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Datasheet for the decision of 30 July 2009

Case Number: T 0806/05 - 3.3.07

Application Number: 98906708.7

Publication Number: 1015098

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Language of the proceedings: EN

Title of invention:
Cast membrane structures for sample preparation

Patent Proprietors:
MILLIPORE CORPORATION

Opponents:
01) Eppendorf AG
02) Schleicher & Schuell MicroScience GmbH

Headword:
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Relevant legal provisions:
-

Relevant legal provisions (EPC 1973):
EPC Art. 54, 56

Keyword:
"Inventive step (no) - Main Request"
"Novelty (no) - Auxiliary Request"

Decisions cited:
T 0681/01

Catchword:
-

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Case Number: T 0806/05 - 3.3.07

D E C I S I O N
of the Technical Board of Appeal 3.3.07
of 30 July 2009

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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 3 May 2005 concerning maintenance of European patent No. 1015098 in amended form.

Composition of the Board:

Chairman: S. Perryman
Members: G. Santavicca
F. Rousseau

Summary of Facts and Submissions

I. The appeal lies from the interlocutory decision of the Opposition Division, according to which European patent 1 015 098 (application N° 98 906 708.7) as amended and the invention to which it relates were found to meet the requirements of the EPC. The decision under appeal was based on the claims of the Main Request, consisting of amended Claim 1 submitted at the oral proceedings held on 14 April 2005 and Claims 2 to 21 as granted.

II. The patent as granted comprised 21 claims, independent Claims 1 and 14 reading as follows:

"1. A housing defining a volume, said housing said housing (*sic*) having a first open end and a second open end spaced from said first open end containing in a portion of said volume a liquid permeable three dimensional cast and adhered in-place structure comprising a porous polymer matrix, said structure having an aspect ratio of less than about 10."

"14. A method of casting a membrane in a liquid impermeable housing, said method comprising:

forming a solution of a polymer;

introducing said solution into said housing; and

subjecting said solution to a phase inversion so as to cause said polymer to precipitate in said housing and form, in-situ, said membrane.".

III. Two notices of opposition to the patent in its entirety were given on the grounds that its subject-matter lacked novelty (opponents 02) and an inventive step (opponents 01 and 02).

IV. Amended Claim 1 underlying the decision under appeal read as follows (compared to Claim 1 as granted, additions shown in bold, deletions in strike-through):

"1. A housing defining a volume, ~~said housing~~ said housing having a first open end and a second open end spaced from said first open end containing in a portion of said volume a liquid permeable three dimensional cast **in-situ** and adhered in-place structure comprising a porous polymer matrix, said structure having an aspect ratio of less than about 10."

V. In the decision under appeal, the finding that the amended patent complied with the requirements of the EPC was reasoned as follows:

(a) No objections under Article 100(b), 100(c) and 84 EPC were raised against Claim 1 as amended, so that Claim 1 was formally admissible (sic).

(b) The subject-matter of Claim 1 was novel, as it differed from the disclosure of D8 (WO-A-90/07965) by being cast *in situ* and having an aspect ratio (average diameter/average thickness) of less than about 10. D9 (US-A-5 334 310) neither disclosed polymer casting *in situ* nor adhesion in place. D10 (US-A-5 645 717) and D11 (EP-A-0 852 334) did not constitute valid prior art.

(c) The novelty of the subject-matter of method Claim 14 had not been disputed, so that it too met the requirements of Article 54 EPC.

(d) As regards inventive step, D1 (US-A-5 552 325) described the closest prior art. The subject-matter of Claim 1 differed from the broadest interpretation of D1 by the features "cast *in situ*"

and "adhered in place". The problem was to provide alternative means for affixing said membrane to a variety of housing sizes, while enabling the retention of the three dimensional polymeric structure. D3 (US-A-5 476 665) and D5 (US-A-4 761 232) disclosed cast separation membranes. However, D3 disclosed knife-casting on a flat surface, which was not a housing. D5 disclosed casting in place of a microporous membrane within macropores, by phase inversion, to increase mechanical strength. However, there was no teaching for housings of much greater dimensions as those of D1. In particular, the polymeric solution of D5, if cast within the container of D1, would flow through its perforated support. Hence, the combination of D1 and D5 did not lead to the claimed subject-matter. The attack based on D4 (WO-A-96/17673) and D5 was less relevant, as D4 did not disclose any of features (e) to (h) of Claim 1.

(e) Since Claim 14 defined the steps required for obtaining the structure of Claim 1, and since the relevant art was that disclosed in D3 and D5, the arguments in support of Claim 1 likewise applied to the method defined in Claim 14. The objections based on the combination of D4 and D5 or on that of D8 and D3 could also not succeed as those prior art documents were less relevant.

(f) The subject-matter defined in the Main request thus was not obvious and involved an inventive step.

