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Datasheet for the decision of 19 February 2013

Case Number: T 2050/07 - 3.3.08

Application Number: 02250686.9

Publication Number: 1229135

IPC: C12Q 1/68, G06F 19/00, G06F 17/00

Language of the proceedings: EN

Title of invention:
Method and system for DNA mixture analysis

Applicant:
Perlin, Mark W.

Headword:
DNA Mixture Analysis/PERLIN

Relevant legal provisions:
EPC Art. 52(2), 54
RPBA Art. 9

Keyword:
"Excluded non-invention (no)"
"Novelty (yes)
"Remittal for further prosecution (yes)"

Decisions cited:
G 0003/08, T 0784/06, T 1658/06

Catchword:
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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 2050/07 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 19 February 2013

Appellant: (Applicant)
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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 24 July 2007 refusing European patent application No. 02250686.9 pursuant to Article 97(1) EPC 1973.

Composition of the Board:

Chairman: R. Moufang
Members: T. J. H. Mennessier
M. R. Vega Laso
D. H. Rees
J. Geschwind

Summary of Facts and Submissions

I. The applicant (appellant) lodged an appeal against the decision of the examining division posted on 24 July 2007, whereby the European patent application No. 02250686.9, entitled "*Method and system for DNA mixture analysis*", with publication number 1 229 135 was refused.

II. Basis for the refusal was the set of claims 1 to 28 filed with the letter of 15 February 2007. This set of claims was considered to be unallowable for lack of novelty (Articles 52(1) and 54(3) EPC 1973).

III. On 3 December 2007, the appellant filed a statement setting out the grounds of appeal which was accompanied by a main request and three auxiliary requests. The main request was identical to the request on which the decision under appeal was based. Oral proceedings were requested as an auxiliary measure.

IV. In a communication dated 22 March 2010 and issued pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA), the Board expressed its preliminary and non-binding views. The Board questioned whether the claimed method of the main request was a mathematical method which as such should not be regarded as a patentable invention (Article 52(2) EPC). It was also doubtful to the Board whether the requirements of Articles 123(2), 84 and 54 EPC were met by claim 1 of the main request. The same comments applied to the auxiliary requests.

V. In reply to the Board's communication, the appellant filed further submissions with a letter dated 28 May 2010. They were accompanied by a new set of claims filed as his sole request with an amended claim 1 compared to claim 1 of the previous main request.

VI. In a communication dated 18 October 2010, the Board made comments about the non-compliance of the request of 28 May 2010 with Articles 54 and 123(2) EPC.

VII. With a letter dated 20 December 2010, the appellant submitted a new set of claims as his main request while the previous main request of 28 May 2010 was re-filed as an auxiliary request. Claim 1 of the main request had been amended compared to claim 1 of the previous main request.

VIII. With a letter dated 6 January 2011, the appellant filed further submissions which were accompanied by four additional auxiliary requests.

IX. With a communication dated 11 July 2011, the appellant was informed that the Board had been enlarged pursuant to Article 9 RPBA to consist of three technically qualified members and two legally qualified members.

X. In a communication dated 23 March 2012, the Board expressed its opinion that there were objections under Article 84 EPC to claim 1 of both the main and the first auxiliary requests.

XI. With a letter dated 31 August 2012, the appellant filed further submissions which were accompanied by a set of 21 claims filed as his sole request. This set of claims

corresponded to the (first) auxiliary request of 20 December 2010 with an amended claim 1, which claim read as follows:

"1. A method of analyzing a DNA sample that contains genetic material from at least two individuals to determine a probability distribution of genotype likelihood or weight in the sample, comprising the steps:

(a) amplifying the DNA sample to produce an amplification product comprising DNA fragments, wherein each allele at a locus is amplified to generate relative amounts of DNA fragments of the alleles that are proportional to the relative amounts of template DNA from the alleles in the DNA sample, and wherein the amplification product produces a signal comprising signal peaks from each allele the amounts of which are proportional to the relative amounts of the alleles;

(b) detecting signal peak amounts in the signal and quantifying the amounts using quantifying means that include a computing device with memory to produce DNA length and concentration estimates from the sample;

