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Datasheet for the decision of 20 May 2015

Case Number: T 2103/12 - 3.5.05

Application Number: 06735440.7

Publication Number: 1859377

IPC: G06F19/00, G06K9/62, G01N15/14

Language of the proceedings: EN

Title of invention:
System, method, and article for detecting abnormal cells using multi-dimensional analysis

Applicant:
Hematologics, Inc.

Headword:
Automated cell testing/HEMATOLOGICS

Relevant legal provisions:
EPC 1973 Art. 83, 84, 111(1)
EPC Art. 123(2)

Keyword:
Added subject-matter - (no, after amendment)
Clarity - (yes, after amendment)
Sufficiency of disclosure - (yes)
Remittal to the first instance for further prosecution - (yes)

Decisions cited:

Catchword:

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Case Number: T 2103/12 - 3.5.05

D E C I S I O N
of Technical Board of Appeal 3.5.05
of 20 May 2015

Appellant: (Applicant)	Hematologics, Inc. 113 1st Avenue North Seattle, WA 98109 (US)
Representative:	Grünecker Patent- und Rechtsanwälte PartG mbB Leopoldstraße 4 80802 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 25 April 2012 refusing European patent application No. 06735440.7 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chair	A. Ritzka
Members:	K. Bengi-Akyuerek
	G. Weiss

Summary of Facts and Submissions

I. The appeal is against the decision of the examining division to refuse the present European patent application on the grounds of added subject-matter (Article 123(2) EPC), lack of clarity (Article 84 EPC) and insufficiency of disclosure (Article 83 EPC) with respect to the claims of a main request and three auxiliary requests.

II. With the statement setting out the grounds of appeal, the appellant filed amended sets of claims according to a main and an auxiliary request. It requested that the decision of the examining division be set aside and that a patent be granted on the basis of the main or the auxiliary request. In addition, the appellant requested that the case be remitted to the examining division for further prosecution based on the main request.

III. In an annex to the summons to oral proceedings pursuant to Article 15(1) RPBA, the board gave its preliminary opinion on the appeal. In particular, it raised objections under Articles 123(2) EPC and 84 EPC 1973, and expressed concerns about the admissibility of the auxiliary request under Article 12(4) RPBA.

The appellant was also informed that the main request fulfilled the requirements of Article 83 EPC 1973 and that the case, in accordance with the appellant's request, could be remitted to the department of first instance if the corresponding objections were overcome.

IV. By its letter of reply, the appellant submitted amended claims according to a main request, replacing the main request on file, along with counter-arguments on an

objection raised in the board's communication under Article 15(1) RPBA (cf. section 2.2.2), and requested that the case be remitted to the examining division for further prosecution based on the main request.

V. Oral proceedings were held on 20 May 2015, during which the appellant filed a new main request, replacing the main request on file, in response to objections raised by the board and discussed at those oral proceedings.

The appellant's final request was that the decision under appeal be set aside and that the case be remitted to the department of first instance on the basis of claims 1 to 6 submitted at the oral proceedings as its main request or, in the alternative, of claims 1 to 19 filed as auxiliary request with the statement setting out the grounds of appeal.

At the end of the oral proceedings, the decision of the board was announced.

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

"A diagnostic system comprising means to carry out a method of characterizing a test set of biological cells, comprising:

a) mapping each cell in the test set of biological cells to a corresponding point in an n-dimensional space, wherein $n \geq 3$ using a defined protocol wherein at least some of the n-dimensions are fluorescent intensity data of the cells, the corresponding points forming a test set of points;

b) comparing the test set of points to a defined set of clusters of normal biological cells, i.e. a defined

set of normal clusters, in the n-dimensional space, wherein each cluster in the defined set of normal clusters corresponds to a maturation level within a cell lineage, and wherein for the set of normal clusters, a reference centroid line and a radius are defined, the reference centroid line and the radius forming various cluster shapes, wherein the reference centroid line for the set of clusters is based on a set of reference points, and wherein the radius is a function of a position on the reference centroid line, wherein the reference centroid line and the radius are adjusted in an iterative manner using at least one of statistical analysis and user input, wherein the adjusting includes determining a distance from an identified centroid point of each cluster and a nearest point on the reference centroid line;

c) determining for each point of the test set of points based on the determined reference centroid line and radius whether it is outside the defined set of normal clusters based on the comparison; and

d) characterizing the test set of biological cells based at least in part on a determination of an amount of abnormal cells in the test set of biological cells based on the determination of step c)."

Reasons for the Decision

1. MAIN REQUEST

This request was filed during the oral proceedings before the board, in response to the objections raised in the board's communication under Article 15(1) RPBA, and further limits the subject-matter claimed.

Therefore, the board admitted it into the appeal proceedings under Article 13(1) and (3) RPBA.

