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**Datasheet for the decision
of 19 May 2022**

Case Number: T 2100/18 - 3.3.02

Application Number: 11820660.6

Publication Number: 2608816

IPC: A61M1/00, A01N1/02, A61B19/00

Language of the proceedings: EN

Title of invention:

METHOD FOR ENHANCING RED BLOOD CELL QUALITY AND SURVIVAL
DURING STORAGE

Applicant:

Hemanext Inc.
Trustees of Dartmouth College

Headword:

Relevant legal provisions:

EPC Art. 56, 83, 84, 123(2)
RPBA 2020 Art. 13(2), 25(1)

Keyword:

Claims - clarity

Amendments

Inventive step

Amendment after summons

Decisions cited:

Catchword:



Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 2100/18 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 19 May 2022

Appellant: Hemanext Inc.
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Lexington, MA 02421 (US)

Appellant: Trustees of Dartmouth College
(Applicant 2) 37 Dewey Field Road
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Representative: J A Kemp LLP
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 20 March 2018
refusing European patent application No.
11820660.6 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman M. O. Müller
Members: S. Bertrand
R. Romandini

Summary of Facts and Submissions

- I. The appeal by the applicants ("appellants") lies from the examining division's decision to refuse European patent application EP 11 820 660.6 on the basis of the main request.
- II. The following documents are referred to in the present decision:
- | | |
|----|--------------|
| D1 | US 6 162 396 |
| D3 | US 4 228 032 |
- III. In the impugned decision, the examining division concluded that the subject-matter of claim 1 did not involve an inventive step in view of D3 as the closest prior art.
- IV. In their statement setting out the grounds of appeal, the appellants contested the impugned decision and submitted sets of claims in a main request and auxiliary requests 1 and 2.
- V. Following this, the board issued a communication in preparation for the oral proceedings scheduled according to the appellants' request. Objections under Articles 56, 84 and 123(2) EPC and Rule 49(10) EPC were raised in said communication.
- VI. In a further letter dated 5 May 2022, the appellants submitted auxiliary requests 3 and 4. Furthermore, a declaration by Mr S. Cooker was filed.
- VII. Oral proceedings before the board were held on 19 May 2022 by videoconference.

VIII. The appellants' case, where relevant to the present decision, may be summarised as follows.

Admittance

- The main request dealt with the board's formal objections raised in the board's communication under Article 15(1) RPBA 2020. These formal objections had not been raised by the examining division, so the appellants had no reason to make the amendments in the main request earlier in the proceedings.
- The main request should be admitted under Article 13(2) RPBA 2020.

Clarity

- The term "between" used in claim 1 did not introduce any lack of clarity as regards the term "acidified additive solution" and the pH value of 7 since the skilled person would have excluded this pH value from the wording of claim 1.

Added subject-matter

- Claim 1 was based on claim 1 as filed in combination with paragraphs [0015] and [0017].

Inventive step

- D3 was the closest prior art.
- The distinguishing feature of claim 1 was the CO₂ depletion of the red blood cell sample prior to storage in step (a) of claim 1.
- The declaration by Mr S. Cooker provided technical data demonstrating that 2,3-DPG levels were

increased when CO₂ was depleted prior to storage in comparison with CO₂ depletion during storage.

- The technical problem was to provide an enhanced method for storing blood.
- The problem was solved over the whole scope of claim 1 since the skilled person would have added an amount of acidified additive solution so as to maintain 2,3-DPG levels. This excluded overdoses of acidified additive.
- D1 and D3 did not teach how to enhance the method for storing blood disclosed in D3.
- The claimed subject-matter involved an inventive step.

IX. The appellants requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the main request filed as auxiliary request 4 with the letter dated 5 May 2022.

Reasons for the Decision

1. The appellants' only claim request is the main request filed as auxiliary request 4 with the letter of 5 May 2022. It comprises claims 1 to 10.
2. Admittance

The claims of the main request are identical to the claims of the previous main request filed with the statement of grounds of appeal, except that:

- the feature "*wherein 2,3-diphosphoglycerate (2,3-DPG) acid levels are maintained at higher levels*

during storage compared to a control sample in which carbon dioxide is not depleted prior to storage" was introduced into claim 1 of the main request,

- the unit was converted into an SI unit and the feature "*less than or equal to*" was added to claims 5 and 6 of the main request,
- the unclear term "*approximately*" was deleted from claims 6 and 7 of the main request,
- the features "*obtained from anti-coagulated whole blood*" and "*and optionally resuspended in physiological fluid*" were added to claim 8 of the main request,
- claim 9 of the main request was restricted to a step of removing leukocytes,
- the feature "*further comprising storing said oxygen- and carbon dioxide-depleted red blood cell sample*" found in claim 12 of the previous main request was replaced with "*said storing is*" in claim 10 of the main request, and
- claims 2, 10, 13 and 14 of the previous main request were deleted.

