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D E C I S I O N
of 17 January 2001

Case Number: T 1027/97 - 3.3.5

Application Number: 93909274.8

Publication Number: 0591505

IPC: B01F 13/08

Language of the proceedings: EN

Title of invention:
Capillary mixing device

Applicant:
Roche Diagnostics Corporation

Opponent:
-

Headword:
Capillary mixing device/ROCHE

Relevant legal provisions:
EPC Art. 56

Keyword:
"Inventive step - no"
"Obvious solution of a technical problem"

Decisions cited:
-

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1027/97 - 3.3.5

D E C I S I O N
of the Technical Board of Appeal 3.3.5
of 17 January 2001

Appellant: Roche Diagnostics Corporation
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 25 April 1997 refusing European patent application No. 93 909 274.8 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: R. K. Spangenberg
Members: G. J. Wassenaar
J. H. Van Moer

Summary of Facts and Submissions

I. European patent application No. 93 909 274.8, publication No. 0 591 505, was refused by a decision of the Examining Division.

II. The Examining Division held that the subject-matter of the independent claims on file during oral proceedings lacked an inventive step. The reasoning was substantially that the claimed system of carrying out mixing liquids in a capillary chamber resulted from replacing a magnetic stirring rod in the device disclosed in Figure 10 of

D4: US-A-4 946 795

by a magnetic powder, which was obvious in the light of

D5: US-A-3 752 443.

III. The appellant lodged an appeal against this decision. In the statement of grounds of appeal it was agreed that D4 represented the closest prior art but it was argued that it was not obvious to combine its teaching with that of D5. Even if one were to combine the teachings of these prior art documents one would not arrive at the present invention.

IV. In the annex to the summons to attend oral proceedings, the Board expressed the preliminary opinion that the subject matter of the independent claims of the requests on file lacked an inventive step. The appellant's attention was additionally drawn to

D3: US-A-3 219 318.

V. By letter dated 1 November 2000 the appellant filed two new sets of claims as main and auxiliary request. During oral proceedings, which were held on 17 January 2001, claim 3 of the main request was amended and a new auxiliary request was submitted comprising four claims corresponding to the amended claim 3 and claims 4 to 6 of the main request. Claim 3 of the main request is an independent process claim which reads as follows:

"A method of mixing in a capillary chamber comprising:

(a) adding a liquid to be mixed to a system comprising a liquid impervious housing (10) with a chamber (20) in said housing containing a stirrer (25); and

(b) generating a rotating magnetic field by a magnetic device (80, 90, 100); and means (70) for retaining said chamber device (10) in an orientation so that said moving magnetic field causes said move in said chamber over a distance sufficient to effect mixing,

characterized in that the chamber (20) has capillary spacing of 1 mm or less in one dimension and non-capillary spacing in two other dimensions; in that the axis of rotation of the magnetic field passes through the chamber; and in that the mixing in the chamber is caused by a plurality of magnetic or magnetically inducible particles (25) aggregating into masses of particles which rotate, break up upon encountering resistance, and reform into new aggregates as the mixing process continues under the influence of the rotating magnetic field to cause mixing in the liquid."

VI. The arguments of the appellant with respect to the inventiveness of this process claim may be summarized as follows:

Mixing a liquid in a capillary chamber by a magnetic mixing device has been disclosed in D4 using a magnetic stirring bar. Although stirring a liquid by magnetically moving magnetic particles in the liquid was also known in the art, there was no suggestion that such a stirring method could be used in a capillary chamber. In D5 stirring by magnetic particles was performed in a droplet. Without the additional magnet to counteract the centrifugal forces the particles flew out to the edge, which made mixing not effective. In D3 stirring by magnetic particles was performed in relatively large vessels. Moreover, D5 and especially D3 were published long before D4, which indicated that the art was developing away from stirring by magnetic particles. A skilled person would not expect that stirring by magnetic particles could be effective in a capillary chamber. The applicant surprisingly found that in a capillary chamber, under the conditions mentioned in the said process claim, the magnetic particles formed temporary aggregates which were effective mixing means and overcame the problem of blocking by irregularities and lumps in the liquid encountered when using a magnetic stirring bar according to D4.

