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**Datasheet for the decision
of 3 December 2007**

Case Number: T 1018/06 - 3.3.08

Application Number: 03027486.4

Publication Number: 1411356

IPC: G01N 33/50

Language of the proceedings: EN

Title of invention:

Test for the rapid evaluation of ischemic states and kit

Applicant:

Ischemia Technologies, Inc.

Headword:

Ischemia detection/ISCHEMIA

Relevant legal provisions (EPC 1973):

EPC Art. 123(2), 76(1), 84, 83, 54, 56
EPC R. 68(2)

Keyword:

"Main request - added subject-matter - (no)"
"Clarity and sufficiency of disclosure - (yes)"
"Novelty and inventive step - (yes)"

Decisions cited:

G 0001/05, G 0001/06, T 0583/04, T 1360/05

Catchword:

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Case Number: T 1018/06 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 3 December 2007

Appellant: Ischemia Technologies, Inc.
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Representative: Clegg, Richard Ian
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 9 December 2005
refusing European application No. 03027486.4
pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: L. Galligani
Members: P. Julià
T. Karamanli

Summary of Facts and Submissions

I. European patent application No. 03 027 486.4, published under No. 1 411 356 (referred to in the present decision as "the application as filed"), was filed on 10 July 1992 as a divisional application to the European patent application No. 92 915 563.8, published as International application under No. WO 93/03346 (referred to in the present decision as "the earlier application"). In a decision dated 9 December 2005, the examining division refused the application for failing to fulfil the requirements of Articles 84 and 56 EPC.

II. Claim 1 of the set of thirteen claims refused by the examining division read as follows:

"1. A method of detecting the occurrence of ischemia in a patient, comprising the steps of:

(a) contacting a blood, blood-derived body fluid sample including a serum or plasma sample or tissue sample of said patient with metal ions capable of binding to protein metal ion-binding sites selected from the group consisting of thiol, hydroxyl, carbonyl, amino, imidazole, hydroxymethyl and guanidinium groups in said sample, to form a mixture containing protein bound metal ions and non-protein bound metal ions, and

(b) detecting the amount of non-protein bound metal ions using a method that detects free metal ions, whereby the amount of free metal ions is a measure of the amount of available metal ion-binding sites of the protein and amount of oxidatively damaged metal ion

binding sites, thereby indicating the occurrence or non-occurrence of an ischemic state in said sample."

Claim 1 differed from claim 1 as filed by the addition of the wording "or tissue sample" in part (a) of the claim and the deletion of the term "respectively" at the end of part (b) of the claim. Claims 2 to 13 were as originally filed and were directed to preferred embodiments of claim 1.

III. As for the reasons for the refusal, the decision under appeal referred to the communications of the examining division dated 27 July 2004 and 20 July 2005.

In these communications, the applicant had been informed that the subject-matter of claim 1 was considered not to be supported by the description over the whole range of the claim because the application as filed only taught that protein thiol groups were decreased in ischemic events. However, claim 1 included a list of other non-thiol groups for which there was neither a teaching nor information on their possible use in the disclosed method (Article 84 and Rule 29 EPC). Moreover, in the absence of this information, these non-thiol groups did not provide a working solution to the technical problem underlying the application, i.e. the provision of an alternative method to detect ischemic events in a patient. Therefore, the requirements of Article 56 EPC were considered not to be fulfilled.

Since the applicant had not filed any comments or amendments in reply to the second communication of the examining division and had requested, with letter dated

- 21 September 2005, a decision according to the state of the file, the application was refused by the examining division making reference only to its previous communications.
- IV. With letter dated 16 February 2006, the applicant (appellant) filed a notice of appeal and paid the appeal fee on the same day. The statement setting out the grounds of appeal was filed with letter dated 18 April 2006, together with a main request and a first, second and third auxiliary requests.
- V. The decision under appeal was not rectified by the examining division and the case was remitted to the board of appeal (Article 109(2) EPC).
- VI. On 25 October 2006, the board sent a communication pursuant to Article 110(2) EPC stating its preliminary, non-binding opinion. The appellant's attention was also drawn to the pending cases under Ref. Nos. G 1/05 of 16 September 2005 and G 1/06 of 4 April 2006 (consolidated with G 3/06 of 15 May 2006) before the Enlarged Board of Appeal, which were considered of relevance for the question whether the present divisional application met the requirements of Articles 76(1) and 123(2) EPC.
- VII. With letter dated 28 December 2006, the appellant replied to the board's communication and filed a fourth auxiliary request. The appellant requested the board to stay the further appeal proceedings until the Enlarged Board of Appeal had decided on the pending cases, unless the board could positively decide on Article 76(1) EPC based on said latter request.

VIII. With a communication dated 26 January 2007, the appellant was informed that the board did not intend to proceed with the case before the decisions of the Enlarged Board of Appeal were issued.

