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Datasheet for the decision of 17 July 2015

Case Number: T 1554/14 - 3.3.06

Application Number: 03761157.1

Publication Number: 1517740

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Language of the proceedings: EN

Title of invention:
TANGENTIAL FLOW FILTRATION DEVICES AND METHODS FOR LEUKOCYTE ENRICHMENT

Applicant:
NorthWest Biotherapeutics, Inc.

Headword:
Tangential flow filtration device/NW BIOTHERAPEUTICS

Relevant legal provisions:
EPC Art. 52(1), 54(2), 56, 84, 111(1), 123(2)
RPBA Art. 13(3)

Keyword:
Amendments - claim 1 - allowable (yes)
Novelty - claim 1 (yes)
Inventive step - claim 1 (yes)
Remittal to the department of first instance - (yes)

Decisions cited:

Catchword:

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Case Number: T 1554/14 - 3.3.06

D E C I S I O N
of Technical Board of Appeal 3.3.06
of 17 July 2015

Appellant: (Applicant)	NorthWest Biotherapeutics, Inc. 21720-23rd Drive SE, Suite 100 Bothell, WA 98021 (US)
Representative:	Gowshall, Jonathan Vallance Forresters Skygarden Erika-Mann-Strasse 11 80636 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 7 January 2014 refusing European patent application No. 03761157.1 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	B. Czech
Members:	E. Bendl
	C. Vallet

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse the European patent application No. 03 761 157.1.

II. In the reasons given for the refusal, the examining division referred *inter alia* to the following state of the art:

D2: WO 98/13131 A1;
D5: US 4 191 182; and
D9: US 5 695 653.

The examining division concluded that the subject-matter of the respective claims 1 according to the then pending requests was either not clear, not novel in view of D2 (figure 8), and/or not inventive in view of a combination of D9, taken as closest prior art, with D5.

III. In its statement of grounds, the appellant (applicant) submitted that the examining division's findings were erroneous because they were based on a wrong interpretation of the wording of the claims. With the statement of grounds it filed four amended claim requests.

IV. The board summoned the appellant to oral proceedings, indicating its preliminary view regarding *inter alia* the interpretation and clarity of claim 1 (regarding the shape, relative position and/or function of some elements of the claimed device), questioned generally compliance of claim 1 (combination of features) with the requirements of Article 123(2) EPC, called into question novelty and inventiveness of the claimed

device over D2 (figure 8). The board also indicated its intention to remit the case if one of the independent device claims 1 overcame the pending objections.

V. In reply to the board's communication, the appellant submitted three sets of further amended claims to replace the ones on file, arguing that the pending objections were overcome thereby.

VI. At the oral proceedings held on 17 July 2015, remaining objections under Articles 84 and/or 123(2) EPC, maintained/raised by the board against claim 1 of the amended main request then on file and regarding the shape, relative arrangement and/or function of the filter, the crossflow chamber and the inlet, were addressed. In reaction thereto, the appellant filed a new set of amended claims 1 to 56 as its sole claim request, claim 1 thereof reading as follows:

"*1. A tangential flow filtration device for preparing a cell population enriched for leukocytes by selectively removing blood constituents such as plasma, platelets and erythrocytes, comprising:*

a remover unit (1) having a cylindrical cross-flow chamber (3) and a filtrate chamber (4) separated by a circular filter (5), the filter (5) in fluid communication with the cross-flow chamber (3) and the filtrate chamber (4);

the filter diameter is substantially the same as the diameter of the crossflow chamber;

the cylindrical cross-flow chamber (3) having an inlet (6) and an outlet (7), the inlet (6) disposed adjacent to the retentate surface of the

filter to introduce a sample of blood constituents comprising leukocytes into the crossflow chamber (3) in parallel to the retentate surface of the filter (5); and the outlet (7) located adjacent to the center of the filter (5) and perpendicular to the retentate surface of the filter (5),

a pump (14) to pump fluid into the cross-flow chamber (3) through the inlet (6), and configured to introduce the fluid into the cylindrical cross-flow chamber at an input rate of 5 to 100 times the filtration rate;

wherein this arrangement causes the flow of fluid to spiral inward toward the center of the filter creating a vortex motion within the fluid, and

the filter (5) having an average pore size ranging from 3 to 8 microns such that flow of the sample across the filter (5) enriches the sample of blood constituents for leukocytes."

Claims 2 to 56 are dependent or independent claims of of the categories device, method or use. They all refer back to the device according to claim 1.

The appellant submitted that claim 1 meets the requirements of the EPC.

VII. The appellant requested that the decision under appeal be set aside and a patent be granted on the basis of the claims according to the request filed at the oral proceedings.

Reasons for the Decision

1. Admissibility of the claim request at issue

1.1 The request at issue was only filed during the oral proceedings before the board. However, the amendments to device claim 1 were all made in reply to and overcome the objections raised by the board in its communication and at the oral proceedings.

1.2 Therefore, the board decided to admit the amended claim request into the proceedings despite its late filing (Articles 114(2) EPC and 13(1)(3) RPBA).

2. Allowability of the amendments - Claim 1

2.1 The board is satisfied that the subject-matter of amended claim 1 finds a fair basis in the disclosure of the application as filed (published under the PCT as WO 2004/000444 A1) as follows:
- claim 1 (device);
- page 7, lines 1 to 2 (more details regarding purpose of the device);
- general indications on page 12, penultimate paragraph,
- figures 1A to 1C (specific embodiment of the claimed device);
- page 16, penultimate and last paragraphs description (text relating to the figures);
- page 17, first paragraph, and page 18, second paragraph (vortex motion, spiral inward flow);
- page 14, lines 26 - 27, in combination with page 13, line 3 (average pore size for leucocyte enrichment).

2.2 Claim 1 at issue therefore meets the requirements of Article 123(2) EPC.

3. Clarity and support by the description - Claim 1

3.1 The board is also satisfied that as a result of the amendments made, claim 1 at issue is clearly worded and supported by the description. In particular, the individual parts of the tangential flow filtration device are now adequately defined in terms of their shape, dimension, relative arrangement within the device, as well as their function (resulting flow pattern to be achieved).

3.2 Therefore, the requirements of Article 84 EPC are met by claim 1 at issue.

4. Novelty - Claim 1

4.1 The Board is satisfied that none of the documents cited in the first instance proceedings discloses a device with all the features of claim 1 at issue.

4.2 In particular, document D2 (see in particular figures 6 to 10), held to be novelty destroying in the decision under appeal, neither discloses an "*outlet located adjacent to the center of the filter (5) and perpendicular to the retentate surface of the filter (5)*" nor an arrangement which "*causes the flow of fluid to spiral inward toward the center of the filter creating a vortex motion within the fluid*".

4.3 Therefore, the subject-matter of claim 1 at issue is novel (Articles 52(1) and 54(1)(2) EPC).

5. Inventive step - Claim 1

5.1 The invention

The invention (see claim 1) concerns a tangential flow filtration device for leucocyte enrichment.

5.2 Closest prior art

The board accepts that D2 can be considered to represent the closest prior art, as held by the Examining Division. D2 (page 5, last paragraph, to page 7, first paragraph), like the present application, is concerned with devices suitable for leukocyte enrichment by cross-flow membrane filtration of blood including means for preventing fouling or clogging of the surface of the filter membrane (see page 6, second paragraph), whilst preventing substantial damage to the filtered cells. In the embodiment according to figure 8 of D2 (corresponding description on page 22, last paragraph, to page 26, first paragraph), a cylindrical membrane surface is rotated in the liquid to be filtered, and may additionally be oscillated to prevent clogging or fouling of the membrane surface

5.3 Technical problem

The technical problem in the light of D2 can be seen in the provision of a further tangential flow device suitable for preparing a cell population enriched for leucocytes.

5.4 Solution

As the solution to this problem, the application proposes the device according to claim 1 at issue which

is characterised *inter alia* in that its components (see full wording under VI, *supra*) are dimensioned and arranged such that the "*sample of blood constituents comprising leukocytes*" is introduced "*into the crossflow chamber (3) in parallel to the retentate surface of the filter (5)*", so as to cause, "*within the cylindrical cross-flow chamber (3)*", "*the flow of fluid to spiral inward toward the center of the filter creating a vortex motion within the fluid*".

5.5 Success of the invention

The board accepts that the posed technical problem is effectively solved by the claimed device.

In particular, it is plausible that in a filter device with all the features of claim 1, the vortex created upon operation scrubs the surface of the filter to prevent binding or stagnation at the boundary layer of the filter, as indicated on page 18, second paragraph, of the application as filed, and thereby permits efficient leukocyte enrichment without substantial lysis thereof.

Hence it remains to be assessed whether, having regard to the state of the art, the claimed device was obvious to the person skilled in the art.

5.6 Non-obviousness of the solution

5.6.1 Document D2

D2 refers also to the prevention of clogging and proposes either to use the relative movement between two concentric cylinders to create vigorous vortices (Taylor vortices) constantly sweeping the membrane

surface of the membrane surface (page 3, lines 13 to 32) or to create an oscillating pressure (paragraph bridging pages 25 and 26).

D2 does not suggest to modify the devices shown in the figures such as to arrive at a device, wherein, upon operation, the flow of fluid is caused "*to spiral inward toward the center of the filter creating a vortex motion within the fluid*" (see also 4.2, *supra*).

5.6.2 Document D9

D9 discloses devices for separating blood into a plasma-rich and a plasma-depleted fraction (column 1, lines 6 to 7, column 2, lines 13 to 20). The focus of D9 is on the recovery of red cells, platelet concentrate and/or cell free plasma with reduced stress and/or damage to the blood components (column 2, lines 53 to 61). D9 however suggests to remove leukocytes using a suitable, e.g. fibrous porous leukocyte depletion medium (column 7, line 65, to column 8, line 8). In the device illustrated by figure 5 of D9, clogging and/or fouling of the filter is prevented by imparting a spiraling flow path across and parallel to the filter surface to the blood flow by through spiral preformed "flow channels" (column 11, lines 30 to 34 and 43 to 52).

For the board, this arrangement does not, excluding hindsight considerations, suggest to modify the device of D2 in a manner leading to a device falling within the ambit of claim 1 at issue. What D9 suggests is to guide the sample flow along the circular membrane surface through spiraling preformed channels, but not to design and arrange the various components of the filter device such that upon operation a vortex flow

parallel to the filter circular surface is induced in the crossflow chamber.

5.6.3 Document D5

D5 refers to an apparatus for carrying out the separation of blood into a plasma fraction and a cellular fraction including red and white blood cells (column 1, lines 6 to 9 and 25 to 35), rather than for preparing a cell population enriched in leukocytes. Accordingly, the separation is preformed by tangential ultrafiltration, the blood flowing in parallel to the surface of a membrane with a pore size 0.1 to 1 µm, under controlled flow and shear rates to avoid hemolysis on the one hand and membrane clogging on the other hand (claim 1; column 2, lines 26 to 42). Additionally, heparin or some other suitable anticoagulant may be used to prevent clogging of the system (column 9, lines 20 to 27).

However, only rather general indications are given as regards the construction of the ultrafiltration cells and the configuration of the filter membranes used (column 8, line 35 to column 9, line 8).

D5 does not suggest either to design and arrange the various components of the filter device such that upon operation creating a vortex flow parallel to the filter circular surface is induced in the crossflow chamber by carefully positioning inlet and outlet of the sample flow.

5.6.4 As apparent from the above analysis documents D2, D9 and D5 disclose different solutions to prevent filter clogging in cross-flow blood filtration. These documents, taken alone or combination, do not however,

lead to the solution according to claim 1 at issue in an obvious manner.

The board is also satisfied that none of the other prior art documents cited in the decision under appeal discloses any more relevant information.

5.6.5 In the board's judgement, the subject-matter of claim 1 at issue thus involves an inventive step (Article 52(1) and 56 EPC).

6. Remittal to the examining division

In the decision under appeal the examining division dealt only with the the issues of clarity, novelty and inventive step as regards the respective independent (device) claims 1 according to the then pending requests. The board therefore considers is expedient to remit the case to the examining division for further prosecution, including examination of the other pending claims as to their compliance with the formal and substantial requirements of the EPC.

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 for further prosecution on the basis of the main request filed during the oral proceedings (claims 1 to 56).

The Registrar: The Chairman:

D. Magliano B. Czech

Decision electronically authenticated