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D E C I S I O N
of 3 August 2000

Case Number: T 0422/96 - 3.3.4

Application Number: 86111928.7

Publication Number: 0212670

IPC: G01N 33/543

Language of the proceedings: EN

Title of invention:

Method for detecting an analyte moiety by means of signal localization

Patentee:

ENZO BIOCHEM, INC.

Opponent:

Ortho-Clinical Diagnostics, Inc.

Headword:

Method for detecting an analyte/ENZO BIOCHEM. INC.

Relevant legal provisions:

EPC Art. 54, 56

Keyword:

"Main request - novelty (yes): claimed technical effect not made available to the public by prior art"

"Inventive step (yes)"

Decisions cited:

G 0010/91, G 0001/95, G 0007/95, T 0229/85, T 0099/85

Catchword:

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Case Number: T 0422/96 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 3 August 2000

Appellant: Ortho-Clinical Diagnostics, Inc.
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 13 February 1996
rejecting the opposition filed against European
patent No. 0 212 670 pursuant to Article 102(2)
EPC.

Composition of the Board:

Chairwoman: U. M. Kinkeldey
Members: R. E. Gramaglia
S. C. Perryman

Summary of Facts and Submissions

I. The appeal lies against the decision of the opposition division rejecting the opposition against European patent No. 0 212 670 (application No. 86 111 928.7) which was granted on the basis of 12 claims, of which independent claims 1 and 2 read as follows:

"1. A method for detecting the presence of an analyte moiety comprising the steps of:

- (a) fixing to a support either a first analyte moiety or a first analyte-specific moiety;
- (b) forming a complex comprising either:
 - (1) said first analyte moiety and a second analyte-specific moiety, or
 - (2) said first analyte-specific moiety and a second analyte moiety, wherein each of that said second analyte-specific moiety and said first analyte-specific moiety has a signalling moiety capable of generating a signal either directly or indirectly attached thereto;
- (c) forming either specific or viscous medium on said support, wherein said specific medium comprises (1) a solution, (2) a polymer network, and (3) a signal precursor, and wherein said viscous medium comprises (1) a solution, (2) a specific component that imparts the desired viscosity to said viscous medium, and (3) a signal precursor; and

(d) generating a signal by means of said signalling moiety.

2. A method for detecting the presence of an analyte moiety in a sample, wherein said analyte moiety is or comprises either a signalling moiety or a signal precursor, comprising the steps of:

(a) forming either a:

(1) specific or viscous medium on a support when said analyte moiety is or comprises a signalling moiety capable of generating a signal directly or indirectly, wherein said specific medium comprises (a) a solution, (b) a network, and (c) a signal precursor, and wherein said viscous medium comprises (a) a solution, (b) a specific component, and (c) a signal precursor, or

(2) indicative or thick medium on a support when said analyte moiety is or comprises a signal precursor, wherein said indicative medium comprises (a) a solution, (b) a polymer network, and (c) a signalling moiety, and wherein said thick medium comprises (a) a solution, (b) a specific component, and (c) a signalling moiety;

(b) contacting one of said media with said analyte moiety; and

(c) generating a signal by means of said signalling moiety."

Dependent claims 3 to 12 related to specific embodiments of the methods of claims 1 and 2.

II. The following documents are mentioned in this decision:

- (1) US-A-3,966,897;
- (4) US-A-4,381,921;
- (6) US-A-3,654,090;
- (8) WO-A-85/02018;
- (9) Podlesky T.R. et al., Proc. Natl. Acad. Sci. USA, Vol. 75, pages 2035-2039 (1978).