VII. The appellant requested that the decision under appeal be set aside and a patent be granted on the basis of:

Main request:

Claims 1, 2, 4 through 6, filed on 2 November 2000,

claim 3, filed during the oral proceedings.

Auxiliary request:

Claims 1 to 4, filed during the oral proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. *Inventive step of the subject-matter of claim 3 of the main request (claim 1 of the auxiliary request)*

2.1 In agreement with the submissions made by the appellant D4 represents the closest state of the art. This document discloses a method for dilution and mixing of liquid samples in a capillary chamber having one dimension in the range of 0.1 to 1.0 mm and non-capillary spacings in the other dimensions and comprising a magnetically operated stirring bar, actuated by a rotating magnetic field (see Figure 10 in combination with column 3, lines 28 to 33, column 5, lines 35 to 42, column 9, lines 25 to 37 and column 17, lines 29 to 50). D4 does not explicitly disclose that the axis of rotation of the magnetic field passes through the chamber and that means are present to keep the chamber in that position. It is, however, evident that for a proper functioning of the mixing process the chamber and the magnetic field should be placed and kept in that position.

2.2 Starting from D4 the problem underlying the invention can be seen in providing a more flexible mixing operation, which works properly in the presence of

irregularities in the mixing chamber or in the liquid or reagent to be mixed and whereby the form of the chamber is not constrained. Such a technical problem is in agreement with the statements in the application in this respect (page 4, lines 2 to 4; page 5, lines 24 to 29; page 6, lines 16 to 17; page 10, lines 11 to 15). The applicant proposed to solve this problem by using magnetic or magnetically inducible particles as stirring means instead of the stirring bar. The examples, which are performed in agreement with the method according to claim 3, show that a proper mixing operation is possible in an oval chamber (Example 5) and in the presence of a precipitate (Example 6). The Board is therefore satisfied that the process according to claim 3 actually solves the above mentioned problem.

2.3 It remains to be decided whether the claimed solution was obvious to a person skilled in the art. A skilled person generally starts looking for a solution of a technical problem in the same technical field, in this case the mixing of small amounts of fluids in clinical laboratories, and will first consider known processes which do not deviate substantially from his current practice. In the Board's opinion the said skilled person should, therefore, be aware of D5, concerning a magnetic mixer for laboratory use, in particular for the analyses of blood plasma samples; ie a document in the same technical field using the same basic mixing technique. D5 discloses a method of mixing blood plasma with a reagent by magnetic particles actuated by a permanent magnet rotating on an axis centrally between its poles. A volume (droplet) of sample-reagent liquid, containing in addition a multiplicity of magnetic particles, is supported centrally with reference to the magnetic poles for activation of the particles in the

rotating magnetic field (column 2, lines 9 to 41). In the Board's opinion it should be obvious to a skilled person that the use of magnetic particles instead of a rigid magnetic bar makes the stirring more flexible both in the sense that they can easily overcome obstacles in the liquid and in the sense that their action is practically independent from the geometry of the vessel. With respect to the latter property reference can be made to D3, an US patent specification relating to stirring fluids by magnetic particles. D3 discloses that stirring by magnetic particles agitated by a magnetic field varying with time in direction and intensity may be effectively applied to fluids in containers varying in size and configuration practically without limit, from millimetre bore tubes to large vats and tanks of any shape whatsoever, as well as in containers defined by biologic organs or ducts. Although agitation by a rotating magnetic field is not explicitly addressed, it nevertheless discloses that stirring by magnetic particles, whatever method for agitating the particles by a varying magnetic field is used, is particularly suitable for stirring minute quantities of fluids where conventional means possess many drawbacks such as in biological and medicinal solutions (claim 1 and column 2, lines 52 to 58 and column 3, lines 17 to 23). The Board, therefore, holds that in view of the disclosure of D3 and D5 a skilled person trying to solve the above mentioned problem would have replaced the magnetic stirring bar in the method according to D4 with magnetic particles.