VI. In their statement setting out the grounds of appeal, opponents 01 (appellants) enclosed a copy of a new document (EP-A-0 231 684 = D13) as a further novelty destroying evidence and attacked the novelty of the

method of Claim 14 having regard to D5, as well as the inventiveness of the subject-matter of Claim 1 over D5 and D8. In their letter of 26 June 2009, in response to a communication of the Board in preparation for oral proceedings, the appellants argued on the amendments made by the respondents. Finally, by letter of 15 July 2009, the appellants announced that they would not attend the scheduled oral proceedings.

VII. In their letter dated 16 March 2006, the respondents enclosed copy of a new Main Request as well as 6 sets of amended claims as their First to Sixth Auxiliary Requests. Compared to the claims underlying the decision under appeal, in the claims of the Main Request only Claim 1 had been amended, as follows:

"1. A housing defining a volume, said housing having a first open end and a second open end spaced from said first open end containing in a portion of said volume a liquid permeable three dimensional cast *in-situ* and adhered in-place structure **formed by phase inversion and** comprising a porous polymer matrix, said structure having an aspect ratio of less than about 10."

In a letter of 26 June 2009 in reply to a communication of the Board in preparation for the oral proceedings the respondents enclosed additional sets of amended claims as their Seventh to Tenth Auxiliary Requests, consisting of the method claims of their Main, First, Second and Fourth Auxiliary Requests, respectively.

VIII. By letter of 8 May 2009 the Board was informed that the party as of right would not attend the oral proceedings.

IX. Oral proceedings were held on 30 July 2009 in the announced absence of the appellants, and in that of the party as of right as well, pursuant to Rule 115(2) EPC. The respondents maintained their Main Request submitted with letter of 16 March 2006, withdrew their 1st to 6th Auxiliary Requests submitted with letter dated 16 march 2006 as well as their 7th to 10th Auxiliary Requests submitted with letter 26 June 2009, and submitted as the sole Auxiliary Request a set of amended method Claims 1 to 7.

X. Claim 1 of the Auxiliary Request reads as follows (the only amendment to Claim 14 as granted is shown in bold):

"1. A method of casting a membrane in a liquid impermeable housing, said method comprising:

forming a solution of a polymer;

introducing said solution into said housing; and

subjecting said solution to a phase inversion so as to cause said polymer to precipitate in said housing and form, in-situ, said membrane **which is adhered to the housing**.".

Claims 2 to 7, apart from the amended references, correspond identically to Claims 15 to 20 as granted.

XI. The arguments submitted by the appellants in writing may be summarised as follows:

Procedural matters

(a) D13 had been submitted with the statement setting out the grounds of appeal in reaction to e.g. the amendment "*in situ*" inserted in Claim 1 before the

Opposition Division. The proprietors, in their response to the statement setting out the grounds of appeal, did not object to the late filing of D13 but submitted an amended Main Request, showing that D13 was relevant. Hence, D13 was admissible.

Main Request

Amendments

(b) As the amendments "cast *in situ*" and "formed by phase inversion" were process features, Claim 1 of the Main Request was drawn up as a product-by-process claim. However, it was not clear that those process features imparted clear structural distinctions over the prior art (Article 84 EPC). Also, the insertion in Claim 1 of the amendment "cast *in situ*", initially disclosed only in connection with non-filled structures, contravened the requirements of Article 123(2) EPC.

Novelty

(c) Novelty of the subject-matter of Claim 1 of the Main Request was no longer disputed. In particular, D13 did not disclose the formation of a membrane by phase inversion.

(d) The method of Claim 14 was not novel over D5.

Inventive step

(e) As to inventive step, the formation of a porous structure by phase inversion was not disclosed in

D13 but was well known to the skilled person. Hence, starting from D13 and having regard to the common general knowledge, it was obvious to form the porous structure of D13 by phase inversion.

(f) Also D1 could be taken as the closest prior art. Although it did not specifically mention the possibility of forming the membrane *in situ*, that process possibility was not structurally limiting. Hence, the only distinction was the explicit disclosure of the membrane formation by phase inversion. However, that formation was encompassed by the generic disclosure of D1, which mentioned that any suitable known method could be used to form its microporous structure, so that the subject-matter of Claim 1 was obvious over D1.

(g) If the method of Claim 14 was held to be novel over D5, e.g. if the pores did not constitute a housing, it would nevertheless be obvious having regard to D5, at least if combined with D8.

Seventh Auxiliary Request

(h) Claim 1 of the Seventh Auxiliary Request, which corresponded to Claim 14 as granted, concerned a method that was anticipated by D5.

Therefore, the patent should be revoked.