(c) resolving the estimates into one or more component genotypes using automated resolving means, said resolution into one or more genotypes including solving the coupled linear equations **d = G.w+e** for the relevant loci (i), individuals (j) and alleles (k), in which **d** is a column vector which describes the peak quantitation data of a DNA sample from the

signal, **G** is a matrix that represents the genotypes in the DNA sample, with a column j giving the alleles for individual j, **w** is a weight column vector that represents relative proportions of template DNA in the sample and **e** is an error vector, wherein the solution includes calculation of data variance σ^2 from the linear model **d = G.w+e** together with the global minimal solution $\mathbf{Pd} = \mathbf{Gw_0}$, where **Pd** is the perpendicular projection point which is the closest point to **d** in mixture space C(**G**) and $\mathbf{w_0}$ is the minimum weight vector, using linear regression methods, and calculating a probability distribution of the data assuming a normal distribution and that the error is unbiased, so that E(**e**) = 0, but has a dispersion D[e] = $\sigma^2\mathbf{V}$ in which **V** is the covariance matrix of the data; and

(d) determining, using the probability distribution of the data, a probability distribution of genotype likelihood or weight in the DNA sample."

Claims 2 to 21 were dependent on claim 1 and directed to particular embodiments of the invention thereof.

XII. With a communication faxed on 20 September 2012, the Board informed the appellant that the oral proceedings scheduled for 11 October 2012 were cancelled.

XIII. The following document is cited in the decision:

(D6) European application EP 1 128 311 A2, published on 29 August 2001, with a priority date of 15 February 2000 and a filing date of 14 February 2001.

XIV. The submissions made by the appellant, insofar as they are relevant to the present decision, may be summarised as follows:

Requirements of Article 123(2) EPC

The features introduced into claim 1 during the appeal proceedings were disclosed in the application as filed, namely on page 31 as regards the calculation of the data variance, on page 43 as regards the calculation of a probability distribution, on page 44 as regards the assumption of an unbiased error, and on pages 31 and 32 as regards the global minimum solution.

Requirements of Article 54(3) EPC

Document D6 contained no teaching that the computation of the genotype likelihood or probability used a probability distribution that included the signal and the variance.

XV. The appellant requested that the decision under appeal be set aside and the application be remitted to the examining division for further prosecution on the basis of the set of claims filed under cover of the letter dated 31 August 2012.

Reasons for the Decision

Admissibility of the request into the proceedings

1. The request submitted with the letter dated 31 August 2012 was filed in direct reaction to the Board's communication of 23 March 2012 as an attempt to remedy a clarity objection. Therefore, exercising the discretion conferred to it by Article 13(1) RPBA, the Board decides to admit this request into the proceedings.

Article 123(2) EPC

2. The question to be answered is whether the claimed subject-matter is disclosed in the application as filed. Support for the subject-matter of claim 1 is found (i) at pages 7 to 10, where the claimed method is described in general terms, (ii) the passage extending from line 20 on page 11 to line 5 on page 12 that describes the linear mixture model on which the mathematical method underlying steps c) and d) relies, (iii) the passage bridging pages 31 and 32 which, taken together with page 28, lines 2 to 6 details the global minimal solution, (iv) the passages at lines 16 to 22 on page 43 and at lines 14 to 16 on page 44 which specify how to calculate a probability distribution. Thus, Article 123(2) EPC is complied with.

Article 52(2) EPC

3. It is established case law that claimed subject-matter is not excluded from patentability as a non-invention under Article 52(2) EPC for the sole reason that it

contains features which might be considered to be non-technical (see opinion G 3/08, OJ EPO 2011, 10, point 10.13 of the Reasons, and decision T 1658/06 of 14 January 2011, point 3 of the Reasons). In the present case, claim 1 as well as dependent claims 2 to 21 are directed to a method of analysing a DNA sample. This method comprises *inter alia* a step of amplifying the DNA sample, wherein the amplification product produces a signal comprising signal peaks (see step (a)), a step of detecting signal peak amounts and a step of quantifying the amounts using quantifying means that include a computing device to produce DNA length and concentration estimates (see step (b)). Already for the reason that both steps (a) and (b) are obviously performed using dedicated laboratory equipment and devices the claimed method cannot be considered as being devoid of technical character. The Board therefore reaches the conclusion that the subject-matter of none of the claims of the request is to be regarded as a non-invention pursuant to Article 52(2) EPC.

Article 84 EPC

4. The Board is satisfied that the claims are clear and supported by the description and concludes that the request complies with the requirements of Article 84 EPC.

Compliance with Article 83 EPC

5. No objection of insufficiency of disclosure was raised in the decision under appeal, and the Board has no

objections of its own. Thus, the requirements of Article 83 EPC are considered to be met.

Article 54 EPC

6. In the decision of the examining division, novelty of claim 1 of the set of claims filed with the letter of 15 February 2007 was denied in view of document D6 which describes a method of analysing a DNA mixture sample that contains genetic material from at least two individuals.