III. The board issued a communication pursuant to Article 11(2) of the Procedure before the Boards of Appeal expressing its provisional opinion. In response thereto, the respondent filed on 3 July 2000 new claims in the form of a new claim request, of which claims 1 and 2 read as follows (the amendments over granted claims 1 and 2 are shown by way of deletions and in bold):

"1. A method for ~~detecting~~ **enhanced detection of** the presence of an analyte moiety **by limiting the spread of the signal from the point of origin of the signal** comprising the steps of:

- (a) fixing to a support either a first analyte moiety or a first analyte-specific moiety;
- (b) forming a complex comprising either:

- (1) said first analyte moiety and a second analyte-specific moiety, or
 - (2) said first analyte-specific moiety and a second analyte moiety, wherein each of that said second analyte-specific moiety and said first analyte-specific moiety has a signalling moiety capable of generating a signal either directly or indirectly attached thereto;
- (c) forming either specific or viscous medium on said support, wherein said specific medium comprises (1) a solution, (2) a polymer network, and (3) a signal precursor, and wherein said viscous medium comprises (1) a solution, (2) a specific component that imparts the desired viscosity to said viscous medium, and (3) a signal precursor; and
- (d) generating a signal by means of said signalling moiety.

2. A method for ~~detecting~~ **enhanced detection of** the presence of an analyte moiety in a sample **by limiting the spread of the signal from the point of origin of the signal**, wherein said analyte moiety is or comprises either a signalling moiety or a signal precursor, comprising the steps of:

- (a) forming either a:
 - (1) specific or viscous medium on a support when said analyte moiety is or comprises a signalling moiety capable of generating a signal directly or indirectly, wherein said

specific medium comprises (a) a solution, (b) a network, and (c) a signal precursor, and wherein said viscous medium comprises (a) a solution, (b) a specific component, and (c) a signal precursor, or

(2) indicative or thick medium on a support when said analyte moiety is or comprises a signal precursor, wherein said indicative medium comprises (a) a solution, (b) a polymer network, and (c) a signalling moiety, and wherein said thick medium comprises (a) a solution, (b) a specific component, and (c) a signalling moiety;

(b) contacting one of said media with said analyte moiety; and

(c) generating a signal by means of said signalling moiety."

IV. With a letter dated 1 June 2000, the appellant announced that he would not be represented at the forthcoming oral proceedings.

V. The submissions by the appellant can be summarized as follows:

Procedural violation

- During the opposition procedure up to the end of oral proceedings, it had been accepted by the parties and the Opposition Division that the objective problem to be solved by the patent in suit vis-à-vis the closest prior art (document

(1)) was that of "preventing the spread of the signal". However, in the decision under appeal, the opposition division indicated that "preventing the spread of the signal" was not the objective problem to be solved and that "whatever the objective problem may be", it had rather to be established whether the technical differences between the claimed methods and those disclosed by document (1) were obvious or not. The Opposition Division found that these differences were not obvious and rejected the opposition. The decision under appeal was thus based on new grounds on which the appellant was unable to comment, contrary to the provisions of Article 113(1) EPC.

Questions for Enlarged Board of Appeal

- In its letter of 13 June 1996, it was requested that the following questions be referred to the Enlarged Board of Appeal:

"If an Opposition Division decides to maintain a patent, in unamended or amended form, on the basis of reasoning which was developed by the Opposition Division and on which the Opponent was not given an opportunity to present evidence or arguments, on appeal should the matter be referred back to the Opposition Division to allow the Opponent and the Patentee the opportunity to present evidence and arguments relevant to the Opposition Division's reasoning?"

"If an Opposition Division decides to maintain a patent, in unamended or amended form, on the basis of reasoning which was developed by the Opposition

Division and on which the Opponent was not given an opportunity to present evidence or arguments, to what extent can a Board of Appeal allow the introduction at the Appeal stage of evidence and arguments relevant to the Opposition Division's reasoning?"

Sufficiency of disclosure (Article 83 EPC)

- The embodiment of claim 1 was not exemplified. There was thus no guidance as to how to carry it out. The second alternative of independent claim 2 did not work since it was likely to produce false positive results.