XII. The respondents essentially (counter) argued as follows:

Procedural matters

(a) D13 had been filed late and could not be properly admitted as a late filed document, because Claim 1 had been amended to have the same scope of Claim 14 as granted, which contained the feature "phase inversion" and had not been objected to in the statement setting out the grounds of appeal. Nevertheless, D13 disclosed a polymeric matrix that had not been formed by polymer inversion, which was not disclosed in D13, so that D13 was not relevant. Therefore, D13 should not be admitted.

Main Request

Amendments

(b) The amendments in all of the requests were based on the application as filed. Thus, the amended claims met the requirements of Article 123(2) EPC.

(c) The effects of the use of the claimed process steps could be determined with certainty on the finished product. Furthermore, there was no other method of which the proprietors were aware to provide a liquid permeable 3-dimensional structure in the open end of a housing which comprised a porous polymer matrix which was adhered in place other than by casting it *in-situ* and forming it by phase inversion. Other technologies such as cut and stuff would result in loose elements. Polymerization in place was not a phase inversion and nevertheless was mostly used in glass capillaries, the interior surface of which had been functionalized. Those

structures would not be visibly porous, as the one claimed, the porosity of which was visible under the microscope. Hence, the claims were clear.

Novelty

(d) The membrane of D1 had not been cast *in situ* and did not adhere in place. D8 disclosed the polymerization of monomers to form gels, which was different from casting *in situ* a polymer by phase inversion. Hence, the subject-matter of Claim 1 according to the Main Request was novel.

(e) The alleged lack of novelty of the method of Claim 14 over D5 had not been raised in the statement of opposition. Anyhow, D5 did not disclose a housing as defined in the claims of the patent in suit but a macroporous sheet, which could even be wound in form of tube, the macropores of which however did not represent a housing. Since the macropores had to be completely filled in by the microporous membrane, the latter did not fill in only a portion of the housing nor was it contiguous to the second end of the housing either. Hence, D5 did not take away novelty. If the Board held that the feature "housing" did not distinguish the method of Claim 14 from that of D5, Claim 14 would be modified in line with Claim 1.

Inventive step

(f) As regards inventive step, D1 described the closest prior art. The subject-matter of Claim 1 differed from the device of D1 in that the membrane was cast

in situ and adhered in place. The problem to be solved was to provide a system in which the membrane was not mechanically fixed, as in D1, but cast and adhered in the desired place to provide retention and sealing. D1 did not hint at a solution as claimed. D5 had to do with a two-dimensional sheet, having macropores, not representing a housing as claimed, and dealing with sizes that were different from those of D1. Even if D1 mentioned scaling down of pore size, so that the skilled person could consider D5, that document did not straightforwardly applied to D1, at least because it required complete filling of the macropores from face to face and use of a doctor blade, to remove excess material, which was not appropriate for the pipette or multi well trays.

Therefore, the Main Request fulfilled the requirements of the EPC.

Auxiliary Request

Amendments

(g) The limitation "which was adhered" in Claim 1 of the Auxiliary Request emphasized that the structure was fixed in place by the action of casting and not by adhering any preferred structure in the housing.

Novelty and inventive step

(h) Claim 1 of the Auxiliary Request, which was based on Claim 14 as granted, was novel and inventive over D5, as found in the decision under appeal. In

particular, D5 neither disclosed a housing nor a microporous membrane formed within the macropores and adhering to them.

Hence, the Auxiliary Request too fulfilled the requirements of the EPC.

XIII. The party as of right did not submit any arguments.

XIV. The appellants (opponents 01) had requested in writing that the decision under appeal be set aside and the patent be revoked.

XV. The respondents (patent proprietors) requested that the decision under appeal be set aside and the patent maintained in the amended form of the Main Request, comprising Claim 1 submitted with letter dated 16 March 2006 and Claims 2 to 21 as granted, or on the basis of Claims 1 to 7 of the Auxiliary Request submitted at oral proceedings on 30 July 2009.

Reasons for the Decision

1. The appeal is admissible.

Main Request

2. *Novelty*

The appellants in their latest reply no longer disputed the novelty of Claim 1 over D13 and D8. The Board has no reason to take a different position. Since the Main Request fails for lack of an inventive step over D1,

the Board need not give further details on why the housing of Claim 1 is novel over those of D13 and D8, nor to explain why D13 need not be admitted into the proceedings.

As regards the method of Claim 14, its novelty, if any, will be apparent from the following analysis of D1 (Main Request) and D5 (Auxiliary Request), so that further details need not be given here either.

Inventive step

3. The patent in suit concerns cast membrane structures for sample preparation.

Closest prior art

4. The decision under appeal and the respondents at the oral proceedings before the Board have considered D1 as the closest prior art for assessing inventive step. D1 is acknowledged in the patent in suit (Paragraph [0008]) and discloses (Point 4.1, *infra*) centrifuge tubes containing porous selection means in form of cast membrane for separation and recovery of biological samples, as in the patent in suit. Therefore, D1 describes the closest prior art.

