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Datasheet for the decision of 12 December 2019

Case Number: T 0325/15 - 3.3.01

Application Number: 09781380.2

Publication Number: 2303922

IPC: G01N33/68, G01N33/74, C07K14/58

Language of the proceedings: EN

Title of invention:
METHOD FOR THE IN VITRO DIAGNOSIS OF STROKE

Applicant:
Bio-Rad Europe GmbH

Headword:
Diagnosis of stroke/BIO-RAD

Relevant legal provisions:
RPBA Art. 15(3)
EPC R. 115(2), 103(1)(a)
EPC Art. 111(2), 54(2), 56

Keyword:
Oral proceedings - held in absence of appellant
Novelty - (main request: no)
Inventive step - (auxiliary request: no)
Reimbursement of appeal fee - (no)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 0325/15 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 12 December 2019

Appellant: (Applicant)	Bio-Rad Europe GmbH Holbeinstrasse 75 4051 Basel (CH)
Representative:	Lavoix 2, place d'Estienne d'Orves 75441 Paris Cedex 09 (FR)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 22 September 2014 refusing European patent application No. 09781380.2 pursuant to Article 97(2) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	P. de Heij
	T. Sommerfeld

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division, in which European patent application 09781380.2, based on an international application published as WO 2010/012834, was refused under Article 97(2) EPC.

II. At the oral proceedings the examining division considered the then pending main request as not being allowable under Article 56 EPC, while the first auxiliary request was found to comply with the requirements of the EPC. The examining division then issued a communication under Rule 71(3) EPC, informing of its intention to grant a European patent on the basis of said first auxiliary request. In an annex to this communication, the examining division also provided a reason why the main request was found to contravene Article 56 EPC. Instead of providing the required translations of the claims proposed for grant, the patent applicant replied to the communication of the examining division by stating that it did not accept the text intended for grant by the examining division and that it maintained its main request. The examining division then issued the appealed decision.

III. The applicant (appellant) lodged an appeal against the decision of the examining division, requesting that the decision be set aside and that a patent be granted according to the main claim request or, alternatively, according to the auxiliary request, both filed with the statement of grounds of appeal. It also requested reimbursement of the appeal fee in view of a substantial procedural violation.

The **main request** is identical to the claim request that was decided on by the examining division. It comprises 17 claims, of which claim 1 reads as follows:

"1. A method for the *in vitro* diagnosis of stroke and transient ischemic attack (TIA) in an individual, comprising the following steps:

(a) measuring the level of proBNP(1-108), or of fragments of proBNP(1-108) comprising a RAPRSP sequence (SEQ ID NO: 1), in a biological sample of the individual;

(b) comparing the measured level with a cut-off value;

(c) determining therefrom whether a stroke or a TIA has occurred in the individual."

The **auxiliary request** is identical to the claim request that the examining division had considered allowable and had proposed as a basis for the grant of a patent. In relation to the main request, claim 1 has been amended by the insertion of features as shown:

"1. A method for the *in vitro* diagnosis of stroke and transient ischemic attack (TIA) in an individual, comprising the following steps:

(a) measuring the level of proBNP(1-108), or of fragments of proBNP(1-108) comprising a RAPRSP sequence (SEQ ID NO: 1), in a biological sample of the individual;

(b) comparing the measured level with a cut-off value;

(c) determining therefrom whether a stroke or a TIA has occurred in the individual,
wherein the level of proBNP(1-108), or of fragments of proBNP(1-108), is determined using an immunoassay which

comprises an antibody targeting an epitope which comprises the RAPRSP sequence (SEQ ID NO: 1)."

IV. As an annex to the summons to oral proceedings, the board issued a communication pursuant to Article 15(1) RPBA.

With said communication, the board introduced a new document, designated D5, and expressed a detailed negative preliminary opinion on the sets of claims on file, in particular with regard to the lack of novelty of claim 1 of the main request over D5 and the lack of inventive step of claim 1 of the auxiliary request, starting either from D5 or from D1 as closest prior art. The board also gave a preliminary opinion that the request for reimbursement of the appeal fee was not deemed equitable.

V. The appellant did not file any substantive reply to the board's communication but instead informed the board that it would not attend oral proceedings and withdrew its request for oral proceedings, in a letter dated 7 November 2019. In a further letter, dated 8 November 2019, the appellant reiterated that it would not attend oral proceedings.

VI. Oral proceedings took place on 12 December 2019 as scheduled and in the absence of the appellant. At the end of oral proceedings the chairman announced the board's decision.

VII. The documents cited in the examination and appeal proceedings include the following:

D1 WO 2004/094460
D2 WO 2004/014952

D5 WO 03/016910

VIII. The appellant's arguments, in so far as they are relevant to the present decision, may be summarised as follows:

The appealed decision was insufficiently and inadequately reasoned, this being a substantial procedural violation within the meaning of Rule 103 EPC. The examining division decided that claim 8 of the main request lacked inventive step, which was in contradiction with the findings of the examining division in relation to the auxiliary request: despite including a claim 6 directed to the same subject-matter as claim 8 of the main request, the auxiliary request was considered to fulfil all the requirements of the EPC. The same discrepancy was also observed in relation to claim 7 of the main request and claim 1 of the auxiliary request.

With regard to novelty and inventive step, the appellant has only provided arguments in relation to document D1. Such arguments are not relevant to the present decision, which relies on document D5.

IX. The appellant requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the main request or, alternatively, according to the auxiliary request, both filed with the statement of grounds of appeal. It also requested the reimbursement of the appeal fee in view of a substantial procedural violation.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings before the board took place in the absence of the appellant who had been duly summoned but decided not to attend.

