Opponent 2)	Cellular Research, Inc. 4040 Campbell Avenue Suite 110 Menlo Park, CA 94025 (US)
Representative:	CHAPMAN, Desmond Mark Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 18 February 2019 rejecting the opposition filed against**

European patent No. 2623613 pursuant to Article 101(2) EPC.

Composition of the Board:

Chairwoman	R. Morawetz
Members:	M. Montrone
	A. Bacchin

Summary of Facts and Submissions

I. The appeal of opponent 01 ("appellant") lies from the decision of the opposition division rejecting the oppositions against European patent No. 2 623 613 ("patent"). This patent is based on European patent application No. 13 164 430.4, which is a divisional application of European patent application No. 11 810 645.9, published as EP 2 619 327 that was filed as International patent application published as WO 2012/038839.

II. Two oppositions were filed against the patent, and the opposition proceedings were based on the grounds for opposition in Article 100 (a) EPC, in relation to novelty (Article 54 EPC) and inventive step (Article 56 EPC), and Article 100(b) and (c) EPC. The opposition division decided that the grounds of opposition did not prejudice the maintenance of the patent as granted and hence rejected the oppositions.

III. With the statement of grounds of appeal, the appellant submitted *inter alia* arguments that claim 1 as granted lacked novelty or inventive step over the disclosure of document D1 (US 2007/0020640) (Article 100(a) EPC). In support of their case, a new document was filed (D21, Miner B.E. *et al.*, Nucleic Acids Research, 2004, Vol. 32, No. 17, e135).

IV. In reply, the patent proprietor ("respondent") submitted counter arguments and 48 auxiliary requests (auxiliary requests 1 to 42 and 1a, 2a, 3a, 4a, 5a and 6a).

V. With letter dated 13 March 2023, the appellant submitted a new line of argument under added subject-matter against the method of claim 1 (Article 100(c) EPC). Furthermore, a communication of board 3308 dated 14 November 2022 issued under Article 15(1) RPBA 2020 that concerned a divisional application of the application underlying the present case (T 1360/21) was submitted.

VI. Opponent 02 - a party as of right - made no submissions in substance during the written phase of the appeal proceedings.

VII. In a communication pursuant to Article 15(1) RPBA, the parties were informed of the board's preliminary opinion.

VIII. In reply, the respondent submitted arguments against admittance of the appellant's new line of arguments under added subject-matter.

IX. Oral proceedings were held by videoconference with all parties being represented.

X. Claim 1 as granted (main request) reads:

"1. A method for determining the minimum number of individual polynucleotide molecules originating from the same genomic region of the same original sample that have been sequenced in a particular sequence analysis configuration or process, including:

attaching a degenerate base region (DBR) to starting polynucleotide molecules;

amplifying the DBR-attached starting polynucleotide molecules;

sequencing the amplified polynucleotide molecules, wherein the sequence of the DBR as well as a portion of the polynucleotide is obtained;

determining the number of different DBRs attached to a polynucleotide of interest:

using the number of different DBR sequences present in the sequencing run to determine the minimum number of individual polynucleotide molecules originating from the same genomic region of the same original sample that have been sequenced in the particular sequence analysis configuration or process; and

determining a statistical value for an allele call in a genotyping assay that cannot be derived from the read number alone."

In this decision, the six separate process steps of claim 1 are referred to as steps (i) to (vi), in line with the feature analysis of the parties.

XI. Claim 1 of auxiliary request 1 is identical to claim 1 of the main request, except that the feature "*to increase the confidence in an allele call in a genotyping assay*" has been added at the end of the preamble.

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

Admission into the proceedings of a new line of argument under added subject-matter

The feature "*determine the minimum number of individual polynucleotide molecules originating from the same genomic region of the same original sample*" ("minimum number" feature) in step (v) of claim 1 comprised added subject-matter. Although this objection related to a new line of argument, admittance of which was governed by Article 13(2) RPBA, exceptional circumstances justified its admittance into the appeal proceedings. The patent in suit was the "parent" of the divisional European application No. 16 170 857.3 which was granted as EP 3 115 468. Moreover, the methods as defined in claim 1 of both patents were very similar and differed solely in that claim 1 of the "divisional" case contained an additional process step which included the pooling of polynucleotide molecules ("pooling step"). The opposition division in the "divisional" case found that the method of claim 1 of all sets of claims before them contained added subject-matter (decision dated 18 June 2021), a decision confirmed recently by board 3308 in a different composition (T 1360/21). Central to the discussion was that the earlier application (WO 2012/038839) provided no basis for the "minimum number" feature in claim 1 in combination with the other features of the claim. This finding was relevant for the present appeal case too, and if applied would cause the revocation of the patent and of all auxiliary requests on file. Furthermore, the decisions in the "divisional" case were post-dated relative to the appellant's deadline for filing a statement of grounds of appeal in this case.

Main request (patent as granted)

Claim construction - step (vi) of claim 1

The opposition division erroneously construed the "statistical determination" feature of claim 1 (step (vi)) narrowly. Since claim 1 did not specify the statistical value in any way, this feature had to be construed according to its broadest technical sensible meaning based on the patent as a whole regardless of how and when the statistical value was determined in the method as long as this value was associated with degenerate base regions (DBRs) without taking read numbers into account. Nor did step (vi) contain references to any of the previous steps, in particular on which number the statistical value had to be determined. As a consequence thereof, claim 1 did not define a chronological order for step (vi).
The purpose of step (vi) was not to improve the confidence into an allele call. This was achieved by the use of DBRs in preceding steps (iv) and (v) of claim 1. The statistical calculation in step (vi) solely provided a value as such that expressed this confidence as a mathematical number, without any interaction with the technical features of the claim.
Furthermore, since the wording of step (vi) of claim 1 was clear to the skilled person, limitations mentioned solely in the description of the patent could not be read into claim 1. This was in line with the case law, e.g. T 1646/12, Reasons 2.1 and T 169/20, Reasons 1.3.3.