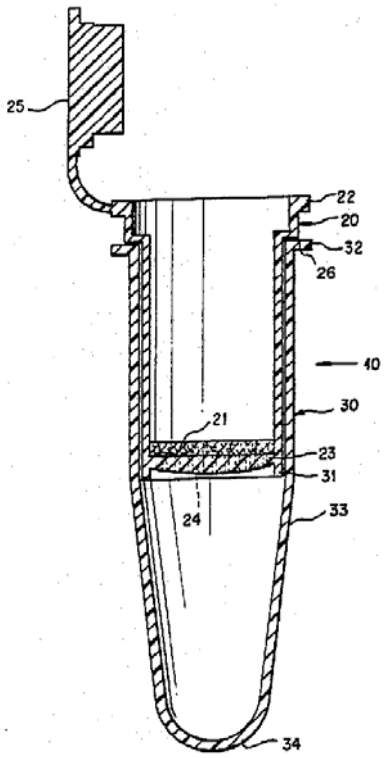
4.1 *Disclosure of D1*

4.1.1 D1 concerns a method for selectively separating and recovering desired biological substances from liquids containing the same which comprises centrifuging said liquid in a centrifuge tube wherein said tube is divided into a separable upper container and lower

container, the bottom of said upper container being comprised of a porous selection means capable of selectively binding desired biological substances thereto while allowing filtrate to pass therethrough, said porous selection means comprising a porous membrane containing an integrally bound particulate affording binding sites distributed throughout said membrane, thereby binding said biological substances to the selection means, and recovering the bound biological substances from the selection means by elution (Claim 1).

Since the membrane, to which the biological material is to be bound, has appropriate size and comprises in its polymeric resinous matrix organic or inorganic entities, preferably in the form of particulate binding sites, integrally dispersed throughout, a network of pores as well as between the particles and the resinous matrix, and between neighbouring particles, with the size distribution of the pores being relatively non-uniform (Column 8, lines 48-58), the polymeric membrane of D1 has a porosity suitable for sample preparation as required in the patent in suit (Paragraph [0024]).

4.1.2 A two-section centrifuge tube of D1 is shown in its drawing, reproduced below, identified as element 10, and comprising an upper section (elements 20 through 25) and a lower section (elements 30 through 34).



The upper section *inter alia* comprises: an upper container 20 which is generally cylindrical; annular lip 22 at the top of upper container 20; a bottom 23 comprising a support member preferably integral with lower container 20 having holes or slits 24 adapted to permit the passage of fluid; and a porous selection means, such as a membrane, 21 (Column 7, lines 32-45).

4.1.3 As to the aspect ratio, (micro)porous membrane 21 may be of any desired thickness consistent with the objectives of the defined process, e.g. in the form of a relatively thin membrane, which either is sufficiently rigid to withstand centrifugal forces applied to it or is laid out on a porous support within the device (Column 4, lines 7-16). As regards the size of the device of D1, it may even be in form of microcentrifuge tubes (microfuges), i.e. of reduced size (Column 3, lines 64-67; Column 7, lines 28-31). It was not disputed that the aspect ratio defined in

Claim 1 is satisfied by the broad disclosure of D1, in particular by membrane 21 shown in the drawing of D1.

4.1.4 The polymeric membrane disclosed by D1 is desirably made of thermoplastic resins (Column 9, lines 1-10).

4.1.5 According to D1 (Column 9, line 53, to Column 10, line 9), the polymeric membrane may be prepared in various ways known in the art, e.g. from US-A-3,862,030, which discloses a method of forming microporous submicron membranes comprising the steps of:

(a) forming a composition comprising a mixture of a polymeric resin, inorganic or organic particles, a solvent and a non-solvent (preferably water);

(b) extruding or molding said composition at room temperature or above to form a membrane comprising a substantially flattened sheet;

(c) passing the flattened sheet through an extraction medium to replace the solvent in the sheet with the extraction medium; and

(d) removing said extraction medium from said sheet.

Hence, the polymeric membrane of D1 can be cast by solvent replacement, i.e. polymer phase inversion, as described in the patent in suit (Paragraph [0028]).

4.1.6 It follows from the above that D1 discloses a housing (upper container 20) defining a volume, having a cylindrical wall, which as shown in section in the drawing should be impermeable to be able to contain the sample to be filtered, a first open end (20,22), a second open end (23,24), spaced from said first open end, and, in a portion of said volume (the lower one), a liquid permeable three-dimensional structure (as

shown in the drawing of D1), comprising a porous polymeric membrane (Point 4.1.4, *supra*), which can be cast by phase inversion (Point 4.1.5, *supra*) and has an aspect ratio of less than about 10 (Point 4.1.3, *supra*). Hence, all structural features explicitly mentioned in Claim 1 of the Main Request are disclosed by D1.