Novelty (Article 54 EPC)

- Column 9, lines 6 to 9 of document (1) disclosed an assay in which a disc of insoluble agarose beads having glucose oxidase (GOD) coupled thereto was embedded in conventional detection strip (gel of agarose). A sample containing glucose was placed in a second well and caused to move to the bead-containing well. Glucose became bound to GOD and oxidised to hydrogen peroxide. In the next step, a leuco dye (the signal precursor) was caused to migrate to the bead-containing well, where it reacted with hydrogen peroxide to produce a dye (the signal). In this assay there was thus no diffusion of the signal because of the presence of the gel of agarose. Therefore, claims 1, 3, 4 and 6 to 12 lacked novelty.
- Claim 2 lacked novelty over document (4). Figure 13 of document (4), in combination with

column 32, lines 7 to 55 and the passage beginning at column 27, line 46 thereof disclosed an assay wherein an antigen comprising a signalling moiety reacted in a viscous medium with a signal precursor, thus generating a signal which remained localized because of the presence of the viscous medium.

- Claims 1, 3, 4, 6, 7 and 9 to 12 lacked novelty in view of document (8). The immunoassays of Examples 15 and 17 to 21 of this document disclosed inter alia an antibody coupled to a peroxidase used to detect, via antinuclear antibodies, HEP-2 cells attached to a solid support. After the formation of the complex, the slide was dipped in a medium comprising the signal precursor and polyethylene glycol (PEG), which formed on the solid support a viscous layer. The peroxidase indirectly caused the formation of a dye (signal) which was prevented from escaping by said viscous layer.

- Document (9) disclosed on page 2035, right hand column, an assay for the acetylcholine receptor wherein cells were fixed to a support and caused to react with labelled bungarotoxin (^{125}I -BTX). A layer containing gelatin and silver halide was then formed. ^{125}I generated a signal (the silver halide was turned into silver), the spreading of which was prevented by gelatin. Claims 1 and 7 were thus not novel over document (9).

Inventive step (Article 56 EPC)

- The problem to be solved vis-à-vis document (1)

was that of adapting the assay of Example 1 of document (1) to the use of an enzyme label instead of a radioactive label. It was obvious to replace a competitive assay involving a radioactive label (Example 1) with a sandwich assay involving an enzyme label of the type disclosed in document (6) for arriving at the claimed subject-matter.

- The claimed methods did not achieve any advantage or unexpected technical effect over the prior art, the more so as the Examples in the patent in suit were not relevant to claim 1.

VI. The submissions by the respondent in support of the claims of the new claim request can be summarized as follows:

Procedural violation

- The decision under appeal was based on grounds on which the parties concerned had an opportunity to present their comments.

Sufficiency of disclosure (Article 83 EPC)

- It was not possible to base the appeal on Article 83 EPC since this ground had not been invoked in the notice of opposition.

Novelty (Article 54 EPC)

- Owing to the limitation introduced in claims 1 and 2 of the new main request (see paragraph III supra), the claims were novel vis-à-vis documents (1), (4), (8) and (9) since none of them disclosed

a method for the enhanced detection of the presence of an analyte moiety by limiting the spread of the signal from the point of origin of the signal.

Inventive step (Article 56 EPC)

- Documents (1) and (8) were silent about the problem of the spread of the signal from the point of origin of the signal, let alone about how to solve it.

- Since the problem of limiting the spread of the signal from the point of origin of the signal to enhance detection of analytes had never been perceived in the prior art, the conventional problem-solution approach failed in the present case since the formulation itself of the problem contributed to the inventive step.

VII. The appellant (opponent) requested that the decision under appeal be set aside, that the appeal fee be reimbursed and that European patent No. 0 212 670 be revoked, or else that the matter be remitted to the first instance for further prosecution or else that the questions set out in the letter of 13 June 1996 be referred to the Enlarged Board of Appeal.

The respondent (patentee) requested that the decision under appeal be set aside that the patent be maintained on the basis of the set of claims filed 3 July 2000.

