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**D E C I S I O N**  
**of 10 January 2001**

**Case Number:** T 0525/97 - 3.3.5

**Application Number:** 89300983.7

**Publication Number:** 0329303

**IPC:** A61M 1/36

**Language of the proceedings:** EN

**Title of invention:**

Device and method for separating leukocytes from platelet concentrate

**Patentee:**

Pall Corporation

**Opponent:**

Terumo Kabushiki Kaisha Head Office  
FRESENIUS AG

**Headword:**

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**Relevant legal provisions:**

EPC Art. 54(1), 54(3), 56, 83, 84  
EPC R. 88

**Keyword:**

"Lack of disclosure (no): enabling analytical methods disclosed"

"Novelty (yes): relevant part of priority document not comprised in European patent application"

"Inventive step (yes) - unobvious modification"

**Decisions cited:**

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Catchword:

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Boards of Appeal

Chambres de recours

Case Number: T 0525/97 - 3.3.5

**D E C I S I O N**  
**of the Technical Board of Appeal 3.3.5**  
**of 10 January 2001**

**Other party:**  
(Opponent 01)

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**Appellant:**  
(Opponent 02)

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**Decision under appeal:**

Interlocutory decision of the Opposition Division  
of the European Patent Office posted 11 March  
1997 concerning maintenance of European patent  
No. 0 329 303 in amended form.

**Composition of the Board:**

**Chairman:** R. K. Spangenberg

**Members:** A.-T. Liu  
J. H. Van Moer

## Summary of Facts and Submissions

- I. European patent No. 0 329 303 was granted with the priority claim of earlier US patent applications dated 17 February 1988 and 25 April 1988. Two notices of opposition were filed against the patent, based on Article 100(a) and Article 100(b) EPC.
- II. The appeal is from the interlocutory decision of the Opposition Division maintaining the patent on the basis of the amended set of 38 claims filed at the oral proceedings of 12 February 1997. Claims 1, 25 and 33 were independent claims for a device, and independent claims 26 to 29 were directed to methods of use of claimed devices. These independent claims read as follows:

"1. A device for the depletion of the leukocyte content of a platelet concentrate comprising a porous synthetic fibrous medium having a CWST of at least 90 dynes/cm, and a negative zeta potential at a pH of 7 to 7.2, the fibers of the medium being modified to present hydroxyl groups together with a lesser number of a second anionic group.

25. A device for the depletion of the leukocyte content of platelet concentrate comprising passing the platelet concentrate through a device comprising a modified, porous, fibrous medium having a CWST of at least 95 dynes/cm, a negative zeta potential at a pH of 7 to 7.2, a pore diameter in the range of from 3.8 to 6 micrometers, and a bulk density of less than 3.6 grams/cc, the fibers of said medium comprising polybutylene terephthalate and having diameters of less than 30 micrometers, the medium having an effective

flow area in excess of 40 square centimeters and the modification of the medium having been effected by the use of a mixture of methacrylic acid and hydroxyethyl methacrylate in which the acid/acrylate monomer weight ratio is between 0.05:1 to 0.35:1.

26. A method for the depletion of the leukocyte content of platelet concentrate comprising passing the platelet concentrate through the device of any one of the claims 1-25.

27. A method for the depletion of the leukocyte content of platelet concentrate comprising passing the platelet concentrate through a fibrous porous synthetic medium having a CWST of at least 90 dynes/cm, and a negative zeta potential at a pH of 7 to 7.2, the fibers of the medium being modified using a mixture of monomers comprising methacrylic acid and hydroxyethyl methacrylate having an acid/acrylate monomer weight ratio of between 0.01:1 to 0.5:1.