7. Document D6 is a European patent application filed by the present appellant and published on 29 August 2001, i.e. after the priority date of the application at issue (2 February 2001). Furthermore, it has a priority date of 15 February 2000, the validity of which has not been challenged by the appellant. Therefore, its content is considered as comprised in the state of the art pursuant to Article 54(3) EPC.

8. Both the method according to claim 1 and the method of document D6 involve (i) an amplification step wherein as a result of the DNA amplification a signal is produced which comprises signal peaks, (ii) a step of detecting the peak amounts in the signal, (iii) a step of quantifying the amounts to produce DNA length and concentration estimates, and (iv) a resolution step which involves a mathematical method basically consisting in representing the estimates in a linear equation, deriving a solution from the linear equation, and resolving the DNA mixture into its components. The methods differ essentially in that in the method according to claim 1, (i) the linear matrix equation

'p = G x w' used in document D6 to represent the linear effect of the concentration estimates - where p is a column vector which describes the peak quantitation data of a DNA sample from the signal, G is a matrix that represents the genotypes in the DNA sample and w is a weight column vector that represents relative proportions of template DNA in the sample - has been amended to include an error vector which models measurement error (see paragraph [0186] of the published patent application) and reads 'd = G.w + e', and (ii) the solution includes calculation of data variance σ^2 from the linear model 'd = G.w + e' together with the global minimal solution '$Pd = Gw_0$'.

9. The argument could be made that the distinguishing features described above are of non-technical nature as being a mathematical method or a method for performing mental activities, and that, in view of the established case law according to which features that do not contribute to the technical character of an invention and do not interact with the technical subject-matter of the claim for solving a technical problem, have to be ignored when assessing inventive step, such features should equally be ignored when assessing novelty. The Board therefore examines whether or not the distinguishing features in the present case make a technical contribution.

10. Both the distinguishing features (i) and (ii) aim at ascertaining the reliability of the claimed method for analyzing DNA samples containing genetic material from two or more individuals and for determining the genotypes involved. By providing estimates of the error 'e', estimates of the variances and standard deviations

can be computed from the data using the global minimal solution 'Pd = Gw_0' and these values can be used to estimate probabilities. This results in a quantitative estimate of the quality of the solution (see paragraphs [0006] and [0194] of the published application). Thus, the distinguishing features constitute a means for improving the confidence of the genotype estimate of the quantitative method analysis of document D6 (see paragraphs [0044] and [0074] of the published application). The board therefore considers that the distinguishing features contribute to the technical character of the claimed invention.

11. In decision T 784/06 of 23 June 2010, the present Board in a different composition had to assess the inventive activity of a five-step method of determining the genotype of a locus within genetic material obtained from a biological sample. The method as claimed was regarded as a mix of technical features (step A) and non-technical features relying on the performance of mental activities based on the application of mathematical methods (steps B to E), the latter features being argued by the patentee to be core features of the invention. It was found that the disclosure of the invention was of such a general nature that it deprived the skilled person of the information he/she needed to understand how to proceed from the first reaction value collected in step A through steps B, C and D to the determination on a probabilistic basis of the genotype of step E. Thus, the Board came to the conclusion that the technical activity of step A did not interact with the mental activities of steps B to E to lead to a tangible

technical result and therefore had to be ignored in the assessment of inventive step.

12. The Board considers that the present case clearly differs from the case underlying decision T 784/06. In contrast to the vagueness of the disclosure of the invention in appeal case T 784/06, the description of the present patent application makes it sufficiently clear how the distinguishing features (i) and (ii) of the method of claim 1 should be implemented and how they interact with the remaining steps of the claimed method in order to provide a common technical result, namely a genotype estimate with an improved confidence compared to the quantitative method analysis known from the prior art.

13. The above consideration leads the Board to consider that the distinguishing features have to be taken into account when assessing novelty of claim 1 and, therefore, it concludes that the method of claim 1 is new. As claims 2 to 21 are dependent on claim 1, the request as a whole complies with the requirements of Article 54 EPC.

Conclusion

14. As the requirements of Article 56 EPC have not yet been assessed by the examining division, the case is remitted to the first instance for further prosecution under the provisions of Article 111(1) EPC in accordance with the appellant's request.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division for further prosecution on the basis of claims 1 to 21 of the request filed under cover of the letter of 31 August 2012.

The Registrar The Chairman

A. Wolinski R. Moufang