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**Datasheet for the decision
of 12 September 2006**

Case Number: T 0143/04 - 3.2.02

Application Number: 95928139.5

Publication Number: 1011415

IPC: A61B 3/11

Language of the proceedings: EN

Title of invention:

Non-invasive method for diagnosing Alzheimer's disease in a patient

Applicant:

Beth Israel Hospital Association

Opponent:-

Headword:-

Relevant legal provisions:

EPC Art. 52(4), 84, 123(2)

Keyword:

"Extended subject-matter (yes)"
"Diagnostic method (yes)"

Decisions cited:

G 0001/04, T 0133/85, T 1197/02

Catchword:

Data processing using an automated apparatus is not actually part of the examination phase which involves the data collection phase, but it results from a subsequent, technical step, intermediate between the data collection and the comparison of these collected data with standard values. Such intermediate steps are not to be considered when assessing the diagnostic character of a diagnostic method (see point 3.2)



Case Number: T 0143/04 - 3.2.02

D E C I S I O N
of the Technical Board of Appeal 3.2.02
of 12 September 2006

Appellant: Beth Israel Hospital Association
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Representative: Lunt, Mark George Francis
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 13 August 2003
refusing European application No. 95928139.5
pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: T. Kriner
Members: M. Noel
A. Pignatelli

Summary of Facts and Submissions

- I. European patent application No. 95 928 139.5 (International Publication No. WO 96/030 70) was refused by the examining division on 13 August 2003 on the basis of Articles 52(4) and 123(2) EPC.

The reasons for the refusal were that all claims then on file defined a diagnostic method and that the omission of some features from the originally filed method claims, with the view to escaping from the definition of a diagnostic method, led to unallowable extension of the claimed subject-matter.

- II. The appellant (applicant) lodged an appeal against this decision by notice received on 8 October 2003 and paid the appeal fee the day after. A statement of grounds of appeal was filed on 16 December 2003 along with amended sets of claims.

- III. Oral proceedings were held on 12 September 2006, at the end of which the appellant requested that the decision under appeal be set aside and that a patent be granted on the basis either of claims 1 to 32 of the main request, or of claims 1 to 31 of the first auxiliary request, or of claims 1 to 33 of the second auxiliary request, or of claims 1 to 19 of the third auxiliary request, all filed during oral proceedings.

- IV. Claims 1 according to the various requests read as follows:

Main and first auxiliary request:

"A non-invasive data collection method when performed exclusively for the purpose of subsequently employing the data collected as a basis for diagnosing the presence or absence of Alzheimer's disease in a living subject, which data collection method comprises:

establishing a baseline pupil diameter for the pupil of the subject;

using automated apparatus to repetitively and episodically image the pupil of the subject and measure pupil diameter, which measurements are made after the administration to the eye of the subject of a neural transmitter mediator in an amount insufficient to cause a significant pupil constriction or dilation if the subject is not afflicted with Alzheimer's disease and during a time when said neural transmitter would have an observable effect on pupil diameter in a subject afflicted with Alzheimer's disease; and

processing said measurements in said automated apparatus to provide a comparison of pupil diameter changes after said administration against said baseline or against Alzheimer's characteristic pupil diameter rates of change."

Second auxiliary request:

"A method of diagnosing Alzheimer's disease in a living subject, which comprises:

establishing a baseline pupil diameter for the pupil of the subject;

using automated apparatus to repetitively and episodically image the subject's pupil and measure pupil diameter, which measurements are made after the administration to the eye of the subject of a neural transmitter mediator in an amount insufficient to cause

a significant pupil constriction or dilation if the subject is not afflicted with Alzheimer's disease and during a time when said neural transmitter would have an observable effect on pupil diameter in a subject afflicted with Alzheimer's disease; and

processing said measurements in said automated apparatus to provide a comparison of pupil diameter changes after said administration against said baseline or against Alzheimer's characteristic pupil diameter rates of change."

Third auxiliary request:

"A kit when for use in a method of diagnosis of Alzheimer's disease, the kit comprising:

- i) at least one neural transmitter mediator, suitable for administration to a targeted eye of a living human subject in an amount insufficient to cause marked changes in pupil diameter over time in a patient not afflicted with Alzheimer's disease, said neural mediator being selected from the group consisting of cholinergic and adrenergic antagonists and agonists; and
- ii) automated apparatus, comprising:
 - a) means to continuously monitor and record, both before and after administration of said mediator, the pupil diameter size of said targeted eye over a plurality of prechosen durations, each duration ranging from less than 1 second to about 5 minutes;
 - b) means to cumulatively record such monitored and measured pupil diameter size information as is obtained over each such duration so as to accumulate primary and secondary

informational data of pupil diameter size for said targeted eye in respect of periods before and after administration of said mediator; and

- c) means to process said primary and secondary informational data to provide average values of at least one parameter selected from the group consisting of pupil diameter dilation, pupil diameter constriction, and the rate of pupil diameter change for said targeted eye as occurred over said time durations, whereby

a marked change in said parameter between said primary and secondary informational confirms or suggests that the living subject is afflicted with Alzheimer's disease."