4.1.7 As regards the process features "cast *in situ*" and "adhered in place" of Claim 1, D1 does not mention that the membrane is cast in the housing of the device, nor how it is mounted therein, let alone whether it is adhered, if at all, to its walls. Those process features however concern the way of assembling housing and membrane, and do not necessarily distinguish the claimed device structurally from the device of D1, for the following reasons:

4.1.8 The feature "cast *in situ*" merely defines where the membrane is cast, without necessarily implying that a different structure is thereby obtained compared to casting e.g. *ex situ*., as mentioned in D1. Hence, casting a membrane *in situ* or *ex situ* does not necessarily change the internal structure nor the shape of the membrane. This is in line with granted Claim 21 of the patent in suit - reading as follows: "21. The method of Claim 17, further comprising removing said porous polymer matrix from said housing and introducing said porous polymer matrix into a second housing." -, thus showing that also the patent in suit as granted protects the possibility of casting *ex situ*. As to the shape of the membrane, any shape is encompassed by Claim 1. Hence, "cast *in situ*" per se is not suitable to distinguish the claimed housing-membrane assembly from that of D1.

4.1.9 As regards the feature "adhered in place", its meaning is not specifically defined in Claim 1, so that it is necessary to read it in the context of the patent in suit.

4.1.10 According to the patent in suit:

(a) The castable membrane should be able to assume the shape of the housing in which it is cast and should be retained in that housing without the use of porous plugs (Paragraph [0017]), wherein the housing can be of a variety of sizes or geometries (Paragraph [0016]).

(b) "Polysulfone is particularly preferred in view of the extent of adherence of the resulting composite structure to polyolefin housing. Other suitable polymer binders include polyethersulfone, cellulose acetate, cellulose acetate butyrate, acrylonitrile PVC copolymer, polyvinylidene fluoride, polystyrene and polystyrene/acrylonitrile copolymer" (Column 6, lines 41-51).

(c) "Adhesion to the housing can be enhanced or an analoguous effect achieved with these composite structures by means known to those skilled in the art, including etching of the housing, such as with plasma treatment or chemical oxidation, mechanical aids such as rims inside the housing, and inclusion of additives into the housing material that promote such adhesion (Column 6, lines 52-58).

(d) Adhesion allows uniform precipitation during casting (Column 7, line 1).

(e) "Polyolefins, particularly polypropylene, are preferred housing material in view of the chemical adhesion that is created when the composite

containing polysulfone is cast-in-place therein" (Column 8, lines 10-16).

(f) "When chemical adhesion of the composite structure to the housing walls is desired but is insignificant or non-existent, plasma treating the housing or a portion thereof can be used to promote adhesion (Column 8, lines 35-40).

(g) "An advantage of adhesion to the housing wall is the ability to "seal" the composite structure to the housing without mechanical means (Column 8, lines 40-43); and, such sealing (by whatever method) prevents the sample from channelling or bypassing the composite structure during operation (Column 8, lines 43-45).

4.1.11 It follows from the above analysis of the disclosure of the patent in suit and from the fact that Claim 1 of the Main Request does not contain any feature restricting explicitly or implicitly its scope to the use of "chemical adhesion", that the feature "adhered in place" per se goes beyond chemical adhesion and merely implies the abilities of casting and retaining the membrane within the housing while sealing the structure (membrane-housing) to prevent the sample from channelling or bypassing the membrane.

4.1.12 As regards D1, on the question whether the membrane of D1 is adhered to the walls of the housing in which it is mounted, it discloses in different instances that:

(a) "where it is necessary or desired to wash the membrane, or to remove the bound substance for completion of the assay, it is preferable to use a removable membrane" (Column 6, lines 34-37).

(b) "most preferably a porous or microporous membrane or a plurality of membranes, which may be removable, having integrally combined therein certain sites that can selectively bind the biological material to be recovered" (Column 6, lines 61-65).

(c) Still according to D1, it is essential that the membrane be incorporated in the device in order to entirely cover the bottom of the housing, "so that the fluid cannot pass from the interior of the upper container 20 through the holes or slits 24 without first passing through the selection means 21" (Column 7, lines 46-48).

The fact it is stated that the membrane of D1 may be removable also suggests to the reader the possibility that it be not removable, i.e. that it is fixed in place. Moreover, D1 requires that a seal be present between membrane and housing, albeit the way of making that seal is not specifically illustrated.

4.1.13 The step of casting a membrane within a housing, in which the membrane is then retained in a sealing way, does not necessarily imply a different retention and seal within the structure (housing-membrane), compared to a membrane adhered in place afterwards, such as that of D1, which membrane must be sealing to prevent bypassing and channelling.