Novelty - claim 1

It was uncontested that document D1 disclosed a method according to claim 1 which comprised process steps (i) to (v). Even if the "statistical determination" feature of step (vi) - although being of a mathematical nature only - was considered for the issue of novelty, Example 6 of document D1 disclosed the method of claim 1

including process step (vi). This working example of document D1 disclosed in paragraphs [0092], [0093], [0098], [0100] and [0106] an allele call in a genotyping assay which included the determination of a statistical value that could not be derived from the read number alone. The statistical value disclosed in paragraph [0100] of document D1 increased the probability that the results obtained were correct. In other words this value was a measure for the accuracy of the method. The probabilistic information of this statistical value increased the confidence in using barcodes for an allele call.

Admittance of auxiliary requests 1 to 42 and 1a, 2a, 3a, 4a, 5a and 6a

Auxiliary requests 1 to 42 were submitted during the first instance proceedings. Both opponents objected during the oral proceedings to the admittance of these sets of claims because they were non-convergent, suffered from additional issues under added subject-matter and lack of clarity (see Minutes of the oral proceedings before the opposition division, points 1.1 and 1.2). The opposition division, however, had not to decide on this issue since the oppositions were rejected.

Auxiliary requests 1a, 2a, 3a, 4a, 5a and 6a were submitted in reply to the statement of grounds of appeal. Reasons were not apparent why these sets of claims could not have been filed already in the first instance proceedings.

Remittal

The admittance of any of the auxiliary requests on file into the appeal proceedings created a fresh case which required remittal to the opposition division for further prosecution.

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

Admission into the proceedings of a new line of argument under added subject-matter

There were no exceptional circumstances apparent why the appellant did not submit this new line of argument under added subject-matter earlier.

Main request (patent as granted)

Claim construction - step (vi) of claim 1

There was no general principle in the case law that any reference to the description and the drawings of a patent were to be avoided when construing a claim from the skilled person's perspective. On the contrary, the claims had to be construed in the context of the patent as a whole as, for example, set out in decision T 1646/12 which stated explicitly that this was sometimes even necessary (see Reasons 2.1).
Claim 1 defined a clear chronologic order for at least performing process steps (i) to (vi). This included step (vi) as last process step which defined as ultimate aim the determination of a statistical value for improving the confidence/reliability of the allele call. This was evident from the claim's structure which did not support a different order. Moreover this order was reflected in the patent as a whole. Thus, paragraphs [0001] to [0003] of the patent mentioned

that the invention related to the field of genotyping large populations of samples wherein the invention was used for increasing the confidence in allele calls. This confidence was increased by using DBRs (see paragraph [0041]) which were counted to give a statistical measure of confidence in allele calls (see paragraphs [0048] and [0068]). When read in this context, the skilled person reasonably construed step (vi) of claim 1 to be the last step of the claimed invention since this step determined the statistical value on the minimum number of individual polynucleotide molecules as indirectly determined by the number of different DBRs (step (v)). Only such an interpretation increased the confidence in the sequencing data obtaining in the preceding steps. Thus the use of step (vi) as last step was the sole reasonable interpretation of claim 1. Other interpretations were artificial. Step (vi) was also not an optional step in claim 1. There were no indications in claim 1 for such an interpretation. On the contrary, due to the use of the term "*and*" at the end of step (v), step (vi) was a mandatory step of claim 1.

Admittance of oral submissions on lack of novelty of opponent 2 at the oral proceedings

Since opponent 2 was a party as of right they should not be allowed to make substantial submissions on the question of novelty in view of document D1 at the oral proceedings. It was evident from the decision under appeal (see point 7.2) that opponent 2 had no objections under novelty as regards the subject-matter of claim 1.

Novelty - claim 1

The disclosure of document D1 differed fundamentally from the method of claim 1. Document D1 used the statistical value to determine certainty of an allele call, i.e. applied a deterministic approach, while step (vi) of claim 1 determined the uncertainty of the allele call and hence applied a probabilistic approach (see patent, paragraphs [0041], [0048] and [0068]). Indications that document D1 relied on a deterministic approach were derivable from paragraph [0005] which disclosed that sequence tags were used to authenticate a nucleic acid sequence and to quantify the relative abundance of polymorphic sequences due to the so called skewing effect of PCR amplification. An example of this quantitative determination was disclosed in Example 1. In essence Example 6 of document D1 taught the same. The statistical value disclosed in paragraphs [0100] and [0101] was a measure of the probability that two cloned products received the same barcode. In a selection of 15 PCR products the probability was 0.047 that two products received the same barcode by chance. This disclosure did not relate to an allele call since neither was the heterozygosity of the locus determined nor the minimum number of individual polynucleotide molecules. Instead PCR products were collected only. The claimed method however determined the minimum number of polynucleotide molecules to determine an allele call, while in document D1 this number was already determined before an allele call was performed. The statistical values in paragraphs [0100] and [0101] in document D1 were an indication of the reliability of the barcode pool. The bigger the pool, the more reliable were the data. This however was different from determining a statistical value for an allele call as defined in step (vi) of claim 1. Irrespective thereof, claim 1 required that step (vi) was performed as last

step of the method while in document D1 this step was carried out before an allele call was performed. Furthermore, the allele call in step (vi) of claim 1 was limited by the definition disclosed in paragraph [0058] of the patent in determining whether a sample was homozygous or heterozygous at a given locus.