V. The appellant argued as follows:

Concerning a non-invasive data collection method according to claim 1 of the main and the first auxiliary requests, the protection sought by the application as originally filed was certainly a method of diagnosing Alzheimer's disease. However, a data collection method was also disclosed in the application as part of the broader method for ultimately making a diagnosis. As presently worded, claim 1 only covered the data collection method when it was intended to form the basis of a subsequent diagnosis, which was entirely consistent with the application as filed.

Therefore, the subject-matter of claim 1 of the main and first auxiliary requests was properly supported by the original disclosure and did not extend beyond the

content of the application as filed. These claims were thus in accordance with the requirements of Articles 84 and 123(2) EPC.

Concerning a method of diagnosing Alzheimer's disease according to claim 1 of the second auxiliary request, the appellant submitted that during the examination phase, which included the collection of data, only the administration of a neural transmitter mediator to the eye of the subject and the capture of images necessitated the presence of the patient. But the subsequent steps of measuring pupil diameter and/or the rate of constriction and of processing the data were performed by automated equipment. Consequently, while being both essential and technical, these steps, did not require the presence of the patient and, hence, were not practised on the human body. Moreover, since the nature of the disease could not be diagnosed absolutely and solely by the diagnostic method of the present invention, despite the original intent in the application, this method was not suitable to unambiguously determine a clinical picture.

Therefore, the method as claimed in claim 1 of the second auxiliary request was not a diagnostic method within the meaning of the opinion G 1/04 and thus was not prohibited by Article 52(4) EPC.

Concerning the kit for use in a method of diagnosis of Alzheimer's disease according to claim 1 of the third auxiliary request, the word "kit" was not explicitly mentioned in the description, and a combination of a mediator and an automated apparatus, as such, was not described as an invention. Nevertheless, such a kit was

inherent in the specification as filed and supported by the combination of features recited for example in claims 15 and 20 as originally filed.

Therefore, the claims to the kit were fairly supported by the application as filed and did not add subject-matter extending beyond the original content, in accordance with the requirements of Article 123(2) EPC.

Reasons for the Decision

1. The appeal is admissible.

2. *Claim 1 of the main and the first auxiliary requests*

This claim relates to a non-invasive data collection method subsequently usable for diagnosing the presence or absence of Alzheimer's disease in a living subject.

The application as filed is repetitively and exclusively directed to the provision and the presentation of a diagnostic method for diagnosing Alzheimer's disease in a patient, based principally upon neurotransmitter (mediator) stimulated changes in pupil diameter or upon light-stimulated pupil constriction velocity (photostimulation). See, for example, page 1, lines 1 to 6 of the application as published under the PCT; page 5, lines 25 to 27; page 11, lines 12 to 23; page 14, lines 13 to 17, etc... .

Although a data collection step consisting in periodically capturing the image of the pupil of the

subject and measuring the pupil diameter, after administration to the eye of the subject of a neural transmitter mediator, is necessary to the making of a diagnosis, the present application never presents this examination phase as being a separate object of the invention for which protection is sought. This examination phase, which involves the collection of data, represents only the first step of a diagnostic method as a whole, as explained in the opinion G 1/04, point 5, and cannot be isolated from its context so as to become the principal object of the invention.

Thus, although a data collection phase is disclosed in the present application it is not disclosed as an independent method, but only as one phase which together with further phases form a method for diagnosing Alzheimer's disease. Consequently the amendment made to claim 1, i.e. of presenting a data collection method as being the main object of the present invention does not find any support in the description, contrary to the requirement of Article 84, second sentence, and extends its subject-matter beyond the content of the application as filed, contrary to the requirement of Article 123(2) EPC.

The Board is aware that during the examination of an application the claims may be amended extensively, provided however, that the subject-matter which results from the amendment remains within the framework of the original disclosure. The rule is that the subject-matter of the invention be the same before and after the modification (see T 133/85, OJ EPO, 1988, 441, in particular point 5). Such is not the case in the present situation since the subject-matter of the

invention has been changed from a diagnostic method to a part of it, i.e. a data collection method, which was never envisaged by the author of the application as originally filed.

3. *Claim 1 of the second auxiliary request*

3.1 In the opinion G 1/04 (OJ EPO 2006, 334) the Enlarged Board of Appeal came, *inter alia*, to the following conclusion (see point 1):

"In order that the subject-matter of a claim relating to a diagnostic method practised on the human or animal body falls under the prohibition of Article 52(4) EPC, the claim is to include the features relating to:

(i) the diagnosis for curative purposes *stricto sensu* representing the deductive medical or veterinary decision phase as a purely intellectual exercise,

(ii) the preceding steps which are constitutive for making that diagnosis, and

(iii) the specific interactions with the human or animal body which occur when carrying those out among these preceding steps which are of a technical nature."