28. A method for the depletion of the leukocyte content of platelet concentrate comprising passing the platelet concentrate through a device comprising a modified, porous, fibrous medium having a CWST of at least 90 dynes/cm, and a negative zeta potential at a pH of 7 to 7.2, a pore diameter in the range of from 3.8 to 6 micrometers, and a bulk density of less than 3.6 grams/cc, the fibers of said medium comprising polybutylene terephthalate and having diameters of less than 30 micrometers, the medium having an effective flow area in excess of 40 square centimeters and the modification of the medium having been effected by the use of a mixture of methacrylic acid and hydroxyethyl methacrylate in which the acid/acrylate monomer weight

ratio is between 0.05:1 to 0.35:1.

29. A method for treating a platelet suspension comprising passing the platelet suspension through a porous, synthetic fibrous medium having a CWST of at least 90 dynes/cm, a negative zeta potential at a pH of 7 to 7.2, and the fibers of the medium being modified to present hydroxyl groups and groups having anionic character at the surface thereof.

33. A device for treating a platelet suspension comprising a porous, synthetic fibrous medium having a CWST of at least 90 dynes/cm, a negative zeta potential at a pH of 7 to 7.2, and the fibers of the medium being modified to present hydroxyl groups and groups having anionic character at the surface thereof."

III. Of the documents which were cited in the opposition proceedings, reference shall be made in the present decision to the following:

D1: Vox Sang. 53: 26-30 (1987)

D2: Vox Sang. 53: 76-82 (1987)

D7: Report on CWST measurement submitted 10 May 1995

D8: Report on zeta potential measurement of fabrics submitted 10 May 1995

D10: EP-A-0 267 286

D14: EP-A-0 313 348 (published 26 April 1989)

D26: Transfusion, Vol. 24, No. 1 (1984), pages 1A to 3A

D27: Vox Sang. 52: 191-194 (1987)

D28: FR-A-2 239 282

- IV. With respect to the ground for opposition pursuant to Article 100(b) EPC, the opposition division held that the patent in suit contained sufficient disclosure enabling the skilled person to determine the pore diameter, CWST value and zeta potential.

The opposition division found that the content of D14 was not novelty-destroying to the claimed devices. The prior use of the IMUGARD IG500 filter was not accepted as proven. Relying on D10 as the closest prior art, an inventive step was recognised for the reason that the modification of the filter medium with a second group having anionic character in addition to the hydroxyl group was not suggested in the available prior art.

- V. With the Statement of the grounds of appeal, the appellant Fresenius AG (opponent 02) reiterated his objections under Articles 100(a) and (b) EPC.

- VI. The appellant's submissions in writing and at the oral proceedings of 10 January 2001 may be summarised as follows:

- The patent in suit did not disclose sufficient teaching for the skilled person to determine the zeta potential.
- The device according to claim 1 lacked novelty with regard to D14, pursuant to Articles 54(3) and (4) EPC.

- The claimed device was distinguished from the previously known IMUGARD IG 500 filter only in that it comprised a synthetic fibrous medium instead of cellulose. The modification was, however, self-evident and did not justify recognising an inventive step.
- The claimed device was only distinguished from D10 in that the polymers in D10 were modified with cationic groups. However, the modification of polymer fiber to contain an anionic group was an obvious alternative, in particular having regard to the disclosure of D28.
- The obviousness of the modification with an anionic group was corroborated by a corresponding passage in the description of the patent in suit, stating the use of cationic polymer as a possible modifier.
- Lastly, the description of the starting materials went beyond the scope of the claims.

VII. The arguments submitted by the respondent were briefly as follows:

- The zeta potential was a parameter commonly used in the art.
- D8 was evidence that the skilled person did not have a problem measuring the zeta potential. Furthermore, a quick and practical method for determining this parameter was recommended in the patent in suit.



- D14 did not disclose a filter comprising fibers being modified to present hydroxyl groups together with a second anionic group.
- The trade name IMUGARD IG500 was used to designate different filters.
- The feature common to all these IMUGARD IG500 filters was that the filter material was cotton.
- The IMUGARD IG500 filters were adhesive to both leukocytes and platelets. Therefore, the skilled person would not consider modifying these filters with the aim to solve the present problem of selectively removing leukocytes from platelets.
- The closest prior art D10 would actually lead away from a leukocyte filter comprising a polymer modified with hydroxyl groups and a second **anionic** group.
- D28 did not concern the problem of selective removal of leukocytes and did not contain a teaching leading to the solution as claimed.
- The mention in the description of modifications using a cationic group was a linguistic error.
- The description of starting materials concerned general background and did not relate exclusively to the claimed invention.

