BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS | BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE | CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

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File Number: T 461/91 - 3.4.2

Application No.: 83 306 178.1

Publication No.: 0 106 662

Title of invention: Non-fluorescent vessels for holding test samples in fluorescent assays

Classification: G01N 21/03, B01L 3/00, G01N 33/52

D E C I S I O N
of 20 May 1992

Proprietor of the patent: DYNATECH LABORATORIES, INCORPORATED

Opponent: Labsystems Oy

Headword:

EPC Articles 123(2); 56

Keyword: "Main request (after amendment)"
"Additional subject-matter - no"
"Inventive step - yes"

Headnote

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number : T 461/91 - 3.4.2

D E C I S I O N
of the Technical Board of Appeal 3.4.2
of 20 May 1992

Appellant : (Proprietor of the patent)
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Decision under appeal :
Decision of Opposition Division of the European Patent Office dated 25 March 1991 and sent by post on 23 April 1991 revoking European patent No. 0 106 662 pursuant to Article 102(1) EPC.

Composition of the Board :

Chairman : E. Turrini
Members : M. Chomentowski
M.V.E. Lewenton

Summary of Facts and Submissions

I. The Appellant is proprietor of European patent No. EP-B1-0 106 662, 106 662, which was granted on the basis of European patent application No. 83 306 178.1.

II. The Respondent (Opponent) filed an opposition against the European patent, in particular on the grounds that the subject-matter of the claims of the opposed patent lacked an inventive step having regard inter alia to the disclosure in

E2 = WO-A-82/00359 and
E4 = GB-A-2 056 670.

III. The Opposition division revoked the patent on the grounds that the amended patent comprised matter which extended beyond the content of the application as filed and that the subject-matter of the claims did not involve an inventive step having regard to E2 and to the general knowledge of the person skilled in the art.

IV. The Appellant (Proprietor) filed an appeal against this decision.

V. In the annex to the invitation to the oral proceedings requested auxiliarily by the parties, the Board of Appeal expressed its provisional opinion that although the subject-matter of the independent claims of the Appellant's requests lacked an inventive step having regard to E4 and E2, an amended main claim resulting from a combination of the features of some of these claims could however be allowable in view of the available prior art.

VI. Oral proceedings were held, at the end of which the Appellant requested that the decision under appeal be set aside and that the patent be maintained,

(1) on the basis of the main request submitted during the oral proceedings with the description and the figures adapted;

(2) on the basis of the auxiliary request submitted during the oral proceedings with the description and the figures adapted.

In relation with the main request and the mentioned adaptation, the Appellant declared that in particular the embodiments illustrated by Figures 3, 6 and 8 to 11 as granted were to be cancelled.

The Respondent requested that the appeal be dismissed.

VII. Main request

Claims 1 and 3 read as follows:

"1. A microtest well structure (20, 70) having a plurality of integral open top wells (26, 72) for receiving and holding microliter quantities of fluid samples during a fluorometric measurement in which each of the samples is exposed to an exciting radiation to be fluorescently excited thereby, said wells (26, 72) being arranged in at least one straight row and being formed as a one-piece molding from a plastics material having a native fluorescence, and means (32) forming a barrier (34) which prevents radiation and/or light directed at the walls (28, 30, 76, 78) of the wells from passing therethrough, characterised in that the barrier forming means comprises pigment particles which are dispersed throughout the

molding and which block or at least reduce the extent of penetration of the exciting radiation into the molding at least to reduce the extent to which the plastics material is fluorescently excited by the exciting radiation during said measurement where the exciting radiation is directed to pass into each well through the open top thereof, said pigment particles being present in an amount ranging from 0.01% to 10% based on the combined weight of plastics material plus the weight of the pigment particles and being at least substantially opaque at least to the peak wavelength of the exciting radiation, and said pigment being substantially non-fluorescent."