4.1.14 If the "adhered in-place" is the result of the "cast *in situ*" step, then kind, extent and degree of adhesion nevertheless remain undefined. Since abilities such as retention within the housing and sealing are also mentioned in D1, and since the mention of "an analogous effect achieved ... by means known to those skilled in

the art" in the patent in suit (Column 6, lines 52-54) encompass a very tight contiguousness, obtained e.g. by simple compression, which in D1 is certainly obtained when the membrane is under the action of the centrifugal force, the feature "adhered in place" per se is not structurally distinguishing over D1.

4.1.15 Claim 1 does not specify what materials are to be used. If chemical adhesion were necessarily meant by "cast *in situ* and adhered in place", then it has not been shown and does not appear plausible that for all possible materials covered by Claim 1 chemical adhesion is obtained or would be different from a sealing mounting in place as required in D1.

4.1.16 Indeed, a structural distinction over the sealing assembly disclosed by D1 can only result if the feature "adhered in-place" means the presence of a particular chemical bonding, e.g. autogenous, between the membrane and the housing, being the result of the choice of a particular couple of materials, for the housing and the membrane respectively, possibly enhanced by any treatment of the housing, as mentioned in specific instances in the patent in suit. This however is not required by Claim 1 of the Main Request.

4.1.17 Since limiting features that are only implicitly encompassed by Claim 1, such as those mentioned in specific instances in the description of the patent in suit, where specific couples of materials for the housing and the membrane are mentioned, may not be read in Claim 1, as established in the case law of the Boards of Appeal of the EPO (Special edition 2 in the Official Journal 2009, Point 3.2, referring to

T 0681/01 of 28 November 2006), and since it has not been shown that the feature "cast in situ and adhered in place" generally distinguish the housing of Claim 1 from that resulting from the broad disclosure of D1, the housing of Claim 1 cannot be treated as novel (Article 54 EPC).

4.1.18 Furthermore, even if the combined process feature "cast *in situ* and adhered in-place" and the relevant structural implications had been shown to distinguish the subject-matter of Claim 1 from that disclosed by D1, that subject-matter would nevertheless be obvious over that of D1, for the following reasons.

Problem and solution

5. The patent in suit mentions problems such as:

(a) To provide a sample preparation device which can concentrate, purify and/or desalt molecules from sample solutions, preferably from very small sample solutions, which can be made in a variety of form or geometries and which is simple and economic to manufacture (Paragraphs [0011] to [0015]).

(b) To provide a method of casting particles in a housing in a variety of housing sizes or geometries (Paragraph [0016]).

(c) To provide a castable membrane that assumes the shape of the housing in which it is cast, and can be retained in that housing without the use of porous plugs (Paragraph [0017]).

(d) To provide a castable membrane on a support or substrate (Paragraph [0018]).

6. Having regard to D1, it is however apparent that:

(a) the problem of providing a castable membrane on a support or substrate is known, addressed and solved even in the prior art acknowledged in D1 (Column 9, line 44, to Column 10, line 26); and,

(b) the problems of (a) providing a sample preparation device which can concentrate, purify and/or desalt molecules from sample solutions, preferably from very small sample solutions, which can be made in a variety of sizes and which is simple and economic to manufacture, (b) of providing a method of casting particles in a housing in a variety of housing sizes, (c) of providing a castable membrane that assumes the shape of the housing in which it is cast, have been addressed and solved by D1 (Examples).

7. Also, the kind, extent and degree of adhesion of the membrane in the housing is not defined in Claim 1 and the use of porous plugs or supports on which to form the membrane are not excluded by Claim 1, nor by the description of the patent in suit either (Column 7, lines 24-25; Example 5, sentence bridging Columns 12 and 13), so that the problem of providing a castable membrane that assumes the shape of the housing in which it is cast, and can be (self)retained in that housing without the use of porous plugs cannot be considered as solved by the structure of Claim 1.

8. Finally, the examples of the patent in suit concern specific housings and membranes not defined in Claim 1, such as pipettes (Examples 1-4, 6,7,10, 11-17), multi-well trays (Example 5), and specific phase inversions, such as casting by evaporation (Example 8) or by

thermal-phase inversion (Example 9), so that those examples only illustrate part of the scope of Claim 1.

9. Hence, the problem to be solved should be reformulated less ambitiously as being to provide a further sample preparation device within the teaching of D1, e.g. to provide a microfuge which can concentrate, purify and/or desalt molecules from sample solutions, preferably from very small sample solutions, which can be made in a variety of form or geometries, by a method of casting particles in a housing, in a variety of housing geometries, to form a membrane that assumes the shape of the housing and can be retained in that housing.

Obviousness

10. It remains to decide whether a housing as claimed was obvious for the skilled person using common general knowledge, having regard to D1 as the closest prior art and addressing the problem to be solved (Point 9, *supra*).