VIII. At the end of the oral proceedings, the appellant requested that the decision under appeal be set aside and that the patent be revoked.

The respondent (patentee) requested that the appeal be dismissed.

## Reasons for the Decision

### 1. *Amendments*

In agreement with the undisputed finding of the first instance, the Board is satisfied that the amendments introduced during the opposition proceedings meet the requirements of Articles 123(2) and (3) EPC.

### 2. *Sufficiency of disclosure*

The appellant has contended that, although the independent claims stipulate a negative zeta potential, the patent in suit does not specify the medium in, and the temperature at which this parameter is to be measured. As a consequence, the patent in suit does not give the skilled person sufficient information for determining the zeta potential.

- 2.1 The Board agrees with the appellant insofar as different values of zeta potential may be obtained for the same substrate if the measurements are carried out in different environments. However, this consideration would mean that the zeta potential may not be clearly defined. Such an objection is, however, one of lack of clarity, which is not a ground for opposition. Since the claims as granted already contain the stipulation of a negative zeta potential, a possible lack of clarity ensuing therefrom could not be considered at this stage of the proceedings. In this respect, the Board follows the reasons set out in T 301/87 (OJ EPO

1990, 335, point 3).

- 2.2 On the other hand, the concept of zeta potential is well known in the art. Furthermore, the other party to the proceedings, Terumo Kabushiki Kaisha (opponent 01), has submitted a report on the zeta potential measurement of five kinds of nonwoven fabrics (D8, page 1, Title and "Samples"). The results shown at page 2 refer to sample A as "Breached (sic) Egyptian cotton (a filter, with the trade name Immugard IG500, manufactured by Terumo Kabushiki Kaisha)". The report does not indicate any problem in determining the zeta potential of the samples. On the contrary, it is stressed that the values obtained on sample A are consistent in duplicate runs (see page 1, point 1).

Moreover, the patent in suit has recognised that the standard methods are complicated to perform and often produce inconsistent data (see page 24, lines 2 to 11). For this very reason, it even offers a useful but simpler analytical method for measuring the zeta potential (page 24, lines 12 to 16).

The appellant has not submitted that the method recommended in the patent in suit is faulty. Neither has he raised any objection to the experimental results obtained by opponent 01 according to previously known methods. The Board therefore concludes that, to the skilled person, the disclosure with respect to the zeta potential is sufficient within the meaning of 100 (b) EPC.

3. *Prior use*

The appellant has observed that the prior use of

IMUGARD IG500 is documented in D1 and D2. However, the trade name of the filters used in the cited documents is, on the one hand in D1, IMMUGARD TFG 500 Y, and on the other hand in D2, IMUGARD IG500. The Board therefore does not see how these documents can possibly relate to the same type of filter.

Nevertheless, the Board notes that all the available citations relating to the prior use of IMUGARD (or IMMUGARD) filters are at least consistent in that they always specify the filter material to be cotton (D1: page 26, left hand column, under the heading: "Introduction"; D2: page 77, left hand column, under the heading: "Preparation of Leukocyte-free platelet concentrates (LF-PC)"; D7: page 1, point 1, under heading: "Purpose of the experiment"; D8: page 2, Table entitled "Result of the zeta potential measurement"; D27: page 191, left hand column, under the heading: "Introduction"). From the available information on IMUGARD filters, the Board can at least regard as proven that this feature is common to the IMUGARD filters.

4. *Novelty*

4.1 It is undisputed that the subject-matter of claim 1 is distinguished from the IMUGARD filters by the stipulation of a synthetic fibrous medium instead of cellulose (or cotton, see also point 3 above).