Admittance of auxiliary requests 1 to 42, 1a, 2a, 3a, 4a, 5a and 6a

Auxiliary requests 1 to 42 were already submitted during the written phase of the opposition proceedings before the final date set by Rule 116 EPC in response to a negative preliminary opinion of the opposition division.

Auxiliary requests 1a, 2a, 3a, 4a, 5a and 6 were filed in reply to the appeal. Claim 1 of each of these sets of claims was at least amended in that the feature "*an allele call*" in step (vi) has been replaced with the feature "*whether a subject is homozygous or heterozygous at a locus*".

This amendment had a basis in the application as filed and was introduced in direct response to the opposition division's surprising finding in the decision under appeal that the term "*allele call*" was a generic expression referring to the determination of the sequence at a specific position which went against the definition disclosed in paragraph [0058] of the patent. Since this construction was found in the decision under appeal for the first time, these claim requests could not have been filed earlier.

The admittance and allowability of both groups of auxiliary requests should thus be decided by the

opposition division in view of the time points when these sets of claims were filed.

Remittal

Due to the substantial changes of the claim requests, a remittal of the case to the opposition division for further prosecution was appropriate.

XIV. Opponent 2's submissions, insofar as relevant to the present decision, may be summarised as follows:

Main request (patent as granted)

Claim construction - step (vi) of claim 1

The "statistical determination" feature of step (vi) had to be construed broadly. It was not required to consult the description to interpret the claim. Claim 1 did not define a chronological order for step (vi), since the claim neither defined a "when" for determining this value nor the "how". It was not mandatory that this value had to be determined on the minimum number of individual polynucleotide molecules as determined in step (v). Step (vi) contained no reference to any of the preceding steps but left it open on which set of data the statistical value had to be determined as long as it was not derived from the read number alone. It was not even necessary that this value increased the confidence into the accuracy of an allele call since this was not the statistical value's sole purpose. Other reasonable uses in the context of an allele call were, for example, the determination of the frequency of certain nucleotides at a given locus. Claim 1 provided no limitation as regards the nature or purpose of the statistical value. Step (vi) was a

mandatory step of the method as defined in claim 1 due to the presence of the term "*and*" at the end of step (v) and had thus to be taken into account for assessing novelty.

Novelty - claim 1

Document D1 anticipated the method of claim 1.

Remittal

A remittal of the case to the opposition division for further prosecution was appropriate.

XV. The parties' final requests relevant for the decision are set out below.
The appellant requested:
- that the decision under appeal be set aside and the patent be revoked;
- that the auxiliary requests filed by the patent proprietor on 23 November 2018 as auxiliary requests 1 to 32a, not be admitted into the appeal proceedings;
- that document D21 filed with the statement of grounds of appeal be admitted into the appeal proceedings;
- that a new line of argument under added subject-matter submitted on 13 March 2023, be admitted into the appeal proceedings.

XVI. The respondent requested:
- that the appeal be dismissed, i.e. that the oppositions be rejected and the patent be maintained as granted (main request); or, auxiliarily,
- that auxiliary requests 1 to 42 (which correspond to auxiliary requests 1 to 32, 11a, 13a, 15a, 17a, 19a, 24a, 26a, 28a, 30a and 32a submitted with the letter dated 23 November 2018) be admitted into the

proceedings and that auxiliary requests 1a to 6a, filed with the reply to the statement of grounds of appeal, be admitted into the appeal proceedings;
- that document D21, filed with the statement of grounds of appeal, not be admitted into the appeal proceedings;
- that the appellant's new line of argument under added subject-matter submitted on 13 March 2023, not be admitted into the appeal proceedings and to be heard with further arguments in response during oral proceedings should the appellant's arguments be admitted;
- that, if the decision under appeal should be overturned, the case be remitted to the opposition division for further prosecution based on auxiliary requests 1 to 42, 1a, 2a, 3a, 4a, 5a and 6a;
- that the party as of right (opponent 2) not be heard on the question of novelty in view of document D1.

XVII. Opponent 2 requested:
- that the decision under appeal be set aside and the patent be revoked and
- that the case be remitted to the opposition division.

Reasons for the Decision

Admission into the proceedings of a new line of argument under added subject-matter

1. The appellant submitted with the letter dated 13 March 2023 a new line of argument within the ground for opposition of Article 100(c) EPC. Since this line of argument is an amendment of the appellant's case filed after the notification of the summons to oral proceedings, admittance of this argument is subject to Article 13(2) RPBA 2020.

2. The appellant submitted in essence that the finding of added subject-matter in a closely related case which concerned a divisional European patent of the application underlying the patent in suit (T 1360/21), represented exceptional circumstances that justified the admittance of a related new line of argument under added subject-matter into these appeal proceedings.

3. The board does not agree.

3.1 The new line of argument is directed against the feature "*determine the minimum number of individual polynucleotide molecules originating from the same genomic region of the same original sample*" ("minimum number" feature) in step (v) of claim 1. This feature had never been objected to under added subject-matter before by the opponents.