Reasons for the Decision

1. The appeal is admissible

Procedural violation (Article 113(1) EPC)

Questions to Enlarged Board of Appeal

2. The decision under appeal analyses the differences perceived between the invention as claimed and the prior art cited by the appellant, and identifies features which are novel. The appellant during the opposition proceedings had the opportunity to comment on the differences it perceived between the claims and the cited prior art.
3. The decision under appeal then goes on to conclude that the skilled person would not be led to modify the prior art to arrive at something falling under the claims. There appears to be no standard problem/solution analysis in the decision, but such an analysis is not a requirement of the EPC.
4. The decision seems adequately reasoned for the purpose of Rule 68 EPC. There is no requirement in the EPC that parties be given preliminary information as to the reasoning that an instance intends to rely on. Article 113(1) EPC requires only that decisions be based on grounds, here lack of inventive step, and evidence on which the parties had an opportunity to comment. This opportunity to comment on the ground of inventive step, and the documents relied on in relation thereto, was afforded the appellant. No substantial procedural violation is seen here such as would justify remittal of the case to the first instance to allow the parties to submit further arguments or evidence to the Opposition Division. The law is clear on this point, and the board sees no cause to refer the first question

suggested by the appellant, or any other on this point, to the Enlarged Board of Appeal.

5. It is the usual practice of the Boards of Appeal to exercise their discretion under Article 114(2) EPC whether or not to allow into the proceedings documents not submitted in due time (that is during the nine month opposition period) in favour of allowing such documents, and arguments based thereon, into the proceedings when these documents have been submitted with the statement of grounds of appeal in answer to comments appearing in the decision under appeal. In accordance with this usual practice, the board has here allowed into the proceedings documents (8) and (9) which the appellant wished to rely on. No question on this, such as that suggested by the appellant, need be referred to the Enlarged Board of Appeal for the purpose of resolving the issues in this case.

Article 123(2)(3) EPC

6. Claims 1 and 2 of the new main request differ from granted claims 1 and 2 by the insertion of the wording "enhanced detection of" and "by limiting the spread of the signal from the point of origin of the signal". A basis therefor is to be found on page 1, lines 8 to 14 of the application as filed. Moreover, since the claims, unlike the granted claims, now include the additional feature according to which the spread of the signal from the point of origin of the signal should be prevented, they are also more limited in scope than the granted ones, so that the requirements of Article 123(2)(3) EPC are fulfilled.

Sufficiency of disclosure (Article 83 EPC) and novelty

(Article 54 EPC)

7. The only ground of opposition was lack of inventive step. No other ground was introduced during the opposition proceedings. While the decision under appeal and the communication by the board discuss novelty, they do so with a view to identifying the features of the independent claims not disclosed in the prior art relied on by the appellant, and not because the issue of lack of novelty had been introduced into the proceedings.

8. In accordance with decisions G 10/91 (OJ EPO 1993, 420), G 1/95 (OJ EPO 1996, 615) and G 7/95 (OJ EPO 1996, 275), a new ground of appeal, such as here lack of novelty or insufficiency, can only be discussed on appeal with the consent of the patentee. This has not been given. Thus insufficiency cannot be discussed on appeal, and the allegation that some claims lack novelty may be considered only in the context of deciding upon the ground of lack of inventive step (see decision G7/95).

Inventive step (Article 56 EPC)

9. Expressed simply, steps (a), (b) and (d) of claim 1 and steps (b) and (c) of claim 2 under consideration relate to known methods for performing (immuno)assays. Both claims comprise the further technical feature that the detection of the presence of an analyte moiety must be enhanced by limiting the spread of the signal from the point of origin of the signal by forming a viscous medium on the support or with the aid of equivalent measures (see step (c) of claim 1 and step (a) of claim 2). The claims at issue thus require that a

technical effect be achieved (enhanced detection of the presence of an analyte moiety in a sample) by preventing the spread of the signal in (immuno)assays. It has thus to be established whether any of documents (1), (4), (8) or (9) discloses the methods of claims 1 and 2 at issue.