4.2 The appellant has remarked that European patent application D14 claims priority from two US applications. Relying on one of these priority documents, the appellant has advanced the argument that D14 is novelty destroying to the subject-matter of

claim 1.

D14, with the earlier priority date of 20 October 1987, was published on 26 April 1989, that is after the priority dates (17 February 1988 and 25 April 1988) of the patent in suit. The content of D14 ensuing from that earlier priority document is therefore comprised in the state of the art for the purpose of Articles 54(3) and (4) EPC. Any part of the priority document which is not comprised in the corresponding European patent application, is not part of the prior art within the meaning of Articles 54(3) and (4) EPC. Neither can the information concerned be taken into consideration under Articles 54(1) and (2) EPC since the appellant has not submitted, let alone proved, that it was available to the public before the priority dates of the patent in suit.

It is undisputed that the description at page 11, lines 45 to 56 of D14 which reviews the prior art of surface grafting, is directly derived from the priority document. In contrast, in the further description concerning the development of the claimed invention, mention is only made in D14 ( page 11, lines 57 to 61) to grafting with "compounds containing an ethylenically unsaturated group, such as an acrylic moiety combined with a hydroxyl group (for example, 2-hydroxyethyl methacrylate, or "HEMA"). A second acrylic monomer, such as methyl acrylate (MA) or methyl methacrylate (MMA), which tends to cause the grafted porous webs to have lower CWST, can be used in combination with HEMA". This is not in dispute. The European patent application D14 itself thus does not disclose a device in which the fibers of the filter medium have been modified to present hydroxyl groups together with a second anionic

group.

4.3 The Board also concurs with the undisputed statement in the decision under appeal that none of the other available prior art documents discloses the stipulated modification in combination with a device comprising a synthetic fibrous medium. The subject-matter of claim 1 is therefore new.

5. *Inventive step*

5.1 Claim 1 is directed to a device for the depletion of the leukocyte content of a platelet concentrate.

5.2 The Board concurs with the parties present at the oral proceedings that D10 therefore represents the closest prior art, disclosing a filter for selectively removing leukocytes with a small loss of platelets (see abstract; page 1, lines 7 to 14; and page 2, lines 2 to 10). The device according to D10 is characterised in that it comprises a fiber having nonionic hydrophilic groups and nitrogen-containing basic functional groups in its peripheral surface portion (page 7, line 11 to page 8, line 13; and claim 1). Although not expressly indicated in D10, it is common ground for the parties that such a device has a positive zeta potential.

5.3 It is undisputed that, with respect to D10, the problem to be solved by the patent in suit can be seen in the provision of an alternative device for selective leukocyte removal.

5.4 The solution proposed in claim 1 is a device comprising a synthetic fibrous medium modified to present hydroxyl groups together with a second anionic group. Such

device is also stipulated to have a negative zeta potential.

5.5 Although the appellant has contested that the claimed device is an improvement over that of D10, he has accepted that it is efficient for the intended purpose of selectively removing leukocytes. In the absence of any evidence to the contrary, the Board therefore presumes that the technical problem as stated in point 5.3 above is solved by the device as claimed. The only remaining question is thus whether the proposed solution is obvious in view of the available prior art.

5.6 As is explained in D10, in order to prevent platelets from adhering to a filter, it is already known to graft-polymerise or coat the filter material with a hydrophilic agent. Such modification, however, renders the material less adhesive not only to platelets but also to leukocytes (page 6, lines 16 to 23). D10 therefore proposes adding to the hydrophilic agent a second modifier which has basic nitrogen-containing groups (see point 5.2 above). D10 is thus very specific in its teaching and does not suggest any other way of modification for selectively removing leukocytes.