3.2 Firstly, it is established case law that proceedings against a parent (this case) and a divisional application (case T 1360/21) are separate independent proceedings. Thus, the facts, evidence, and submissions made or filed in these proceedings are not automatically part of the parent procedure and *vice versa* (see Case Law of the Boards of Appeal, 10th edition 2022 ("Case Law"), II.F.4.1.1 and II.F. 4.1.5). No exceptional circumstances in the sense of Article 13(2) RPBA 2020 can be inferred from decisions relating to a different case, or arguments submitted therein.

3.3 Secondly, the method of present claim 1 has remained the same since the beginning of the opposition proceedings. While opponent 2 raised an objection against the method of claim 1 under added subject-

matter in their notice of opposition, these objections were solely directed against the feature "*determining a statistical value for an allele call in a genotyping assay that cannot be derived from the read number alone*" ("statistical determination" feature) in step (vi) of claim 1, i.e. a different feature. No reasons are apparent why the appellant could not have made their case on added subject-matter already during the first instance proceedings.

3.4 As an additional consideration, the board also sees no possibility to take the new objection of added subject-matter into account in the present appeal proceedings as an effect of *res judicata*. The question whether subject-matter on which a final decision is taken by a board in a given application or patent (here the divisional patent) becomes *res judicata* and could not be pursued in another application or patent (here the parent patent) would in any case not apply in the present case already for lack of identity of facts, particularly of claimed subject-matter and of parties involved (see Case Law, II. F.2.4.3 b), e.g. T 1870/16, Reasons 4.2. and T 1270/20, Reasons 3.8). In particular, the method of claim 1 of the main request differs significantly from that of the divisional patent, since the "pooling step" is missing. Thus, even if after a decision on the claims of the divisional patent, the principle of *res judicata* applied to the claims of the present parent patent, i.e. in "cross-procedural proceedings", which the present board doubts (see also T 2084/11, Reasons 1.3 and T 1666/14, Reasons 2), it would not apply here.

3.5 In light of the considerations above, the appellant should have submitted this new line of argument at the latest with their statement of grounds of appeal. Even

accepting that this issue became clear only at a later stage (on account of the "divisional" case), the appellant had reasons to raise this issue in the present case immediately after the opposition division took their decision with respect to the divisional application in 2021 at the latest. The delay of two more years cannot be justified by waiting for the board's decision in case T 1360/21.

4. The new line of argument under added subject-matter is therefore not admitted into the appeal proceedings (Article 13(2) RPBA).

Main request (patent as granted)

Claim construction - claim 1

5. Claim 1 is directed to "*a method for determining the minimum number of individual polynucleotide molecules originating from the same genomic region of the same original sample that have been sequenced in a particular sequence analysis configuration or process*", which method comprises at least six process steps. These steps and their interrelation are construed as follows:

"*attaching a degenerate base region (DBR) to starting polynucleotide molecules*", ("step (i)");

"*amplifying the DBR-attached starting polynucleotide molecules*" [the molecules from step (i), comment added by the board], ("step (ii)");

"*sequencing the amplified polynucleotide molecules ...*" [the molecules from step (ii), comment added by the board], ("step (iii)");

counting "*the number of different DBRs attached to a polynucleotide of interest*" [using presumably the sequencing data from step (iii), comment added by the board], ("step (iv)"); and

"*determining the minimum number of individual sequenced polynucleotide molecules originating from the same genomic region of the same original sample*" by "*using the number of different DBR sequences present in the sequencing run*" [using presumably the sequencing data from step (iii), comment added by the board], ("step (v)"); and

"*determining a statistical value for an allele call in a genotyping assay that cannot be derived from the read number alone*", ("step (vi)").

6. Process step (i) attaches a "*DBR*" to starting polynucleotide molecules which serves as a nucleotide-based label (see patent, paragraph [0005]). Since step (i) does not define the type and number of DBRs used, for example, that they have to be unique or consist of at least two nucleotides, DBR-tags can be different and/or identical and have a length of at least one nucleotide, while different DBR-tags are counted only (see step (iv) and patent, paragraphs [0062] and [0063]).

7. Process steps (ii) and (iii) describe that DBR-labelled polynucleotide molecules are amplified and sequenced, respectively.

8. Steps (iv) and (v) refer to different numbers (number of different DBRs "*attached to a polynucleotide of interest*" vs the number of different DBRs *per se* used

for determining the minimum number of sequenced individual polynucleotides, respectively). In the absence of any further specification in steps (iv) and (v), the number of different DBRs as determined in step (iv) must correspond to the minimum number of individual polynucleotides.

9. Due to the back-references of terms, such as DBR and DBR-attached polynucleotides in steps (i) to (v), these process steps define a chronological order in which the claimed method has to be performed.

10. It is disputed between the parties whether step (vi) of claim 1 (i.e. the "statistical determination" feature) likewise underlies this chronological order, i.e. whether or not step (vi) has to be performed as last step in the method as defined in claim 1.

11. The respondent submitted that step (vi) in claim 1 had to be carried out as last process step. This was the necessary result of the claim's structure which mentioned this feature as its last step and the skilled person's interpretation of claim 1 in the context of the patent's teaching as a whole. Reference in this regard was made to the patent, paragraphs [0001] to [0003], [0041] and [0048] and the case law of the boards of appeal, in particular decision T 1646/12.