IX. After the decisions of the Enlarged Board of Appeal G 1/05 and G 1/06 (both to be published in the OJ EPO) were issued on 28 June 2007, the appellant was summoned to oral proceedings.

X. With letter dated 2 November 2007, the appellant made further submissions together with a document describing details of the commercial product ACB (Albumin Cobalt Binding) Test Reagent Pack as well as the test and the colorimetric detection method based on this product. The appellant further filed a new main request and new first and second auxiliary requests. Claim 1 of the **main request** read as follows:

"1. An in vitro method of detecting the occurrence of ischemia in a patient, comprising the steps of:

(a) contacting a serum, plasma, fluid or tissue sample from said patient with an excess amount of metal ions capable of binding to protein metal ion-binding sites in said sample, to form a mixture containing protein bound metal ions, including thiol group-bound metal ions, and non-protein bound metal ions, and

(b) detecting the amount of non-protein bound metal ions using a method that detects free metal ions, whereby the amount of free metal ions is a measure of the amount of available metal ion-binding sites of the

protein and amount of oxidatively damaged metal ion binding sites, thereby indicating the occurrence or non-occurrence of an ischemic state in said sample."

Claims 2 to 11 and 13 were as filed and were directed to preferred embodiments of claim 1. Claim 12 was also dependent on claim 1 and was identical to claim 12 as filed except for defining the metal ion used as cobalt ion.

XI. Oral proceedings took place on 3 December 2007.

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

Main request

Article 123(2) EPC

The characterization of the claimed method as an "*in vitro*" method was supported by the whole content of the application as filed. Paragraphs [0017] and [0018] of the application as filed referred to general protein metal ion-binding sites, including thiol groups, and provided a formal support for part (a) of claim 1.

Whereas the reference to "*an excess amount of metal ions*" in claim 1 was supported by paragraph [0019], a formal basis for the type of sample from the patient, including "*fluid or tissue*", was found in paragraphs [0014] and [0023]. The features of claim 1 were thus supported by the application as filed.

Article 84 EPC

The application disclosed a simple method for detecting the occurrence of an ischemic event in a patient, which comprised only two steps, namely (a) contacting a sample from the patient with metal ions capable of binding to protein metal ion-binding sites, and (b) detecting the quantity of non-protein bound (unbound) metal ions. The introduction of thiol groups into claim 1 ("*including thiol group-bound metal ions*") reflected the technical feature that was described in the application as essential to the disclosed method. The objection for lack of clarity raised by the examining division was thereby overcome. The references to "*an in vitro method*" and to "*an excess amount of metal ions*" did not introduce any ambiguity in claim 1. The meaning of "*an excess amount*" was clearly defined in paragraph [0019] of the application. The introduction of cobalt as the metal ion in claim 12 reflected the fact that the pH range indicated in this claim was the pH range given in paragraph [0030] for the specific binding of cobalt ion to the protein.

Articles 54 and 56 EPC

The examining division did not raise any objection for lack of novelty and, in the decision under appeal, identified both the closest prior art (document D3, US 4 492 753) and the technical problem to be solved. The solution proposed in the application was acknowledged to be neither disclosed nor hinted at in any of the cited prior art documents and thus, not to be obvious. Subject-matter regarding to thiol groups was explicitly recognized to be inventive in the

decision under appeal. The claimed subject-matter was however considered to comprise embodiments that did not solve the technical problem and therefore, inventive step was not acknowledged. The main request necessarily required now the presence of thiol groups and, for this reason, the objection for lack of inventive step was moot.

XIII. The appellant (applicant) requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request or, in the alternative, of the auxiliary request 1 or 2, all filed with a letter of 2 November 2007.

Reasons for the Decision

Procedural issues

1. The decision under appeal is a so called "decision on the state of the file". Although this decision does not contain any reasoning within the meaning of Rule 68(2) EPC but refers only to two previous communications of the examining division, these communications contain a fully reasoned exposition of the examining division's objections to the refused application and the refutation of any rebuttal by the applicant. It is thus not necessary to construct the applicable reasons by mosaicing various arguments from these communications nor do they leave any doubt which arguments apply to which claims. In line with the established case law (cf. *inter alia* T 583/04 of 6 June 2006 and T 1360/05 of 16 February 2006), the board considers that the

decision under appeal satisfies the requirement of Rule 68(2) EPC.

Main request

Articles 123(2) and 76(1) EPC

2. According to the decisions of the Enlarged Board of Appeal G 1/05 and G 1/06 (both to be published in the OJ EPO), *"it is a necessary and sufficient condition for a divisional application ... to comply with Article 76(1), second sentence, EPC that anything disclosed in that divisional application be directly and unambiguously derivable from what is disclosed in each of the preceding applications as filed"* (cf. G 1/06, Order). Moreover, *"amendments to divisional applications are allowed under Article 123(2) EPC to the same extent as amendments of any other non-divisional applications ... a divisional application can be directed by amendment to aspects of the earlier application also disclosed in the divisional application as filed but not encompassed by the claims of the divisional application as filed"* (cf. G 1/05 or G 1/06, point 9.2 of the Reasons).