The Board does not ignore the fact that D28 generically discloses the possibility of coating absorbent particles with polymers comprising a hydrophilic monomer such as HEMA and a comonomer such as acrylic or methacrylic acid (page 3, line 1 and page 4, lines 36 and 37). This particular combination of monomers is, however, only one among the wide choice proposed in the prior art (see page 2, line 20 to page 5, line 35). Furthermore, the general teaching of D28 is about the use of absorbents for blood perfusion. The coated

particles are applied to the process of removing toxic agents from the blood without substantially altering the blood composition. In particular, it is important that the platelets and other cellular components (such as leukocytes) do not adhere to the surface of the coated particles (page 1, lines 10 to 14 and 20 to 22; page 2, lines 5 to 12; page 19, lines 3 to 8). A skilled person, seeking suggestions for removing leukocytes from platelets, would not have any incentive to look into D28, much less to make a particular selection among the multitude of combinations of monomers offered in this document.

Since the skilled person cannot infer the solution as proposed in claim 1 from D10 or from any other prior art document (including D28), the Board concludes that the subject-matter of claim 1 involves an inventive step.

5.7 The appellant has also asserted that the device according to claim 1 lacks an inventive step in view of the IMUGARD filters. The Board, however, notes that the relevant page 2A of D26 is an advertisement by Terumo, displaying the properties of the new IMUGARD IG500 filter. It specifically states that "the IMUGARD also effectively removes platelets" (see paragraph 3 of the caption). The Board therefore finds that the skilled person, seeking a solution to the problem of selectively removing leukocytes from platelet concentrates, would not be led to consider this particular type of filter. The documents relating to IMUGARD filters, in particular D26, are thus not relevant for the assessment of inventive step.

6. The above findings with respect of claim 1 apply



mutatis mutandis to the other independent claims for a device, claims 25 and 33, and to the independent method claims 26 to 29 which all stipulate the same new and inventive feature as claim 1, namely a synthetic fibrous medium modified with hydroxyl groups and a second anionic group.

Claims 2 to 24 and 34 to 37 are dependent claims relating to specific embodiments of the device according to claim 1 and 33, respectively. Likewise, claims 30 to 32 are dependent claims relating to specific embodiments of the method according to claim 29, and claim 38 a dependent claims relating to specific embodiments of the method according to any of the method claims 26 to 29. The patent can therefore be maintained with these claims.

7. *Description*

7.1 The appellant has raised the objection that the description at page 10 lines 10 to 13 of the patent in suit would allow for other starting materials than those stipulated in the claims.

The Board interprets the appellant's objection as being raised under Article 84 EPC, requiring that the claims be supported by the description. Since the description concerned has not been amended as a result of the oppositions, such objection cannot be taken into consideration at this stage of the proceedings (see also point 2.1 above).

Notwithstanding the preceding remark, the appellant has moreover submitted that the wording at page 10 line 10, indicating that "A variety of starting materials other

than fibers can be considered", should be interpreted as referring to the possible choice of starting materials in general terms. The subsequent statement that "considerations of cost, ... point to fibers as a preferred starting material" would then indicate the selection made by the patentee (page 10 line 11 to 13). In view of the explanation, the Board considers that the latter statement may be read as reflecting the restriction made in the claims which stipulate devices comprising a fibrous medium.

- 7.2 The appellant has alleged that the description at page 23, line 10 of the patent in suit clearly indicates that the modification with a second agent carrying a cationic group is also envisaged in the patent in suit, as an alternative to the modification with one carrying an anionic group.

Whilst the cited passage indeed concerns the modification according to the patent in suit, the description states expressis verbis that "it may be possible to achieve the preferred degree of surface modification with less than 0.1% of HEMA and other than .019% of MAA **or other cationic polymer**" (emphasis added). There is, however, no doubt, that MAA is an anionic and not a cationic monomer. Thus, it is clear to the skilled reader that, not only the term "cationic" is erroneous but also that the correct expression must be "anionic". The objectionable expression is thus an obvious error within the meaning of Rule 88 EPC. In such case, the onus is on the respondent to submit a request for correction, if he so wishes.

**Order**

**For these reasons it is decided that:**

The appeal is dismissed.

The Registrar:

The Chairman:

S. Hue

R. Spangenberg