"3. A microtest well structure for conducting assays of immunological substances in a frontal approach-type energy measurement instrument, wherein a labelled reactant is immunologically reacted with an immuno-logical substance which is directly or indirectly immobilized on a solid phase to yield a light-emitting reaction product wherein the energy release of said reaction product is measured to determine the quantity of the substance, said structure (20, 70) having a plurality of open-top wells (26, 72) for receiving and holding microliter quantities of fluid samples during a measurement, said wells being molded from a plastics material having a native fluorescence and sufficient protein-binding properties to serve as the solid phase in said assay, and barrier means (32) which prevents radiation and/or light directed at the walls (28, 30, 76, 78) from passing therethrough, characterised in that the barrier means (32) is substantially opaque and substantially non-fluorescent and is dispersed throughout the plastics material for enhancing the signal-to-noise ratio of the system during said measurement, said barrier means comprising pigment particles dispersed in those regions in an amount ranging from 0.01% to 10% based on

the combined weight of plastics material plus the weight of the pigment particles."

Claims 2 and 4 to 8 are dependent claims.

VIII. The Appellant submitted the following arguments in support of his request. E2 does not address the problem of native fluorescence of the material of the well of the test structure and is moreover concerned by a structure including a window. Thus, even if the problem was otherwise known, the skilled person was not incited to disperse pigment particles in the window part of the test structure and make it non-transparent and there is moreover no indication in E2 that it is necessary to select the pigments and their amount in such a way that they block the exciting light so that no spurious effect arises. E4 does not pertain to the relevant technical field and is thus not concerned by the problem of native fluorescence of the material of the test structure; a combination of the arrangement of E4, comprising a non-transparent and light-reflecting foil of synthetic material, with the transparent structure of E2, would necessitate further modifications for arriving at the disputed test structure and would thus be the result of an "ex-post facto" analysis.

IX. The Respondent submitted the following arguments in support of his request. E2 discloses a test structure for fluorescence measurements comprising wells of the same materials as in the patent in suit, and thus the known structure shall also suffer from the same drawbacks, which are known in the art; since the walls of the wells can be made partly or wholly impervious to the beams of measurement by colouring and since the window can be made to have filtering properties, the skilled person would be incited to disperse pigments in the structure and would

arrive to the disputed test structure in an obvious way. The person skilled in the art could also start from E4, which discloses a microtest well structure for luminescence measurements formed as a non-transparent and light-reflecting one-piece molding from a plastics material and, adapting it for a fluorescence measurement, for instance by referring to E2, he would also arrive at the disputed test structure in an obvious way.

Reasons for the Decision

1. The appeal is admissible.

2. Allowability of the amendments

2.1 The Claims 1 and 3 result from the combination of the features of Claims 1 to 4 as granted and Claims 21 to 23 and 27 as granted, respectively, and are restricted to the embodiments illustrated by Figures 1, 2, 4 and 5 as granted wherein, according to the description as granted, the pigment particles are dispersed throughout the molding in an amount ranging from 0.01% to 10% based on the combined weight of plastics material plus the weight of the pigment particles (see column 7, lines 49 to 62; column 8, lines 36 to 42; column 12, lines 16 to 35). Therefore, the Board is satisfied that the claims of the European patent have not been amended in such a way as to extend the protection conferred (Article 123(3) EPC). The Board is also satisfied that, since the embodiments illustrated by Figures 1, 2, 4 and 5 are disclosed in the application as filed, the European patent has not been amended in such a way that it contains subject-matter which extends beyond the content of the application as filed (Article 123(2) EPC).

3. Claim 1

3.1 Novelty

3.1.1 No microtest well structure comprising all the features mentioned in Claim 1 is known from the prior art. Therefore, the Board is of the opinion that the subject-matter of Claim 1 is novel in the sense of Article 54 EPC. Moreover, the Respondent has not submitted any objection concerning the novelty of said subject-matter.

3.2 Inventive step

3.2.1 A microtest well structure (1) having a plurality of integral open top wells (2) for receiving and holding microliter quantities of fluid samples during a fluorometric measurement in which each of the samples is exposed to an exciting radiation to be fluorescently excited thereby, is known from E2 (see page 1, lines 1 to 18; page 1, line 26 to page 3, line 26; page 4, lines 9 to 30; page 7, line 8 to page 8, line 16; Figure 3; see also page 5, line 22 to page 7, line 7; Figures 1 and 2); said wells (2) are arranged in at least one straight row and are formed as a one-piece molding from a plastics material having a native fluorescence; means (29) forms a barrier which prevents radiation and/or light directed at the walls (30) of the wells (2) from passing therethrough.