10. The appellant argues in essence that for the methods disclosed in documents (1), (4), (8) or (9) the technical effect, namely the "limitation of the spread of the signal from the point of origin" of the signal would automatically take place in the course of their being carried out by a skilled person, having regard to the fact that all these (immuno)assays involve a layer of agarose gel (document (1)), gelatine (documents (4) and (9)), or a viscous solution containing PEG (document (8)), which limit the spread of the signal from the point of origin of the signal.

11. The board, however, was persuaded during oral proceedings that even assuming that documents (1), (4), (8) or (9) convey to the skilled person the **partial** technical effect stated in claims 1 and 2 at issue that a viscous medium or a gel limits the spread of the signal from the point of origin of the signal, a disclosure of the claimed direct correlation between this partial effect and the enhanced detection of analytes in (immuno)assays is to be found **nowhere** in these documents. Therefore, it must be concluded that no prior art document makes available to the public methods of **enhancing detection of analytes** in (immuno)assays by limiting the spread of the signal from the point of origin of the signal. The subject-matter of claims 1 and 2 and dependent claims 3 to 12 is thus not anticipated by these documents.

12. The technical contribution made by the subject-matter of claims 1 and 2 vis-à-vis the conventional "precipitable or soluble" assays referred to on page 1, lines 5 to 14 of the patent in suit, is the enhanced detection of analytes in performing (immuno)assays. Achieving this advantageous technical effect thus corresponds to the technical problem the patent in suit purports to solve. It is solved by carrying out (immuno)assays according to the methods of independent claims 1 and 2 at issue comprising a step of limiting the spread of the signal from the point of origin of the signal by forming a viscous medium on the support or through equivalent measures (see step (c) of claim 1 and step (a) of claim 2). The experimental results listed in eg Table II of the patent in suit show enhanced visualization as a blue fluorescence (see page 10, line 51) of the signal in enzyme assays involving an agarose layer preventing the spread of the signal from the point of origin of the signal (experiments D, E, F) vis-à-vis enzyme assays involving no such agarose layer (experiments A, B, C). The board is thus satisfied that the technical problem the patent in suit purports to achieve has been solved.

13. Defining the technical problem solved by the patent in suit as "the prevention of the signal from spreading from the point of origin of the signal" as argued before the Opposition Division would already contain a pointer to the solution or would partially anticipate the solution, contrary to the rationale emerging from decisions T 229/85 (OJ EPO 1987, 237) and T 99/85 (OJ EPO 1987, 413).

14. The board also disagrees to the appellant's contention that the problem to be solved by the patent in suit is

that of adapting the assay of Example 1 of document (1) to the use of an enzyme label instead of a radioactive label, because this approach does not take into account the objective technical progress made in the subject-matter of claims 1 and 2 (see paragraph 12 supra). There is no guarantee that someone, unaware of the solution now claimed, would make such an adaptation in such a way as to ensure enhanced detection of an analyte by limiting the spread from the point of origin of the signal.

15. As to whether or not the methods of claims 1 and 2 at issue follow in an obvious manner from the prior art, it should be noted that none of the documents before the board even relates to the problem of enhancing detection of analytes in (immuno)assays, **let alone** suggests a correlation between enhanced detection of analytes in (immuno)assays and limitation of the spread of the signal from the point of origin of the signal. Therefore, the method of neither independent claim 1 or 2 can be derived in an obvious way from the cited prior art. This also applies for claims 3 to 12 dependent on one or the other of claims 1 and 2. Accordingly the requirements of Article 56 EPC are satisfied by the claims now put forward.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The requests of the appellant for reimbursement of the appeal fee and for referral of questions to the Enlarged Board of Appeal are refused.
3. The matter is remitted to the first instance with the order to maintain the patent on the basis of the set of claims filed 3 July 2000.

The Registrar:

The Chairwoman:

U. Bultmann

U. M. Kinkeldey