10.1 Contrary to the finding of the Opposition Division in the decision under appeal (Reasons, Point 2.33), the size and shape of the centrifuge tube is not a critical feature of the device of D1, which discloses that:

(a) The relatively thin membrane of D1 can be sufficiently rigid to withstand centrifugal forces applied to it or is laid out on a porous support within the device (Column 4, lines 7-16).

(b) The device of D1 may be in form of microcentrifuge tubes (microfuges), i.e. of reduced size (Column 3, lines 64-67; Column 7, lines 28-31).

(c) "Advantageously, the device can thus be scaled down **greatly** (emphasis added) for highly effective use in microfuges to recover minute amounts of biological substances" (Column 3, lines 64-67).

(d) "However, because very small amounts of biological materials are generally being handled, tubes of a "micropreparative" scale, for use in microfuges, may be utilized to great advantage" (Column 7, lines 28-31)).

Hence, (very) small (micro) size devices are contemplated in D1, if not even preferred.

10.2 According to D1, the materials used in forming the device may be made of glass or metal, more desirably plastics such as polyethylene, (especially high density), polypropylene, polystyrene, polycarbonate, polytetrafluoroethylene, methyl or polymethyl methacrylate, or like materials as are employed in the manufacture of commercial centrifuge or microcentrifuge tubes. Because of DNA's ability to bind to glass, it is preferred that the tube not be made of this material when the intended use is with DNA or other like materials which bind to silica (Column 8, lines 35-47). Hence, the device of D1 is made of materials as those mentioned for making the housing described in the patent in suit (Paragraph [0031]).

10.3 Always according to D1, the polymers which form the matrix of the membrane are desirably thermoplastic resins made from commercially available polyvinylchloride, or a copolymer thereof with small amounts of monoethylenic monomers such as vinyl acetate, vinylidene chloride, propylene, ethylene, or mixtures thereof. Alternatively, the matrix may be formed from

such materials as polytetrafluoroethylene (PTFE), cellulose acetate or triacetate, polyamides, such as nylon, polysulfone, cellulose nitrate, mixtures or alloys thereof, or the like (Column 9, lines 1-10). Examples of suitable porous materials for the membrane of D1 include cast polymeric microporous membranes formed from such materials as nylon, cellulose derivatives, or modified polyvinylidene fluoride. Hence, the materials used for the membrane of D1 correspond to those mentioned for making the membrane of the patent in suit (Paragraph [0025]).

10.4 It follows from the two paragraphs above that a number of same materials for, respectively, the membrane and the housing are envisaged in D1 and the patent in suit.

10.5 As the housing of the device of D1 becomes smaller, in particular micro, it becomes not only more and more difficult to sealingly mount in it a membrane that has been cast *ex situ*, but also uneconomical. Also the provision of additional means to enhance the seal, if any, becomes more difficult if those means have to be made within the housing. Casting *in situ* by phase inversion, which as acknowledged in D1 was known, is suitable also for small sizes.

10.6 Hence, the skilled person, aiming at implementing the teaching of D1 in the area of the mentioned micro housings to provide a further device, would use a method of casting the membrane *in situ*., i.e. in the housing directly, instead of casting it *ex situ* and then mount in the housing, because casting *in situ* is simple and economical for small sizes.

10.7 Since the membrane should retain the desired biological material, while being itself sealingly retained, at least during the filtration cycle, to prevent channelling or its by-passing, the choice of compatible materials for housing and membrane is important. The materials for housing and membrane in D1 and in the patent in suit however overlap to a great extent. It has never been disputed that the binding properties of the particular couple of polymers disclosed in D1 and in the patent in suit were known. The fact that the materials to be combined should be matched is a usual requirement, at least to prevent any thermal mismatch, which requirement is easily fulfilled in the present case. Not only do the materials in D1 and in the patent in suit largely overlap, but also specific combinations for sampling devices are already known, as acknowledged in D1. At least in cases of samples containing DNA and the like material, plastics are the material of choice (D1, Column 8, lines 44-47; Point 10.2, *supra*).

10.8 Since the skilled person would arrive at the claimed subject-matter in an obvious way starting from D1, the housing defined in Claim 1 of the Main Request cannot be inventive over D1.

11. As regards the method of Claim 14 as granted, it follows from the disclosure in D1 (Point 4.1.5, *supra*) that a method of casting a membrane in a liquid impermeable housing ("molding" implies a mold, which is a housing), comprising forming a solution of a polymer (step (a), *supra*), introducing said solution into said mold (step (b), *supra*); and subjecting said solution to a phase inversion so as to cause said polymer to precipitate in said housing and form, *in situ*, a

membrane (step (c), *supra*), was already known. Hence, the method of Claim 1 as granted was not novel. The Board has not persisted in objecting that lack of novelty because the appellants, in that case, were ready to amend Claim 14 in line with Claim 1.