3.2.2 Since E4 (see page 2, lines 96 to 111; Claims 1 to 4; Figure 3), which is concerned with a microtest well structure (5) having a plurality of integral open top wells (2) for receiving and holding microliter quantities of fluid samples during a luminescence measurement, does not disclose any technical feature relating to fluorometric measurement in which samples are exposed to

an exciting radiation to be fluorescently excited thereby, it is considered as pertaining to a closely related, but however different technical field and is thus less relevant.

3.2.3 According to the patent in suit (see column 1, line 63 to column 2, line 18, as granted) the known microtest well structures are to be used in particular for fluorometric measurements wherein fluorescent radiation impinges on the walls of the wells containing the sample, which also may emit fluorescent radiation resulting in spurious light emissions which interfere with and impair an accurate measurement of the intensity of the light emitted from the excited test sample itself; these spurious light emissions have the objectionable effect of creating a noise signal in the fluorometer's detector to significantly reduce the signal-to-noise ratio.

3.2.4 This problem of the native fluorescence of the material of the test structure is not mentioned in E2, but it is acknowledged in the patent in suit (see column 2, lines 19 to 34 and column 3, lines 1 to 13, as granted) as being known in the art and as being solved previously in particular by selecting other materials for the set of cuvettes, thereby either increasing the costs of the devices or, for some materials, leaving significant spurious light emissions.

3.2.5 Starting from the structure known from E2, the microtest well structure of the patent in suit intends to solve the problem; in particular, the barrier means is formed so that it comprises pigment particles which are dispersed throughout the molding, and thus also in the bottom of the wells; said pigment particles are substantially non-fluorescent and are at least substantially opaque at least to the peak wavelength of the exciting radiation, thus

blocking or at least reducing the extent of penetration of the exciting radiation into the molding; therefore, the extent to which the plastics material is fluorescently excited by the exciting radiation during said measurement where the exciting radiation is directed to pass into each well through the open top thereof is at least reduced and thus, the Board is of the opinion that the problem mentioned in the patent in suit is credibly solved and that its solution is non-obvious for a skilled person, due to the reasons set out in the following paragraphs.

3.2.6 The Respondent has argued that, since E2 (see page 2, lines 6 to 10) uses for the wells some of the materials mentioned in the patent in suit, the known structure shall also suffer from the same drawbacks; E2 (see page 1, line 31 to page 2, line 10) suggests that walls of the wells can be made partly or wholly impervious to the beams of measurement, as compared to the window required to be transparent, in particular by making them of a different colour, and the only method for doing this appears to be the introduction of pigments in the material of said parts of the wells; since the wells are to be used in fluorometry, the person skilled in the art would be incited to select pigments which are substantially non-fluorescent in order not to disturb the measurements; moreover, the range of the amount of pigment in Claim 1 in dispute appears to be the range commonly used in the field; it is further to be noted that E2 (see page 7, line 37 to page 8, line 16; Figure 3) specifies that the bottom part (34) of the well (2) can be made of the same material as the well and may be used as a filter, e.g. for selecting the wavelength of the measurement radiation; thus, the person skilled in the art was incited by E2 to provide the window with filtering properties and thus, as generally known in the art, by providing colouring elements therein; therefore, the problem was already

solved in E2, i.e. the spurious effect was suppressed, in accordance with the same features as those of Claim 1 in dispute, said features being either disclosed in E2 or being obvious in consideration of the problem, which was anyway known in the art.

3.2.7 However, the patent in suit (see column 10, lines 23 to 30 and column 11, lines 18 to 21 and 32 to 37, as granted) specifies that the exciting light in the embodiment of Figures 1 and 2 is directed through the open end of each of the plate's wells and that, to conduct a fluorometric measurement, a fluorometer of the frontal approach type such as the one schematically shown in Figure 7 is required. The patent in suit (see column 11, line 38 to column 12, line 43, and more in particular column 12, lines 23 to 35, as granted) also specifies that the pigment particles for the embodiment of Figures 4 and 5 are the same and dispersed in the same amount as in the embodiment of Figures 1 and 2; thus, a fluorometer of the frontal approach type is required for all the disclosed embodiments and, therefore, the bottom wall of each of the wells of the disputed test well structure is only intended to block the exciting rays, thereby directly avoiding that spurious fluorescent radiation be emitted by the bottom wall towards the detector located above the opening of the well. On the other hand, the bottom wall (34) of the wells (2) of Figure 3 of E2 (see page 7, line 19 to page 8, line 16; see also Claim 3) is intended to have technical features of sufficient transparency, derivably at least for the fluorescent rays emitted by the sample under measurement, which are to transit through said window before arriving at the detector (12). In E2, the exciting radiation and/or the spurious radiation emitted by the window and/or a part of the fluorescent response of the sample can be filtered by the window, but there is no indication about the specific filtering properties which