The claims of this request differ from those of the main request underlying the appealed decision essentially in that the option of using an "adjustment of the data set" in connection with the iterative adjustment in step b) of claim 1 has been removed (supported e.g. by page 43, line 28 to page 44, line 5 of the application as filed) and in that claim 1 now specifies that (emphasis added by the board)

A) the reference centroid line and the radius are defined for the set of normal clusters;
B) the reference centroid line and the radius form various cluster shapes;
C) the radius is a function of a position on the reference centroid line;
D) adjusting includes determining a distance from an identified centroid point of each cluster and a nearest point on the reference centroid line;
E) the determination whether the respective test points are outside the defined set of normal clusters is done based on the determined reference centroid line and radius.

Amendment A) is supported e.g. by page 42, lines 20-23, while amendments B) and C) are based on page 44, lines 9-11 of the application as filed. Amendment D) is based on page 43, lines 11-26 in conjunction with Fig. 21, acts 810, 812, 814 and 826. Lastly, amendment E) finds its support e.g. at page 44, lines 18-20 of the original application. Hence, the board is satisfied that the above amendments comply with Article 123(2) EPC.

Thus, present claim 1 of the main request comprises the following features (as labelled by the board):

A diagnostic system comprising means to carry out a method of characterising a test set of biological cells, comprising the steps of:

a) mapping each cell in the test set of biological cells to a corresponding point in an n-dimensional space, wherein n ≥ 3 using a defined protocol wherein at least some of the n-dimensions are fluorescent intensity data of the cells, the corresponding points forming a test set of points;

b) comparing the test set of points to a defined set of clusters of normal biological cells, i.e. a defined set of normal clusters, in the n-dimensional space, wherein

1) each cluster in the defined set of normal clusters corresponds to a maturation level within a cell lineage;

2) a reference centroid line and a radius are defined for the set of clusters;

3) the reference centroid line for the set of clusters is based on a set of reference points;

4) the reference centroid line and the radius form various cluster shapes and the radius is a function of a position on the reference centroid line;

5) the reference centroid line and the radius are adjusted in an iterative manner using at least one of statistical analysis and user input;

6) adjusting includes determining a distance from an identified centroid point of each cluster and a nearest point on the reference centroid line;

c) determining for each point of the test set of points based on the determined reference centroid line and radius whether it is outside the defined set of normal clusters based on the comparison;
d) characterising the test set of biological cells based at least in part on a determination of an amount of abnormal cells in the test set of biological cells based on the determination of step c).

1.1 Article 123(2) EPC

1.1.1 The examining division held that features b5) and d) contravened Article 123(2) EPC, since, with regard to feature b5), the relevant passages of the original specification disclosed that the statistical analysis or the user input was used for adjusting the reference *points* rather than the reference centroid line and the radius and, with regard to feature d), the original application disclosed merely a method for defining the normal clusters and determining whether each of the points in a data set were contained within said clusters rather than determining an amount of abnormal cells and the characterisation of the test cells based on that amount (cf. appealed decision, section III.10).

1.1.2 As to feature b5), the board however finds that the application as filed in fact teaches that the reference centroid line may be refined using statistical analysis (cf. page 42, lines 2-3) and that the radius may be entered by the user (cf. page 44, lines 14-16). Therefore, feature b5) is considered to be originally disclosed.

1.1.3 As to feature d), the original application teaches that a *percentage* of abnormal cells or a *number* of abnormal

events is indicated to the user (see e.g. page 29, lines 17-19 and page 53, lines 12-15) and that it may be determined whether too many cells are classified as abnormal to ascertain whether a defined normal cluster set should be redefined (cf. page 45, lines 8-12 in conjunction with Fig. 22, act 914). From this the board concludes that both the characterisation of cells as abnormal and the determination of an amount of abnormal cells are sufficiently disclosed in the original application. Therefore, also feature d) is found to be supported by the application as originally filed.

1.1.4 In view of the above, the board judges that the objections raised under Article 123(2) EPC in the decision under appeal are unfounded.

1.2 Article 84 EPC 1973

1.2.1 The examining division found that claims 1, 4, 5 and 7 then on file were not clear (cf. appealed decision, section III.11), with the following reasons provided:

- As to features b3) and b4) of claim 1, the reference centroid line and the respective radius were not clearly defined, since no definition was given of the "reference points" or of a method for generating a reference centroid line based on those reference points, nor was it specified how the magnitude of the radius should be defined. Thus, the skilled reader was not enabled to determine how the set of normal points is used to define the reference centroid line and the radius.

- As to feature b5) of claim 1, it was unclear what the corresponding iterations were based on, thereby raising questions about what triggered an

iteration, what was different between the different iterations and how the statistical analysis and user inputs were used to adjust the reference centroid line and the radius.

- As to the features of former dependent claim 4 (corresponding to present claim 3), it was unclear how, based on a representation of some "normal cells", any conclusions with regard to diagnosing cancer could be drawn, what should be understood by characterising and diagnosing a set of cells and the transition from comparing individual points with a set of normal clusters to said characterisation and diagnosis of the entire set of cells.

- As to the feature of former dependent claim 7 (corresponding to present claim 6), it was defined in terms of the result to be achieved, i.e. diagnosing cancer.