The present decision is based on facts and evidence put forward during the written proceedings, in particular in the board's communication pursuant to Article 15(1) RPBA, and on which the appellant has had the opportunity to comment. In accordance with Rule 115(2) EPC, the board decided to continue the proceedings in its absence.

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

3. Main request - novelty

3.1 Document D5 discloses a number of possible diagnostic markers for stroke, including BNP (B-type natriuretic peptide or brain-type natriuretic peptide), and methods for the diagnosis of stroke by analysing the presence or amount of one or more such markers in a test sample obtained from the subject (claims 1 and 3). Paragraphs [0113] to [0115] of D5 are specifically concerned with BNP. Paragraph [0113] teaches that both the precursor form "pre pro BNP" (which is designated proBNP(1-108) in the present application) and "NT pro BNP" (which is the 76-amino acid N-terminal peptide that results from

proteolysis of the precursor form), as well as any other peptides derived therefrom, "are collectively described as markers related to or associated with BNP". Paragraph [0114] also clarifies that while "The term "BNP" as used herein refers to the mature 32-amino acid BNP molecule itself (...) the skilled artisan will recognise, however, [that] other markers related to BNP may also serve as diagnostic or prognostic indicators in patients with stroke". Finally, paragraph [0142] "describes the statistical analysis of data generated from immunoassays specific for BNP, ..." and teaches the thresholds used for the assays. Hence, document D5 discloses a diagnostic method for stroke comprising all of the features of claim 1 of the main request.

3.2 The main request is thus not allowable for lack of novelty (Article 54(2) EPC).

4. Auxiliary request - inventive step

4.1 The present claims are directed to methods for the in vitro diagnosis of stroke and transient ischemic attack (TIA) in an individual. According to the established case law of the boards of appeal, the closest prior art is usually a document which has the same purpose as the claimed invention. Hence, in the present case, the closest prior art should be a document also directed to the diagnosis of stroke and transient ischemic attack. Document D5, entitled "Diagnostic markers of stroke and cerebral injury and methods of use thereof", is specifically concerned with the diagnosis of stroke and therefore a more suitable starting point for the discussion of inventive step than document D1, which was considered the closest prior art in the appealed decision.

4.2 The difference from the subject-matter of claim 1 of the auxiliary request is that D5 does not make use of an antibody targeting an epitope which comprises the RAPRSP sequence (SEQ ID NO:1). The RAPRSP sequence spans amino acids 73 to 78 of the proBNP(1-108) and thus is only partially present in the mature BNP 1-32 form (which spans amino acids 77 to 108 of the proBNP(1-108) peptide). Hence an antibody targeting an epitope which comprises the RAPRSP sequence makes it possible to measure the level of proBNP(1-108), but is directed to an epitope which is not part of the mature form, as explained above. Document D5, on the other hand, teaches in paragraph [0134] (Example 2) that "Assays for BNP were performed using murine anti-BNP monoclonal antibody 106.3", wherein "The hybridoma cell line secreting mAb 106.3 was generated from a fusion between FOX-NY cells and spleen cells from a Balb/c mouse immunized with human BNP 1-32 conjugated to BSA". Clearly such an antibody recognises both the proBNP(1 -108) peptide (which also comprises the mature form BNP 1-32) and the mature form BNP 1-32 itself.

4.3 The application states that an antibody as claimed, i.e. directed against an epitope comprising the RAPRSP sequence, is advantageous, "in that it enables the specific detection of proBNP(1-108) and of all the fragments of proBNP(1-108) according to the invention, with the notable exception of BNP(32), NT-proBNP(1-76) and their respective fragments, thereby ensuring obtaining the full diagnosis benefits of proBNP(1-108) and its various fragments" (page 9, lines 4 to 8). There is however no teaching or data in the application or elsewhere on file which would allow to conclude that the use of this discriminatory antibody has any advantages over the use of the antibody of D5 in the context of stroke diagnosis. Hence the technical

problem is formulated as the provision of an alternative diagnostic method for stroke. The solution is the method as claimed and the board is satisfied that the claimed solution solves the technical problem.

4.4 However, the board comes to the conclusion that the claimed subject-matter does not involve an inventive step. Merely replacing the antibody of the closest prior art D5 with another equally suitable antibody, which was furthermore known in the prior art and had already been used for diagnostic purposes (D2, as discussed in the application on page 8, line 32 to page 9, line 4), appears to be a trivial modification of the diagnostic method disclosed in D5.

4.5 The auxiliary request is thus not allowable for lack of compliance with Article 56 EPC.

5. Request for reimbursement of the appeal fee

5.1 According to Rule 103(1)(a) EPC, the appeal fee shall be reimbursed in full where the board of appeal deems an appeal to be allowable, if such reimbursement is equitable by reason of a substantial procedural violation. As in the present case the appeal is dismissed, the appeal fee cannot be reimbursed.

5.2 In addition, the decision is not insufficiently or inadequately reasoned either. The examining division only had to decide on the allowability of the main request. This was considered not to be the case for the reason that the subject-matter of claims 8 and 10 lacked inventive step. This part of the reasoning is understandable and not contradicted by any other part of the decision. The board agrees that there seems to be a contradiction on the one hand between the findings

of the examining division with regard to the main request in the appealed decision and on the other hand concerning the auxiliary request as expressed during the oral proceedings and in its Rule 71(3) EPC communication. However, this contradiction is not part of the grounds for the decision. Therefore, a lack of reasoning is not present.

5.3 The request for reimbursement of the appeal fee is thus refused.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

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

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated