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Datasheet for the decision of 23 November 2010

Case Number: T 1202/04 - 3.3.05

Application Number: 98930151.0

Publication Number: 1024872

IPC: B01D 21/26

Language of the proceedings: EN

Title of invention:
Systems and methods for collecting diluted mononuclear cells

Applicant:
Baxter International Inc.

Opponent:
-

Headword:
Blood separation system/BAXTER

Relevant legal provisions:
EPC Art. 54, 56, 123

Relevant legal provisions (EPC 1973):
-

Keyword:
"Novelty (yes)"
"Inventive step (yes) - general statements in the prior art do not provide incentive"

Decisions cited:
-

Catchword:
-

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Case Number: T 1202/04 - 3.3.05

D E C I S I O N
of the Technical Board of Appeal 3.3.05
of 23 November 2010

Appellant: Baxter International Inc.
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Deerfield, Illinois 60015 (US)

Representative: Dee, Ian Mark
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 24 June 2004 refusing European patent application No. 98930151.0 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: G. Raths
Members: E. Waeckerlin
S. Hoffmann

Summary of Facts and Submissions

I. The appeal is from the decision of the examining division to refuse the European patent application No. 98 930 151.0.

II. In the decision under appeal, the examining division gave no explicit reasons for the refusal, but referred instead to its communications dated 16 May 2002, 2 February 2004 and 8 June 2004. In these communications the following two documents were cited:

D1: WO 96 32199 A;

D2: US 5 573 678 A.

III. Notice of appeal was filed by the appellant with letter dated 9 August 2004. Independent claims 1 and 4, respectively, attached to the notice of appeal, read as follows:

"1. A blood separation system comprising a chamber (12) for rotation about a rotational axis (28), the chamber including an inlet region (72) where whole blood enters for separation into packed red blood cells, a plasma constituent, and an interface (58) carrying platelets and mononuclear cells between the packed red blood cells and the plasma constituent,

a first collection container,

a second collection container,

a pump (P1 - P6),

a controller (222) operable to convey whole blood into the inlet region while removing packed red blood cells and the plasma constituent from the chamber, the

controller including an interface control unit (220) operative (i) in a first condition to retain platelets and mononuclear cells in the chamber to enable removal of platelet-poor plasma from the chamber in a path that leads to the first container and not the second container; (ii) in a second condition to retain mononuclear cells in the chamber while enabling removal of platelet-rich plasma from the chamber in a path that bypasses the first and second containers; and (iii) in a third condition to enable removal of mononuclear cells from the chamber in a path that leads to the second container and not to the first container, and the controller further operating the pump to direct platelet-poor plasma from the first container to the second container to dilute the removed mononuclear cells in the second container."

"4. A method for collecting diluted mononuclear cells comprising the steps of

rotating a chamber (12) about a rotational axis (28),

conveying whole blood into an inlet region of the chamber for separation into packed red blood cells, a plasma constituent, and an interface (58) carrying platelets and mononuclear cells between the packed red blood cells and the plasma constituent,

maintaining the interface in a first condition in the chamber to retain platelets and mononuclear cells in the chamber to enable removal of platelet-poor plasma from the chamber in a path that leads to a first container and not to a second container,

maintaining the interface in a second condition in the chamber to retain mononuclear cells in the chamber while enabling removal of platelet-rich plasma from the

chamber in a path that bypasses the first and second containers,

maintaining the interface in a third condition in the chamber to enable removal of mononuclear cells from the chamber in a path that leads to the second container and not the first container, and

directing platelet-poor plasma from the first container to the second container to dilute the removed mononuclear cells in the second container."

IV. In the communications dated 16 May 2002 and 2 February 2004, respectively, the examining division held that the blood separation system according to claim 1 differed from the system disclosed in document D1 *"merely in that the admixture of platelet-poor plasma to the mononuclear cells is effected automatically via a pump"*. In the examining division's view, automatic admixture of the platelet-poor plasma to the mononuclear cells by means of a pump represented a *"rationalization"* which did not require *"inventive skill"*. For this reason, the examining division denied that the claimed blood separation system involved an inventive step.

V. In its statement of grounds of appeal dated 19 October 2004, the appellant contested the conclusions of the examining division. D1 did not disclose a system or method in which the concentration of the collected mononuclear cells is adjusted after they are removed from the separation channel. Nothing in D1 suggested to dilute the collected mononuclear cells with plasma collected previously in a container. There was also no teaching to provide a system or a method in which platelet-rich plasma is removed from the separation

channel so that only platelet-poor plasma is used to dilute the collected mononuclear cells. In the system of D1, platelet-poor plasma is never collected without also collecting platelets. According to D1 the platelets and the platelet-poor plasma are both harvested continuously whilst the mononuclear cells are being intercepted and accumulated in the accumulation phase of the process.

The appellant argued that the claimed system and method provide technical advantages compared to the system of D1. Thus, a pure concentration of mononuclear cells is obtained. Moreover, the mononuclear cell product remains pure after dilution with platelet-poor plasma as a diluting liquid.

The appellant concluded that both the claimed system and the method involved an inventive step.

VI. The appellant requested that the decision under appeal be cancelled in its entirety and that European patent application no. 98 930 151.0 be allowed on the basis of the claims that were attached to the grounds of appeal as annex A.

Reasons for the Decision

1. Allowability of the amendments effected to the claims - Article 123(2) EPC

1.1 Claim 1 has been amended to specify that the blood separation system comprises a **pump**. A basis for this amendment can be found, for example at page 9, lines 10

to 17 and page 11, lines 3 to 5 of the description, as well as in Figure 6, reference signs P1 to P6, of the application as published by the International Bureau (hereinafter called "application as originally filed"). Furthermore claim 1 has been amended to specify that both the platelet-poor plasma and the platelet-rich plasma are removed **from the chamber**. The basis for this amendment can be found at page 2, lines 7 to 17 of the application as originally filed.

Moreover, claim 1 has been amended to specify that the controller operates **the pump** to direct platelet poor plasma from the first container to the second container. The basis for this amendment can be found at page 52, lines 16 to 23 and Figure 26 of the application as originally filed.
Finally, a number of reference signs have been included in claim 1 to increase the intelligibility (Rule 43(7) EPC). These reference signs are illustrated, for example, in Figures 1, 4, 16A, 16B, 17 and 19, respectively, of the application as originally filed.

1.2 In claims 2, 3, 5 and 6 a number of reference sings have been included. These reference signs are illustrated in Figures 1, 16A, 16B, 17 and 19, respectively.

1.3 Claim 4 has been amended to achieve conformity of the wording with the amended claim 1.

1.4 Dependent claims 7 and 8 have been added during the examination of the application. These claims relate to embodiments of the claimed system and method, wherein a portion of the platelet-rich plasma is re-circulated

into the inlet region of the chamber. Support for this feature can be found at page 28, lines 27 to 31, page 30, lines 23 to 31 and page 50, lines 12 to 21 of the application as originally filed.

1.5 With letters dated 29 October 2002, various amendments have been effected to the description and the drawings.
The phrase *"which is incorporated herein by reference"* has been deleted from the description on pages 7, 8, 14, 20, 22, 31 and 35.
On page 7, lines 2 - 9, the text referring to the *"spirit"* of the invention and to the *"range of equivalency of the claims"* has been deleted.
On pages 7, 8, 14, 20, 22, 31 and 35 the text *"which is incorporated herein by reference"* has been deleted.
On pages 10 and 11 the reference signs *"C3"*, *"VA1"* and *"VA30"* have been corrected to read *"C9"*, *"V1"* and *"V30"*, respectively (see Figures 6 and 9).
On pages 15, 16, 26, 29, 39, 41, 49, 51, 53, 55, 56 and 57, as well as in Figures 6, 19, 21, 22, 23, 24A, 24B, 24C, 25, 26, 27, 29, 30 and 31 the reference signs for the clamps *"C"* have been replaced by *"CL"* in order to distinguish the clamps (now *"CL"*) from the channels *"C"*.
On page 19, the mistaken reference sign *"50"* has been deleted and the reference sign for the interface *"26"* corrected to read *"58"* (see page 18, lines 18 - 20 and Figures 16A, 16B).
On page 20, the reference sign for the blood processing compartment *"134"* has been corrected to read *"38"* (see page 8, lines 32 - 33).

1.6 Together with the grounds of appeal dated 19 October 2004, an amended page 1 of the description containing

an acknowledgment of the disclosure of document D1 has been filed by the appellant.

1.7 The board is satisfied that none of the amendments effected to the claims, the description and the drawings extends beyond the content of the application as originally filed. Therefore, the requirement laid down in Article 123(2) EPC is met.

2. Novelty - Article 54 EPC

2.1 Document D1 discloses a blood separation system (see D1, page 5, lines 18 - 22) comprising a chamber for rotation about a rotational axis (see D1, Figure 1, reference sign 15 *"centrifuge"*), the chamber including an inlet region where whole blood enters for separation into packed red blood cells, a plasma constituent, and an interface carrying platelets and mononuclear cells between the packed red blood cells and the plasma constituent (see D1, Figure 1, reference signs 10, 12, 13 and 14; page 2, lines 33 - 37), a first collection container (see D1, Figure 1, reference sign 20 *"plasma collect reservoir"*), a second collection container (see D1, Figure 1, reference sign 23 *"WBC collect reservoir"*), various pumps (see D1, Figure 1, reference signs 13, 19, 22), and a controller operable to convey whole blood into the inlet region while removing packed red blood cells and the plasma constituent from the chamber (see D1, Figure 1, reference sign 26 *"control system"*; 16 and 16A *"RBC reserve"*; 18, 19, 20 *"plasma collect reservoir"*). The controller includes an interface control unit operative to retain platelets and mononuclear cells in the chamber to enable removal of platelet-poor plasma from the chamber in a path that

leads to the first container and not the second container (see D1, page 3, lines 7 - 14; page 11, line 33 to page 12, line 21; page 15, line 33 to page 16, line 4; page 16, line 19 to page 17, line 22; Figures 2, 4A, 4B, 4C). The interface control unit is also operative to retain mononuclear cells in the chamber while enabling removal of platelet-rich plasma from the chamber in a path that by passes the first and second containers (see D1, page 15, lines 21 - 33; Figure 1, reference signs 15, 21, 22, 8, 17). Furthermore, the interface control unit is operative to enable the removal of mononuclear cells from the chamber in a path that leads to the second container and not to the first container (see D1, page 14, line 15 to page 15, line 2; page 17, lines 11 - 22; Figure 1, reference signs 15, 21, 22, 23).

There is no disclosure in D1, however, of a controller operating the pump to direct platelet-poor plasma from the first container to the second container to dilute the removed mononuclear cells in the second container.

Therefore, the blood separation system of claim 1 is novel having regard to the disclosure of D1.

2.2 The method for collecting diluted mononuclear cells set out in claim 4 comprises the feature of directing platelet-poor plasma from a first container to a second container containing mononuclear cells, thus obtaining the product of the method, namely diluted mononuclear cells. Since this feature is not disclosed in D1, the method of claim 4 is novel having regard to D1.

2.3 Document D2 belongs to the technological background of the claimed subject-matter. The board is satisfied that the contents of D2 are not prejudicial to the novelty of both the system of claim 1 and the method of claim 4 of the application.

2.4 Claims 2, 3, 5, 6, 7 and 8 are dependent claims referring to the independent claims 1 and 4, respectively. Therefore, they meet the requirement of novelty.

3. Inventive step - Article 56 EPC

3.1 The invention is concerned with blood processing systems, in particular with a system for the separation of whole blood on the one hand (see claim 1), and a method for collecting diluted mononuclear cells obtained from the separation of whole blood (see claim 4).

3.2 D1 discloses a system and a method for the centrifugal processing of a liquid, for example whole blood, to collect species which are sparse within the liquid, for example mononuclear cells (see D1, claims 1, 6; page 5, lines 18 - 22).

3.3 The board regards D1 as representing the closest prior art, as did the appellant.

3.4 Starting from D1, the technical problem underlying the application may be defined as the provision of a system and a method for the separation of whole blood leading to a product of mononuclear cells which remains pure

after dilution with plasma (see description, page 2, lines 24 - 30).

3.5 As the solution to this technical problem, the application proposes a blood processing system according to claim 1 and a method according to claim 4, characterised in that

- whole blood is separated into distinct fractions of packed red blood cells, platelet-poor plasma, platelet-rich plasma and mononuclear cells;
- thereby the process is operated under process conditions to retain platelets and mononuclear cells in the separation chamber whilst allowing for the removal of platelet-poor plasma (see claim 1, condition (i); claim 4, lines 11 to 15);
- the platelet-poor plasma is collected in a first container and subsequently used for diluting the collected mononuclear cells in a second container (see claim 1, lines 27 to 30; claim 4, lines 26 to 29);
- the platelet-rich plasma is

a) removed in turn under conditions to retain mononuclear cells in the separation chamber; and

b) eliminated from the process through a path that bypasses both the container for the platelet-poor plasma and the container for the mononuclear cells (see claim 1, condition (ii); claim 4, lines 16 to 20).

3.6 The appellant argued that the technical problem set out above is successfully solved by the claimed system and method, because only platelet-poor plasma is used to dilute the collected mononuclear cells to the desired concentration, thereby avoiding the contamination of the mononuclear cells with platelets (see grounds of

appeal dated 19 October 2004, page 4, section 4.1.1, fifth paragraph).

3.7 In the absence of any evidence to the contrary, the board accepts this explanation. In particular, it is plausible to the board that the separation of the plasma into two fractions under the specific conditions set out in claim 1, namely into a platelet-rich plasma fraction and a platelet-poor plasma fraction, allows for the use of the platelet-poor plasma thus obtained for the purpose of diluting the mononuclear cells. Thus, the level of platelets in the diluted mononuclear cell product will be low. Moreover, contamination of the mononuclear cells with red blood cells is prevented by removing the latter from both the platelet constituents and the mononuclear cells (see claim 1, lines 12 to 13). Therefore, the resulting product will be in a relatively pure state.

Therefore, the board is satisfied that the technical problem posed is solved by the claimed subject-matter.

3.8 It remains to be decided whether the claimed solution is obvious having regard to the prior art.

3.8.1 In the blood processing system and method according to D1, the mononuclear cells are accumulated behind a barrier and, once a sufficient volume of the mononuclear cells has accumulated, they are caused to spill over the barrier into a collection well (see D1, page 7, lines 9 to 11).

During the period in which mononuclear cells are being accumulated, both platelets and plasma flow

continuously past the barrier. The platelets accumulate in a well beyond the barrier. Subsequently they are removed from the blood processing system through a collect line and returned to the donor. The remaining platelet-poor plasma is collected by another collect line (see D1, page 8, lines 8 - 12; page 10, line 36 to page 11, line 1; page 14, lines 32 - 35; page 24, lines 14 - 17). During the collection of mononuclear cells, platelet-poor plasma is also collected at the plasma exit port (see D1, page 7, lines 9 - 11). In the blood processing system and method of D1, platelet-poor plasma is never collected whilst both platelets and mononuclear cells are retained in the separation chamber. According to D1 platelets and platelet-poor plasma are both collected continuously whilst the mononuclear cells are being accumulated during the accumulation phase (see D1, page 8, lines 8 - 17).

3.8.2 The board agrees with the appellant's argument according to which nothing in D1 provides an incentive to operate under specific process conditions to retain platelets and mononuclear cells in the separation chamber whilst allowing for the removal of platelet-poor plasma.

3.8.3 The board is aware of the statement contained in D1, according to which *"it may also be desirable to collect some plasma in order to dilute the white blood cell collection to a desired volume before freezing it"* (see D1, page 24, lines 20 - 22). In the board's view this statement confirms what is already known from the general technical knowledge of the skilled person, namely that plasma is a suitable diluent for the *"white blood cell collection"*, i.e. blood fractions containing

mononuclear cells. In view of the fact that the statement referred to above is of a very general nature, it cannot be regarded as a pointer towards the solution of the technical problem underlying the present invention.

3.8.4 It follows from the above that the disclosure of D1 does not provide the skilled person with an incentive to look for the claimed system and method in order to solve the technical problem posed.

3.9 The board concludes, therefore, that the subject-matter of independent claims 1 and 4, respectively, involves an inventive step as required by Articles 52(1) EPC and 56 EPC.

3.10 Dependent claims 2, 3 and 5 define particular embodiments of the system of independent claim 1, whereas dependent claims 6, 7 and 8 define particular embodiments of the method of independent claim 4. These claims derive their patentability from the independent claims 1 and 4 to which they refer.

4. Auxiliary request for oral proceedings

Since the appeal is allowed on the basis of the set of claims submitted by the appellant together with the grounds of appeal dated 19 October 2004, there is no need to hold oral proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent on the following basis:
Claims 1 to 8 annexed as Annex A to the grounds of appeal dated 19 October 2004;
Page 1 of the description filed together with the grounds of appeal dated 19 October 2004;
Pages 7, 8, 10, 11, 14, 15, 16, 19, 20, 22, 26, 29, 31, 35, 39, 41, 49, 51, 53, 55, 56 and 57 of the description filed with letter dated 29 October 2002;
Pages 2 to 6, 9, 12, 13, 17, 18, 21, 23 to 25, 27, 28, 30, 32 to 34, 36 to 38, 40, 42 to 48, 50, 52 and 54 of the description of the application as originally filed;
Sheets 6, 14, 16 to 24 and 26 to 28 of the drawings filed with letter dated 29 October 2002;
Sheets 1 to 5, 7 to 13, 15 and 25 of the drawings of the application as originally filed.

The Registrar: The Chairman:

C. Vodz G. Raths