2.4 The Board agrees that in the method of D5 mixing takes place in a droplet and not in a vessel. The volume of a droplet is, however, not substantially different from the volume of the mixing chamber used in Figure 10 of

D4. Since the stirring action of the magnetic particles is practically independent of the geometry of the liquid, as testified by D3, the skilled person would not expect essential differences in stirring action whether the geometry of the liquid is defined by the walls of a capillary chamber or by the surface tension of the liquid itself as in the case of a droplet. Thus, there are no obvious reasons which would deter the skilled person from applying the mixing method as taught in D5 to a liquid in a capillary chamber as disclosed in D4.

2.5 The Board also agrees that D5 further teaches the use of an additional magnetic field perpendicular to the rotational magnetic field to maintain a more homogeneous distribution of the magnetic particles in the liquid during mixing. The wish to maintain a homogeneous distribution of the magnetic particles in D5 is associated with the specific optical detection means for determining the formation of fibrin in blood plasma. A non-homogeneous distribution of magnetic particles prior to the fibrin formation may cause false signals (column 1, line 66 to column 2, line 6 and column 5, line 44 to column 6, line 36). There is no indication in D5 that without the additional magnetic field to maintain a more homogeneous distribution the stirring action is insufficient. Thus for other reactions and/or detection means, whereby a homogeneous distribution of the magnetic particles during mixing is not essential, the skilled person would have recognized that the additional magnetic field used in the method according to D5 was not necessary and he would first try to solve the above mentioned technical problem by merely replacing the magnetic stirring bar in the method of D4 by magnetic particles.

2.6 Claim 3 requires that during mixing the magnetic particles form aggregates, which rotate, break up upon encountering resistance and reform into new aggregates as the mixing process continues. The application does not indicate that, apart from applying the other features mentioned in claim 3, additional measures should be taken in order to obtain aggregates with the required property. According to the application the aggregate clusters are simply formed during the mixing operation. It is only the shape of the aggregates that are formed (which is not limited by claim 3) which is determined by the rotation rate and the viscosity of the liquid being mixed (page 9, line 27 to page 10, line 19). Under these circumstances the Board cannot regard the formation of the aggregates and the properties thereof mentioned in claim 3 as an additional limiting feature. A narrative statement in a claim, merely indicating a result which is automatically achieved by the substantial features of the claim, cannot contribute to inventive step. Moreover, it follows already from D5 that without an additional magnetic field the distribution of the magnetic particles during the mixing operation becomes inhomogeneous, which implies the formation of some kind of aggregates. But even if the skilled person was not aware of the formation of aggregates, this lack of knowledge would not have influenced his decision to apply magnetic particles instead of a magnetic bar to solve the above mentioned problem. The incentive to use magnetic particles as stirring means follows from their known use for that purpose and is thus independent from the knowledge of any details about their distribution in the liquid to be treated.

2.7 It is also true that D3 and D5 were published many years before D4, but that does not mean that they represent forgotten art. Although the use of magnetic particles as stirring means has several obvious advantages as discussed above, they also have obvious drawbacks such as pollution of the liquid, rendering the liquid opaque and separation difficulties after mixing. Thus for most applications stirring by magnetic particles is not the first choice; only in special circumstances where other mixing devices fail the skilled person will consider the use of magnetic particles as mixing means. The lack of more recent literature about this particular mixing means may simply reflect the situation that their use is only advantageous in rare circumstances. It does not mean that their use was completely forgotten in the art or that a skilled person would not have found it without inventive activity when looking for an alternative for conventional mixing by a magnetic stirring bar. Rather, the claimed method is to be considered as a straight-forward adaptation of the method according to D4 (published in August 1990, ie less than two years before the priority date of the present application) to difficulties encountered in particular situations.

2.8 For these reasons the Board holds that the subject-matter of claim 3 of the main request and the identical claim 1 of the auxiliary request, lacks an inventive step within the meaning of Article 56 EPC, so that both the main and auxiliary request must fail.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

S. Hue R. Spangenberg