1.2.2 As regards features b3), b4) and b5) of claim 1 and in view of amendments A) to C), the board holds that the corresponding reference centroid line and the radius are broadly defined but not unclear. In particular, the skilled reader understands from feature b3) that several points in the underlying coordinate system are first selected in one of a number of ways (e.g. user-based, statistically, etc.) and that then a centroid line is drawn through those points. Feature b4) sufficiently indicates that multiple radiuses may be assigned to any cluster, while their magnitudes depend on the shape of the cluster. Finally, feature b5) adequately describes that the reference line and the radius are iteratively determined as a function of input data such as statistical or user

data. Hence, the board concludes that it is clear for the skilled person what falls within the terms of those features.

In this context, the board additionally notes that a claim cannot be reasonably expected to furnish each and every implementation detail, like an overly detailed recipe, to enable a skilled reader to properly establish the scope of protection sought in the sense of Article 84 EPC 1973. Rather, in order to meet the requirement of Article 84 EPC 1973 that the claims should be clear, the board considers that it suffices that the skilled reader is in a position to derive from the wording of a claim what falls within its ambit.

1.2.3 As regards present claim 3, the board finds that its wording relates not only to "normal cells" but also to "test cells" (see the second exposing, measuring and mapping steps in claim 3), and it is therefore satisfied that the skilled reader understands that the solution according to that claim, i.e. the comparison of test cells with normal cells, could - at least in part - be used for diagnosing cancer according to e.g. empirical medical studies or the doctor's experience.

1.2.4 As regards present claim 6, the board is satisfied that the features of this claim, i.e. the clusters being a hyperellipsoid, and the referenced claims (i.e. present claims 1 to 5) specify a possible solution (rather than solely the achieved result) which indeed could be employed for diagnosing cancer, depending on medical circumstances.

1.2.5 In view of the above, the objections raised under Article 84 EPC 1973 in the decision under appeal are

considered to be overcome or unfounded.

1.3 Article 83 EPC 1973

1.3.1 The examining division also took the view that features b2) and b3) of claim 1, i.e. the definitions of the "reference points" and the "reference centroid line", were not sufficiently disclosed, since the original application did not indicate how reasonable reference points were selected to define a reference centroid line, what qualified a point as a reference point compared to other points, and since the terms "reference points" and "reference centroid line" were not known in the relevant art of statistics. Also, the original specification did not disclose any process of generating a reasonable reference centroid line from the reference points selected because a plurality of points could be connected in a variety of ways to obtain a line through the points (cf. appealed decision, section III.12).

1.3.2 The board finds that, in the present case, the notional "skilled person" to which the application is supposed to be addressed is a team made up of an expert in *statistics and mathematical modelling* (see also statement setting out the grounds of appeal, page 6, last sentence) and an expert in *computer automation* (see e.g. "diagnostic system 104" in Fig. 1 of the present application). The skilled person would readily recognise that the application as filed teaches that the reference points may be selected by a user after viewing various representations of the data set (as preferred alternative) or may be statistically selected by diagnostic system 104 or by a combination thereof (cf. page 40, lines 8-13 or page 42, line 25 to page 43, line 2 in conjunction with Figs. 20A and 20B)

and that they are iteratively adjusted (cf. Fig. 19, act 616 and Fig. 21, act 816). Moreover, the board subscribes to the view of the appellant that the skilled person in the field of statistics and mathematical modelling, from his common general knowledge, would know that "reasonable" reference points are to be selected in such a way that the reference points are within a cluster and that their number and position are sufficient to represent the cluster's shape (i.e. typically being close to the centroid points of the corresponding clusters), and that the selection of the initial reference points is not critical for the final cluster representation, as the reference centroid line and the radius are supposed to be iteratively adjusted until convergence. In this respect, the board adds that the application as filed also demonstrates that ten reference points are simply connected with each other to define an "initial reference centroid line 702" (cf. Figs. 20A and 20B) and that a "redefined reference centroid line 704" is determined e.g. by geometric bending (cf. page 44, lines 3-6).

Therefore, the board judges that the above-defined skilled person would readily derive from the application as filed and his common general knowledge at least one way of selecting reference points and drawing a reference centroid line - whether reasonable or not - to put the present invention into practice through a mere automation of the underlying statistical/mathematical model.

1.3.3 Hence, the board holds that the main request is allowable under Article 83 EPC 1973.

2. *Remittal of the case for further prosecution*

2.1 The appellant requested that the case be remitted to the examining division for further prosecution based on the main request (cf. points II and V above).

2.2 Compliance with the requirements of Article 52(1) EPC, in particular as regards novelty and inventive step, was neither discussed nor decided in the decision under appeal. The board therefore judges that, under the present circumstances, it is not appropriate to take a final decision for the first time on the matters of novelty and inventive step in the second-instance proceedings. For these reasons and in order not to deprive the appellant of a complete examination of the claims on file by two instances, the board decides, in the exercise of its discretion conferred by Article 111(1) EPC 1973 and in accordance with the appellant's request, to remit the case to the department of first instance for further prosecution.

2.3 As the board is remitting the case to the examining division on the basis of the main request, it is not necessary to consider the present auxiliary request further.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution on the basis of claims 1 to 6 submitted as main request at the oral proceedings before the board.

The Registrar: The Chair:

K. Götz-Wein A. Ritzka

Decision electronically authenticated