11.1 The board does not agree.

11.2 For the reasons set out above, based on the wording of the process steps cited in claim 1, steps (i) to (v) have to be carried out in a consecutive order. This holds not true for the "statistical determination" feature of step (vi). Neither any of process steps (i) to (v) nor the preamble of claim 1 mentions the terms

cited in step (vi). Claim 1 is also silent on using formal identifiers for the at least six process steps, such as, for example, (a) to (f). Nor can the use of step (vi) as last process step be derived from the structure of claim 1 in any other way. On the contrary, the use of the term "*including*" in claim 1 which immediately follows the preamble leaves the order of the steps open since this term in the context of patent claims is commonly understood to have the same meaning as comprising. Thus based on the structure and the wording of claim 1, the performance of the "statistical determination" feature as last process step in claim 1 is not required.

11.3 As regards the argument that step (vi) has to be the last step based on the skilled person's necessary understanding of claim 1 as a whole in the context of the patent's teaching, the following is relevant.

11.4 The terms "*statistical value*", "*allele call*", "*genotyping assay*" and "*read number*" as mentioned in step (vi) of claim 1 are widely used in the field of performing a genetic analysis of chromosomes/genomes. The skilled person reading claim 1 is familiar with these terms and aware of their meaning. These terms are thus clear in themselves and in their relation to each other. In a situation like the present one, it is established case law that terms in a claim must be given their broadest technical sensible meaning, and that a definition in the description which is absent from a claim cannot give these terms and, hence, the claim as a whole a more narrow/restrictive meaning. This is particularly relevant in assessing novelty and inventive step of subject-matter claimed over the cited prior art (see Case Law, I.C.4.1 and I.C.4.8).

11.5 Nor does step (vi) of claim 1 specify "how" and "when" the statistical value is to be determined, except for indicating the purpose of its determination, i.e. "*for an allele call in a genotyping assay that cannot be derived from the read number alone*". Accordingly, step (vi) includes the determination of statistical values in any way and at any time of the claimed method as long as such a value serves the indicated purpose.

11.6 Following the criteria established by the case law set out in point 11.4 above, the board construes the meaning of the features in step (vi) and their relation to each other on account of the wording used in the claim and the claim's structure. In other words, the context of claim 1, having in mind the technical context of the invention, as also presented in the description. Moreover, the construction of the statistical determination feature according to step (vi) corresponds to the unambiguous wording of claim 1 and is technically sensible (see point 11.5 above). In this case thus it is neither necessary nor justified to rely on isolated passages of the description to interpret the claim more narrowly, let alone to read into claim 1 further limitations as derivable from paragraphs [0041] and [0048] of the patent only which are absent from the claim (see also T 169/20, Reasons 1.3.3, relied on by the appellant).

11.7 Claim 1 does therefore not define a chronological order as to when the statistical value defined in step (vi) has to be determined.

11.8 This does not change when the findings in decision T 1646/12 are taken into account. This decision sets out in point 2.1 *inter alia* that features in a claim should be construed in a context: "*Auf Patente*

angewandt bedeutet dies, dass Begriffe eines Anspruchs bzw. der Anspruchswortlaut als solcher kontextuell, d.h. im Gesamtzusammenhang des Anspruchssatzes bzw. der Beschreibung auszulegen sind. Sie können daher in der Regel nicht völlig losgelöst von der Beschreibung betrachtet werden" (Applied to patents this means that terms of a claim or the claim wording as such must be interpreted contextually, i.e. in the overall context of the claim sentence or description. Therefore, as a rule, they cannot be considered completely detached from the description; translation provided by the board). This decision warns however that:"*In diesem Zusammenhang gilt es zwei Extreme zu meiden. Zum einen ist es nicht zulässig, die Ansprüche und die Beschreibung gewissermaßen als kommunizierende Gefäße zu betrachten, zum Beispiel, indem man einschränkende Merkmale, die zwar in der Beschreibung beschrieben sind, aber nicht in den Ansprüchen, in letztere hineinliest (siehe dazu "Rechtsprechung der Beschwerdekammern des EPA", 7. Auflage, 2013, II.A. 6.3.4). Eine solche Übertragung von einschränkenden Merkmalen kann nicht durch Auslegung, sondern nur durch eine Änderung der Ansprüche erreicht werden. Zum anderen kann man den Anspruch auch nicht als von der Beschreibung völlig getrennt betrachten*" (In this context, two extremes must be avoided. Firstly, it is not permissible to regard the claims and the description as communicating vessels, so to speak, for example by reading limiting features mentioned in the description but not in the claims into the latter (see "Case Law of the Boards of Appeal of the EPO", 7th edition, 2013, II.A.6.3.4). Such a transfer of limiting features cannot be achieved by construction, but by amending the claims only. Secondly, the claim cannot be considered as being completely separate from the

description either; translation provided by the board, emphasis added).

11.9 In arguing that the skilled person, based on the disclosure of paragraphs [0041] and [0048] of the patent, would interpret claim 1 such that step (vi) had to be carried out after the other process steps because the statistical value had to be determined on the minimum number of individual polynucleotide molecules as indicated by the number of different DBRs (although this information is lacking in claim 1), the respondent applies the first of the two extremes identified in decision T 1646/12. Already for this reason alone, the respondent's argument fails.

11.10 Furthermore, as set out above (see point 11.5), step (vi) and claim 1 as a whole lacks any indication of how and when "*a statistical value*" has to be determined, for example, on which data, let alone on which of the numbers indicated in steps (iv) and/or (v) of claim 1. Nor does step (vi) define any "quantity" or "quality" of the value, or a reference which indicates the value's significance. In view thereof, step (vi) comprises any statistical value irrespective of when and how the value has been obtained, except that the value must be used for an allele call in a genotyping assay that cannot be derived from the read number alone.