11.1 Therefore, the amended claims of the Main Request are not allowable.

Auxiliary Request

Novelty

12. Claim 1 of the Auxiliary Request (Point X, *supra*) corresponds to Claim 14 as granted with the further limitation that the cast *in situ* membrane is adhered to the housing.

13. D5 discloses a porous structure comprising a macroporous substrate defining an interconnected network of macropores and a microporous matrix defining a network of interconnected micropores filling and contained entirely within said network of macropores so that outside edge of said microporous matrix is at the outside surface of said substrate (Claim 1).

13.1 The material of said substrate and the material of said microporous matrix can consist essentially of synthetic resin (Claim 2), wherein said macroporous substrate consists of a first synthetic resin and said microporous matrix consists of a second synthetic resin different than said first synthetic resin (Claim 3). In particular, said macroporous substrate can consist

essentially of polyethylene and said microporous matrix can consist essentially of polyvinyl chloride (Claim 4).

13.2 The microporous matrix can be formed within said network of macropores (Claim 5) by impregnating said network of macropores with a solution of the material of said microporous matrix and a solvent for said material of said microporous matrix and by forming said microporous matrix from said solution (Claim 6).

13.3 D5 also discloses a method of making a porous structure comprising providing a macroporous substrate defining a network of interconnected macropores, filling said network of macropores with a solution including a material capable of being formed into a microporous matrix from said solution while leaving none of said solution on the surface of said substrate, and forming a microporous matrix of said material from said solution entirely within said network of macropores (Claim 7). Said solution can further comprise a pore former and a solvent for said pore former and for said material, and said step of forming said microporous matrix includes coagulating said material in said solution into a matrix and extracting said pore former and said solvent from said matrix (Claim 8).

13.4 In the method of D5, the step of impregnating the macroporous substrate with the solution can include immersing said substrate in the solution in a vacuum chamber (Claim 9) and the step of forming a macroporous matrix can include the step of causing said solution while contained in network of micropores to imbibe moisture from the surrounding atmosphere (Claim 10), wherein the imbibing of water by said solution causes

said solution to separate into two phases, a first phase being rich in said material and a second phase being rich in water, and wherein said first phase is coagulated into said microporous matrix (Claim 11). The solution can comprise a solvent for said material and a diluent homogenously miscible with said solvent and in which said material is not soluble (Claim 12).

13.5 The interconnected network of macropores of the structure of D5 has a definite, measurable pore volume, specifically from 34 to 46% (Column 4, line 4), in which the microporous phase is contained, hence housed. Furthermore, the macropores are interconnected, so that they have at least two open ends. The impermeable wall of that macroporous structure is constituted by the set of wall sections of the particles adjacent to the pores making the macropore volume. Therefore, the macropore network of the struture of D5 is a housing encompassed by the term "housing" of Claim 1 of the Auxiliary Request.

13.6 D5 specifically mentions the formation of a solution of polymer (Claims 6 and 7, Points 13.2 and 13.3, *supra*), the introduction of that solution into the macropore network (housing) (*idem*, *supra*; Claim 9, Point 13.4, *supra*) as well as the precipitation or coagulation of the polymeric material, by phase inversion, in the housing, i.e. *in situ* (Claims 8, 10 and 11, Points 13.3 and 13.4, *supra*; Column 2, line 49).

13.7 It remains to decide whether or not the microporous matrix adheres to the walls of the macropore network.

14. Since the structure of D5 can act as depth filter (Column 1, lines 45-47), the microporous structure should tightly seal the macropore network, otherwise it would not function. Even when the casting solution is diluted too much, which is not preferred because a microporous matrix does not completely fill the macropore network, the walls of the pores are nevertheless coated (Column 6, line 22), which implies affinity between the material of the macropore structure and that of the microporous structure. Furthermore, a macroporous substrate of polyethylene and a microporous matrix of polyvinylchloride (PVC) are exemplified in D5 (Column 4, lines 1-8), and will have some adhesion enough to satisfy the requirement of "adhesion" of Claim 1 of the Auxiliary Request.

15. Therefore, the method of Claim 1 of the Auxiliary Request lacks novelty over that of D5.

16. D1 (in particular Column 9, line 53 to Column 10, line 10) (Points 4.1.5 and 11, *supra*) does not directly and unambiguously disclose a method in which a porous membrane is cast *in situ* and adhered to the mold (otherwise it could not be removed), so that the method of Claim 1 is novel over that illustrated by D1. But, for the reasons given in Points 10, *supra*, which apply *mutatis mutandis* to the method of Claim 1, the method of Claim 1 of the Auxiliary Request is not inventive.

17. Therefore, the grounds of lack of novelty and/or of an inventive step prejudice the maintenance of the patent in suit.

18. In view of the above decision, the Board need not decide whether or not the amended claims of both requests comply with Articles 84 and 123(2) EPC. It is also apparent that D13 need not be admitted into the proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

S. Fabiani S. Perryman