This means that a diagnostic method in the sense of Article 52(4) EPC has to comprise the following steps (G 1/04, point 5 of the reasons):

(a) the examination phase involving the collection of data,

- (b) the comparison of these data with standard values,
- (c) the finding of any significant deviation, i.e. a symptom, during the comparison, and
- (d) the attribution of the deviation to a particular clinical picture, i.e. the deductive medical or veterinary decision phase,

wherein the steps of a technical nature belonging to steps (a) to (c) must satisfy the criterion "practised on the human or animal body" (see conclusion, point 3).

As further specified in opinion G 1/04 (see conclusion, point 4):

"Article 52(4) EPC does not require a specific type and intensity of interaction with the human or animal body; a preceding step of a technical nature thus satisfies the criterion "practised on the human or animal body" if its performance implies any interaction with the human or animal body, necessitating the presence of the latter".

The criterion "practised on the human or animal body" is to be considered only in respect of method steps which are of a technical nature (see points 6.4.1 and 6.4.4 of G 1/04). Thus it neither applies to the deductive decision phase, nor to the above-mentioned steps b) and c) which consist in comparing the data collected in the examination phase with standard values and in finding a significant deviation resulting from the comparison. These activities are predominantly of a

non-technical nature and normally not practised on the human or animal body (see point 6.4.1 of G 1/04).

It results therefrom that in most cases only step a) which refers to the examination phase and involves the collection of data can actually be of a technical nature and, therefore, concerned with the criterion "practised on the human or animal body" (see T 1197/02, point 2.2).

3.2 Claim 1 at issue relates to a method of diagnosing Alzheimer's disease in a living subject.

Step (a) mentioned above is achieved in claim 1 by repeatedly and episodically imaging the subject's pupil and measuring the pupil diameter with an automated apparatus, said measurements being made after the administration to the eye of the subject of a neural transmitter mediator.

At least the administration of the mediator and the capture of the image of the pupil, which are of technical nature, require the presence of the patient. Contrary to the appellant's contention, it is not correct to artificially dissociate the examination phase into a measuring step and a processing step, so as to further assert that the operation of processing the data with automated equipment does not require the presence of the patient and that, therefore, it is not practised on the human body.

Data processing using an automated apparatus is not actually part of the examination phase which involves the data collection phase, but it results from a

subsequent, technical step, intermediate between the data collection and the comparison of these collected data with standard values.

Such intermediate steps are not to be considered when assessing the diagnostic character of the method (see T 1197/02 supra, point 2.2). In most of the claims to a diagnostic method, such technical, intermediate steps exist and may be introduced for completeness between the steps (a) to (d) mentioned above. But only the steps (a) to (d) are essential to identify a diagnostic method according to G 1/04 and are to be considered correspondingly.

Step (b) which refers to the comparison of the data collected (and processed) with standard values is to be found in claim 1 in the last feature: "processing said measurements (in said automated apparatus) to provide a comparison of pupil diameter changes after said administration against said baseline". The standard values are obtained by the feature: "establishing a baseline pupil diameter for the pupil of the subject".

Step (c) which refers to the finding of any significant deviation, i.e. a symptom, during the comparison, is to be found in claim 1 in the features according to which the comparison is made after a neural transmitter mediator is administered in an amount and during a time suitable for said neural transmitter to have an observable effect on pupil diameter in a subject afflicted with Alzheimer's disease.

Step (d) which refers to the attribution of the deviation to a particular clinical picture, i.e. the

diagnosis, results clearly from the method as claimed:
"A method of diagnosing Alzheimer's disease in a living subject".

3.3 It results therefrom that claim 1 according to the second auxiliary request includes all the features of a diagnostic method practised on the human or animal body as defined in the opinion G 1/04. Such a method is prohibited by Article 52(4) EPC.

3.4 The appellant's argumentation according to which the claimed method should not be regarded as a diagnostic method in the sense of Article 52(4) EPC, since it was not suitable, by itself, to unambiguously determine Alzheimer's disease, is not convincing. Neither Article 52(4) EPC nor G 1/04 requires that only reliable diagnostic methods which by themselves lead to an unambiguous result are excluded from patentability. Therefore the question whether or not a diagnostic method is absolutely reliable is not relevant for the assessment of patentability of the method with respect to Article 52(4) EPC.

4. *Claim 1 of the third auxiliary request*

This claim relates to a kit for use in a method of diagnosis of Alzheimer's disease, comprising essentially a neural transmitter mediator for administration to a targeted eye of a living human subject, and an automated apparatus comprising means to continuously monitor and measure pupil diameters, means to cumulatively record therefrom informational data and means to process said informational data.

Such a combination of features is supported partially by claim 11, 15 or 20 as originally filed. However, these claims refer to a method for diagnosing Alzheimer's disease and not to an apparatus, let alone to a kit comprising a substance (mediator) and said apparatus in combination. The application as filed is, as already pointed out, exclusively concerned with a diagnostic method using a number of known substances and apparatuses. A kit, in particular a kit comprising a mediator and an apparatus is not even mentioned in the application originally filed.

As a consequence, a kit for use in a method of diagnosis of Alzheimer's disease is not supported and extends the claimed subject-matter beyond the content of the application as filed, in contravention to Article 123(2) EPC. Therefore, claim 1 of the third auxiliary request is not acceptable either.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

V. Commare

T. Kriner