12. An allele call in general as referred to in step (vi) aims at determining the variation (polymorphism) of a certain nucleotide sequence at a specific genome/ chromosome locus, i.e. a nucleotide variation at a specific position and/or region (see e.g. patent, paragraph [0058], and decision under appeal, point 7.4.2). Step (vi) does not specify the sample type.

Thus the sole restriction as set out in the preamble of claim 1 is that an allele call must be done in "*the same original sample*" irrespective of its source (i.e. derived from one or more organism(s) of whatever ploidy (1N, 2N, 3N, 4N etc.)).

13. The respondent submitted that the term "*allele call*" was defined by paragraph [0058] of the patent as "*determining whether a subject is homozygous or heterozygous at a locus*" which limited claim 1. The board disagrees. As set out above, it is established case law that terms in a claim must be given their broadest technical sensible meaning, and that a definition in the description which is absent from a claim cannot give the claim a more narrow/restrictive meaning.

14. A genotype assay comprises any sequencing-based assay that determines one or more sequence variation(s) (i.e. allele(s)) at (a) specific site(s) within a genome/ chromosome. Thus, an allele call in a genotyping method according to step (vi) of claim 1 relates to any sequencing-based method that determines a specific sequence variation (polymorphism) at a particular genomic locus (position or region) of the same sample. Since the number of different DBRs indicates the minimum number of individual polynucleotides (see above), the number of different DBRs is associated with the sequence variation(s) (i.e. allele(s)) at a particular locus in the same sample too.

15. The term "*read number*" in step (vi) of claim 1 is commonly understood in the field to refer to the number of sequence-based observations ("*reads*") of (a) sequence variation(s) (allele(s)) in a polynucleotide (see also patent, page 12, line 46).

16. The appellant contested that step (vi) of claim 1 was a mandatory process step since the terms "*allele call*", "*genotyping assay*" and "*read number*" did not appear elsewhere in claim 1. Since there was no link between step (vi) and the other process steps in claim 1, the appellant submitted that an embodiment of claim 1 comprised that the purpose of the method of claim 1 set out by the preamble (see above) was achieved solely by process steps (i) to (v).

17. The board does not agree. Claim 1 mentions the term "*and*" at the end of step (v) and avoids the use of any "or" between the different process steps. Consequently, based on the structure of its wording, claim 1 necessarily requires that step (vi) has to be performed. Step (vi) is thus a mandatory process step of claim 1. The appellant's argument thus fails.

Admittance of oral submissions on lack of novelty of opponent 2 at the oral proceedings

18. The respondent requested that the party as of right (opponent 2) not be heard on the question of novelty in view of document D1. It was submitted that opponent 2 did not appeal against the decision of the opposition division rejecting the oppositions. In addition, during opposition proceedings, opponent 2 did not maintain their objections against novelty of claim 1 in view of document D1, on account of the interpretation given by the opposition division that step (vi) was mandatory, as indicated in the opposition division’s decision (see point 7.2).

19. The board cannot follow this argument.

19.1 According to the procedural principles governing the appeal proceedings before the Boards of Appeal of the EPO (e.g. G 9/92, OJ EPO 1994, 875) the scope of an appeal is defined by the appellant's requests, which the non-appealing parties are not allowed to exceed.

19.2 A non-appealing party, which is party as of right, does therefore not have the same procedural status in all respects as does an appellant, e.g., it does not have an independent right to continue appeal proceedings if the appellant withdraws its appeal (see G 2/91, OJ 1992, 206 and G 9/92, OJ 1994, 875). However it does have the right to be heard (on account of the principle that all parties must be treated fairly and equally).

20. Since opponent 2's requests and submissions with regard to lack of novelty of claim 1 in view of document D1 remained within the scope of the appeal as defined by the appellant's submissions, the board found no reason why these should not be heard and taken into account. In particular, the board found no procedural obstacle to consider opponent 2's submissions, since they remained both within the framework of the appellant's submissions and of the board's communication under Article 15(1) RPBA.

Novelty - claim 1

21. It is uncontested between the parties that document D1 discloses the method of claim 1 which comprises process steps (i) to (v). It is further uncontested that the term "*barcodes*" disclosed in document D1 and the term "*DBR*" as mentioned in claim 1 are synonyms.

22. The respondent submitted that the method of claim 1 was novel over document D1 because this document, in

particular, Example 6 did not disclose a step of determining a statistical value for an allele call in a genotyping assay.

23. Novelty over document D1 depends thus on the question whether this document discloses the "statistical determination" feature of step (vi).

24. As set out above under claim construction (see point 14), an allele call in a genotyping method comprises any sequencing-based method that determines a specific sequence variation (polymorphism) at a particular genomic locus (position or region).

25. Document D1 states in paragraph [0005] that "*Barcoding permits, for example, quantification of the relative abundance of genomic methylation patterns or polymorphic sequences by correcting for skewing that can arise from PCR amplification or the cloning of the products*" (emphasis added). In other words, barcoding permits a counting of sequence variations (alleles). The term "*skewing*" refers to errors that arise from a PCR over-amplification of one or more starting polynucleotides derived from limited sample amounts (see e.g. paragraphs [0003], [0006] and [0093] of document D1). Thus the barcoding in document D1 addresses *inter alia* the problem that the relative abundance of a sequence polymorphism can not reliably be determined from the read number of the sequences (i.e. the sequencing data) alone because a PCR skewing effect may over-represent starting polynucleotides obtained from limited sample amounts. The same problem is addressed in the patent (see e.g. paragraph [0002]).