3. Although in the application as filed there is no explicit reference to the claimed method as being an *"in vitro"* method, the content of the description as a whole clearly relates to a method of this nature. In particular, the type of samples referred thereto (*"any tissue, serum, plasma or fluid sample"*) as well as their preparation (*"tissue samples may be obtained from body organs"*) (cf. paragraph [0023] of the application as filed) and the methods described for detection of the ion metal binding to the protein (colorimetric,

atomic absorption spectroscopy) directly point to "*in vitro*" methods. This is further supported by the sole example of the application as filed, which refers to sera and plasma from patients "*obtained by peripheral venipuncture*" and used "*in a test tube or cuvette*" (cf. paragraphs [0050] to [0052] of the application as filed).

4. Paragraph [0018] of the application as filed refers to general metal ion-binding sites of a protein and mentions some examples thereof, including the thiol groups present on the amino acids that constitute the protein. Paragraph [0017] of the application as filed proposes the possible biological mechanism underlying the disclosure of the invention and reference is also made to thiol groups. The importance of thiol groups is further emphasized in paragraphs [0025] and [0026]. The use of an "*excess amount of metal ion*" is described in paragraph [0019]. The other features of claim 1 are present in claim 1 as filed and in claim 1 refused by the examining division (cf. Section II *supra*), for which no objections were raised under Article 123(2) EPC in the decision under appeal nor are any apparent to the board.

5. Thus, the requirements of Article 123(2) EPC are fulfilled. Since the description of the application as filed is identical to that of the earlier application, the requirements of Article 76(1) EPC are also met.

Article 84 EPC

6. Claim 1 requires the mixture - which contains protein bound metal ions and results from contacting a sample from the patient with an excess amount of metal ions - to include thiol group-bound metal ions. The sample from the patient is thereby explicitly required to contain proteins having available thiol groups for metal ion binding. This requirement excludes samples from the patient containing only proteins that do not have available thiol groups, and which, according to the description, *"will not be effective in binding metal ions and therefore ineffective in the present method"* (cf. paragraph [0026] of the application as filed). This is in line with the statements found in paragraph [0025] of the application as filed, namely that *"optimum results are obtained with samples containing a large concentration of proteins having thiol groups available for metal ion binding"* and that *"any sample containing a substantial concentration of proteins having available thiol groups may be used in the present invention"*.

7. The exclusion of ineffective samples, i.e. samples containing only proteins that do not have available thiol groups for metal ion binding, restricts the scope of claim 1 to subject-matter for which technical support is actually found in the application as filed. Therefore, the objection for lack of clarity and for lack of technical support raised by the examining division in the decision under appeal is overcome.

8. No further objections were raised under Article 84 EPC by the examining division nor are any apparent to the board. The requirements of Article 84 EPC are thus considered to be fulfilled.

Article 83 EPC

9. The examining division did not raise any objection under this article in the decision under appeal. Example 1 of the application as filed shows that the claimed method differentiates patients having an ischemic episode or with myocardial infarction as well as patients with unstable angina from control patients and from normal patients with non-cardiogenic chest pain (cf. paragraph [0053] and Table 1 of the application as filed). These results are confirmed by the information on the commercial product "ACB (Albumin Cobalt Binding) Test Reagent Pack" provided by the appellant (cf. Section X *supra*).
10. Therefore, the conditions of Article 83 EPC are considered to be met.

Article 54 and 56 EPC

11. The examining division acknowledged the novelty of the disclosed method of detecting the occurrence of ischemia in a patient. In view of the prior art on file, the board does not see any reason to deviate from that view and novelty is acknowledged for the claimed subject-matter (Article 54 EPC).
12. The objection for lack of inventive step raised in the decision under appeal was based - only and exclusively

- on the presence of embodiments that did not provide a working solution to the technical problem underlying the invention (cf. Section III *supra*). The exclusion of those samples which in the application are disclosed as ineffective samples, i.e. samples without proteins having available thiol groups for metal ion binding, restricts the claimed subject-matter to what actually solves the technical problem identified in the decision under appeal. Thereby, the objection of lack of inventive step raised by the examining division is overcome.

13. In the decision under appeal, the examining division acknowledged that the claimed method, when based on - or regarding to - thiol groups was neither disclosed nor hinted in any of the cited prior art and thus, not obvious and inventive. In view of the prior art on file, the board does not see any reason to deviate from that finding and inventive step is acknowledged (Article 56 EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to grant a patent with the following claims and a description to be adapted thereto:

Claims 1 to 13 filed as main request with the letter of 2 November 2007.

The Registrar:

The Chairman:

A. Wolinski

L. Galligani