are intended for said window, i.e. about which of said plurality of radiations is/are to be inhibited. In this respect, the Respondent has argued that the transparency of a part of the structure is dependent on the measurement method, and not on said part; however, the patent in suit (see column 1, line 63 to column 2, line 5 and column 10, lines 31 to 37, as granted) mentions that the exciting radiation is in the usual range and is selected depending upon the material to be fluoresced, and there is no indication in E2 that the radiation should be selected in a different way; moreover, the fluorescent response of the sample to be tested is generally known as being specific for the sample. As argued by the Appellant, E2 does not address the problem of native fluorescence of the material of the well, even if the problem was otherwise known; therefore, starting from E2, to arrive at the device of Claim 1 in dispute, it was necessary to look for otherwise known pigment particles and to select them in order to inhibit specifically the exciting radiation while leaving in particular the fluorescent response of the sample inhibited. Indeed, the Board is of the opinion that the indications contained in E2, in particular the disclosed different type of test method and the minimal information about the mentioned filtering, were not sufficient for inciting the person skilled in the art to carry out these steps. In particular, there is no indication in E2 or other prior art documents to utilise substantially non-fluorescent pigment particles.

3.2.8 The Respondent has also argued that, starting from E4 (see page 2, lines 96 to 111; Claims 1 to 4; Figure 3), which discloses a microtest well structure (5) having a plurality of integral open top wells (2) for receiving and holding microliter quantities of fluid samples during a luminescence measurement, whereby said wells (2) are arranged in at least one straight row as a one-piece

molding from a plastics material (a foil (5) of synthetic material) and form a barrier (non-transparent and light-reflecting) which prevents radiation and/or light directed at the walls of the wells from passing therethrough, the person skilled in the art would be incited to disperse pigment particles in the foil of synthetic material and, when adapting the test structure for the closely related field of fluorescence measurement, for instance by referring to E2, would select the right pigments in the adequate range of amount. However, as credibly argued by the Appellant, E4 does not pertain to the relevant technical field and is thus not concerned by the problem of native fluorescence of the material of the test structure; moreover, the foil of synthetic material of E4 (see Claim 4) is thin, 0.01 to 0.5 mm, and the skilled person would be incited, for obtaining light-reflecting properties in such a thin foil, to add a metallic layer such as the alternative aluminium layer mentioned in E4 (see Claim 4), rather than to disperse pigments in said thin foil; indeed, a combination of the arrangement of E4, including a non-transparent and light reflecting foil of synthetic material, with the transparent structure of E2, would necessitate further modifications for arriving at the disputed test structure, which are not derivable from the prior art without knowing the patent in dispute, and this would thus be the result of an "ex-post facto" analysis.

3.2.9 Therefore, the Board is of the opinion that the subject-matter of Claim 1 in dispute involves an inventive step in the sense of Article 56 EPC.

4. The Board is of the opinion that Claim 3, which is directed to a microtest well structure of the same type as that of Claim 1 wherein the effect of enhancing by the barrier means the signal-to-noise ratio of the system

during the measurement is stressed, is also allowable for the same reasons.

5. Claims 2 and 4 to 8 are dependent claims which relate to particular embodiments of the invention defined by Claim 1 and Claim 3, respectively, also imply an inventive step for the same reasons.

6. Therefore, taking into account the amendments made by the Appellant with respect to the main request, the patent and the invention to which it relates meet the requirements of the Convention and the patent as amended may be maintained (Article 102(3) EPC).

6.1 Thus, since the main request is considered as being allowable, it is not necessary to take into account the Appellant's auxiliary request.

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 maintain the patent on the basis of the main request submitted in the oral proceedings, with the description and the drawings to be adapted, in particular by deleting the embodiments illustrated by Figures 3, 6 and 8 to 11.

The Registrar: The Chairman:

P. Martorana E. Turrini

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