26. Paragraph [0021] of document D1 reports that the length of the barcode sequence and the number of random

nucleotides used in the barcode determines the probability of uniquely tagging polynucleotides, and hence, the ability to uniquely identify target nucleic acids.

26.1 Example 6 of document D1 discloses a method wherein a PCR product of the FMR1 locus is "*bar-coded*", i.e. sequence-tagged (see paragraph [0092]). Paragraph [0093] reports that this addresses the "*increased risk of redundancy and contamination when amplifying limited amounts of template DNA, for example, when the goal is to compare and quantify sequences from different cells represented in the same DNA sample...*" (emphasis added). These problems are solved by introducing into DNA fragments barcodes and batch-stamps as molecular labels prior to PCR amplification. It is further stated that "*This encoded information enables the genomic origin of each sequence obtained from PCR and subsequent bacterial cloning to be tracked. Each genomic fragment is marked prior to amplification, allowing us to identify contaminant and redundant sequences and to quantify accurately the proportion of cells carrying a particular sequence variant by counting only distinctly tagged sequences*" (emphasis added). In other words, the introduction of barcodes and batch-stamps increases the accuracy and hence confidence in quantifying allelic sequence variations in the same DNA sample from the same genomic locus (FMR1) (see also paragraph [0006] of document D1).

26.2 In the discussion part of Example 6 in paragraph [0106] of document D1 it is further stated that "*Here, a similar concept was applied to the labeling of individual genomic fragments with distinct sequence tags. The ability to bar-code and "batchstamp" genomic DNA sequences from individual alleles is useful in*

situations where the amount of template DNA is limited, thus identifying contaminants and redundant sequences arising from template re-cloning" (emphasis added).

26.3 Thus Example 6 discloses a method that quantifies sequence variations at the same genomic region (FMR1) in the same sample which represents an allele call in a genotyping assay that falls within the ambit of claim 1.

27. The sole remaining issue to be addressed is whether Example 6 also involves "*determining a statistical value*" "*that cannot be derived from the read number alone*", as specified in step (vi) of claim 1.

27.1 Example 6 mentions in paragraph [0100] that barcodes are used "*to encode each ligated genomic fragment with information that distinguishes it from other sequences within a sample, allowing the evaluation of cloned sequences for redundancy and contamination*". This aim is achieved by replacing a 6 nucleotide long loop of a hairpin linker "*with 7 nt randomly selected from A, G, and T. Cytosine was not used because its identity would be ambiguous after bisulfite conversion. With a random 7 nt barcode, the number of possible codes is 2187; in selecting 15 cloned PCR products from one DNA sample, the probability that two of these will be different genomic fragments labeled with identical 7 nt barcodes is 0.047 (for details of this probability calculation, see Miner et al., Nucl. Acids Res. 32(17):e135, 2004, Supplementary Materials)*".

27.2 Thus, this passage teaches the skilled person that with a probability of 0.047 any two or more sequences of 15 amplified barcoded starting polynucleotides carry the same barcode by chance (i.e. because two individual

starting polynucleotides in the sample are tagged by the same barcode). In other words, the statistical value of 0.047 indicates that there is a low probability that by using the 7-nt random barcode of Example 6 two starting molecules have received the same barcode. This likewise implies that the finding of different barcodes indicates with high probability that the tagged polynucleotides are different and therefore improves the confidence in the allele call of the genotyping assay (see also decision under appeal, point 8.6.2.3). Such a 7-nt random barcode is used in the experimental part of Example 6 (see [0103] in conjunction with Figure 4).

27.3 Furthermore the statistical value mentioned in paragraph [0100] of document D1 cannot be derived from the read number alone. This is so because the statistical value is normally determined before the polynucleotides are barcoded, amplified and sequenced, i.e. the read numbers of an allele call. This statistical value is thus independent from the read number and can therefore not be derived from the read number alone. It follows further from the teaching in paragraph [0100] of document D1 that the statistical value is normally not determined as last step (although this is not excluded) of the allele call in the genotyping assay but rather as a first step. A reason for this is that the probability that different genomic fragments are labeled with identical barcodes is influenced by the size of the pool of random-sequence barcodes which has to be large enough to allow reliable allele calls.

28. The respondent submitted that Example 6 of document D1 disclosed a deterministic approach in quantifying redundant sequences due to a PCR skewing effect (see

also [0005] of document D1) contrary to the probabilistic approach applied by the claimed method. While Example 6 provided exact results that did not leave room for any uncertainty, claim 1 was directed to determine a statistical value that estimated the uncertainty of the results obtained for an allele call. Both methods differed fundamentally from each other.

28.1 The board does not agree. As set out above under claim construction (see point 11.5), the statistical value as defined in step (vi) of claim 1 is not defined in any way except that it determines a value for an allele call in a genotyping method that cannot be derived from the read number alone. Step (vi) of claim 1 is therefore not limited in using statistical values that are determined on the minimum number of starting polynucleotides as indicated indirectly by the number of different DBRs.

28.2 Paragraph [0100] of document D1 mentions a statistical value. Since a statistical value describes *per se* how probable a certain fact is (here: the probability that two out of 15 cloned PCR products from one DNA sample will be different genomic fragments labeled with identical barcodes), paragraph [0100] of Example 6 discloses not exact results but allows an estimation of how reliable the obtained results are under the selected conditions.

28.3 This is further supported by the disclosure of the term "*probability*" in paragraph [0100] and the expression "*a highly accurate method*" in the last sentence of paragraph [0103]. These terms indicate to the skilled person that it is very likely, i.e. highly probable - but not certain - that the results obtained are correct which differs from the respondent's assertions that

Example 6 discloses exact results and a deterministic approach.

28.4 Also the mentioning of "*PCR products*" in paragraph [0100] of document D1 does not exclude that Example 6 relates to an allele call. The use of PCR products for sequencing in order to obtain an allele call likewise falls within steps (ii) and (iii) of claim 1.

28.5 Since the method of claim 1 neither defines a chronological order nor a reference on which data the statistical determination feature of step (vi) has to be performed (i.e. no "when" and "how", see claim construction above), Example 6 of document D1 is considered to be detrimental to the novelty of claim 1.

29. Thus claim 1, and hence the claims as granted lack novelty over the disclosure of document D1 (Article 100(a) in conjunction with Article 54 EPC).

Auxiliary request 1

30. Claim 1 of auxiliary request 1 is identical to claim 1 of the main request, except that the feature "*to increase the confidence in an allele call in a genotyping assay*" has been added at the end of the preamble.

Admittance of auxiliary request 1

31. The appellant requested that auxiliary requests 1 to 42 not be admitted into the appeal proceedings which includes auxiliary request 1. In view of the board's conclusion on the issue of lack of novelty (see points 32 and 33 below), there is no need to provide reasons

for the admittance and consideration of auxiliary request 1.

Novelty

32. Since the amendment in claim 1 of auxiliary request 1 does not affect the statistical determination feature in step (vi) but the preamble of claim 1 only, the subject-matter of claim 1 lacks novelty over the disclosure of document D1 for the same reasons as outlined above for claim 1 of the main request.

33. Auxiliary request 1 thus contravenes the requirements of Article 54 EPC.

Admittance of auxiliary requests 1a, 2a, 3a, 4a, 5a and 6a

34. Auxiliary requests 1a, 2a, 3a, 4a, 5a and 6a have been filed for the first time in reply to the appeal. Accordingly they are new in the proceedings.

35. It is established case law that the function of an appeal is to give a judicial decision upon the correctness of a separate earlier decision taken by an examining or opposition division. Appeal proceedings are not an opportunity to re-run or re-open the proceedings before any of these divisions (see Case Law, V.A.1.1).

36. Claim 1 of each of these auxiliary requests has been amended at least in that the feature "*an allele call*" in step (vi) has been replaced with the feature "*whether a subject is homozygous or heterozygous at a locus*".

37. The respondent submitted that these sets of claims could not have been submitted earlier because amended claims 1 addressed the opposition division's broad interpretation of the term "*allele call*" in step (vi) of claim 1 which was found for the first time in the decision under appeal only. Moreover, the opposition division's interpretation was surprising, in particular since it deviated from the definition given in the patent (see paragraph [0058]).

38. The board does not agree. It is evident from the course of events in the opposition proceedings that the appellant (then opponent 1) submitted already with their notice of opposition (see point 4.12 on page 4) that document D1 disclosed an allele call since this document referred in paragraphs [0005], [0093] and [0106] to the "*quantification of the relative abundance of genome methylation patterns or polymorphic sequences*". Furthermore, the appellant (then opponent 1) reiterated this argument that an allele call concerned any quantification of genomic polymorphic sequences in their reply to the preliminary opinion of the opposition division annexed to the summons (see submission of 23 November 2018, page 3, first paragraph).

39. In view of this course of events, the opposition division's broad interpretation of the term "*allele call*" was not an issue that came up for the first time in the decision under appeal only. Rather the opposition division merely adopted the interpretation of one of the opposing parties. Therefore auxiliary requests 1a, 2a, 3a, 4a, 5a and 6a filed in appeal could have been filed already at first instance.

40. The board fails to see any reason that could have prevented the respondent from filing these requests sooner. Since the respondent's filing of the new auxiliary requests is not in line with the case law cited above, auxiliary requests 1a, 2a, 3a, 4a, 5a and 6a are not admitted into the appeal proceedings (Article 12(4) RPBA 2007, which applies in the present case in accordance with Article 25(2) RPBA 2020).

Remittal

41. The opposition division did not decide on the admittance of auxiliary requests 2 to 42 which correspond to auxiliary requests 2 to 32, 11a, 13a, 15a, 17a, 19a, 24a, 26a, 28a, 30a and 32a submitted with the letter dated 23 November 2018 because the patent was maintained as granted. Nor had the opposition division for this reason to decide on the allowability of any of these sets of claims.

42. In a situation like the present one, not remitting the case to the opposition division would require the board to perform these tasks in both first- and last-instance proceedings and to effectively replace the opposition division rather than review the decision under appeal in a judicial manner, as required by Article 12(2) RPBA 2020. It follows that special reasons within the meaning of Articles 11 RPBA 2020 present themselves for remitting the case.

43. Consequently, the board considers it appropriate to exercise its discretion under Article 111(1) EPC to remit the case to the opposition division for further prosecution.

Admittance of document D21

44. The respondent requested that document D21 not be admitted into the appeal proceedings. In view of the board's conclusion that the subject-matter of claim 1 lacked novelty over Example 6 of document D1 alone (see point 28.5 above), there was no need to decide on document D21's admittance.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division for further prosecution.

The Registrar: The Chairwoman:

L. Malécot-Grob R. Morawetz

Decision electronically authenticated