The submission of the main request after notification of the summons to oral proceedings represents an amendment to the appellants' case.

- 2.1 In line with Article 13(2) RPBA 2020, which applies to the case at hand in accordance with the transitional provisions set out in Article 25(1) RPBA 2020, any amendment to a party's appeal case made after notification of a summons to oral proceedings will, in principle, not be taken into account unless there are

exceptional circumstances, which have been justified with cogent reasons by the party concerned.

- 2.2 In the board's communication under Article 15(1) RPBA 2020, an objection of lack of clarity of claims 1, 6, 7 and 12 of the previous main request, an objection under Rule 49(10) EPC and an objection of added subject-matter for claims 1 and 9-12 of the previous main request were raised (points 6, 7 and 8 of the communication). The appellants then filed the main request on 5 May 2022. The appellants submitted that the main request dealt with the board's formal objections raised in its communication under Article 15(1) RPBA 2020. These formal objections had not been raised by the examining division, so the appellants had no reason to make the amendments in the main request earlier in the proceedings.

The board agrees that this represents, in the sense of Article 13(2) RPBA 2020, exceptional circumstances justifying the late filing of the main request during oral proceedings.

- 2.3 For this reason, the board decided to admit the main request filed during oral proceedings into the appeal proceedings.

3. Article 123(2) EPC

- 3.1 Claim 1 of the main request reads as follows:

"1. A method for enhancing red blood cell quality and survival during storage, the method comprising:

*(a) depleting a red blood cell sample **comprising an acidified additive solution having a pH between 5.5 and 7.0** of both oxygen and carbon dioxide; and*

(b) transferring said oxygen- and carbon dioxide-depleted red blood cell sample to an oxygen- and carbon dioxide-impermeable environment ~~for storage, thereby enhancing red blood cell quality and survival during storage,~~ and

(c) storing said depleted red blood cell sample in said oxygen- and carbon dioxide-impermeable environment at a temperature between 1°C and 6°C, wherein 2,3-diphosphoglycerate (2,3-DPG) acid levels are maintained at a higher level during storage compared to a control sample in which carbon dioxide is not depleted prior to storage".

(Emphasis added by the board; struck-through text and bold text represent deletions and additions, respectively, compared with claim 1 as filed).

Paragraph [0017] of the application as filed reads as follows: "... when the instant method is carried out in the presence of **acidified additive solution (i.e., an additive solution of between pH 5.5 and 7.0, or more desirably between 6.25 and 6.75), 2,3-DPG levels of the RBCs are maintained at higher levels than controls (e.g., a sample wherein carbon dioxide is not depleted)**". (Emphasis added by the board).

Paragraph [0015] refers to "*Desirably the sample is **stored between 1°C and 6°C** to further enhance the survival of the red blood cells*". (Emphasis added by the board).

Therefore, claim 1 of the main request is based on claim 1 as filed in combination with paragraphs [0015] and [0017] of the application as filed; see in particular the parts highlighted by the board.

- 3.2 Claims 2 to 4 and 7 of the main request are based on claims 3, 5, 7 and 12 as filed, respectively. Claims 5 and 6 of the main request are based on page 8, lines 27-30 of the application as filed. Claim 8 of the main request is based on the combination of claim 14 as filed and the passage on page 6, lines 8 to 10 of the application as filed. Claim 9 of the main request is based on page 6, lines 18 to 20 of the application as filed. Claim 10 of the main request is based on paragraph [0018] of the application as filed.
4. Article 84 EPC
- 4.1 In the communication under Article 15(1) RPBA 2020, the board was of the preliminary opinion that the feature "acidified additive solution having a pH of between 5.5 and 7.0" in claim 1 of the previous main request was unclear. More specifically, the term "acidified" meant that the solution was made acidic and an acidified additive solution could not have a pH of 7.0.
- 4.2 In fact, in addition, according to the decision "Athletic Alternatives, Inc. v. Prince Manufacturing, Inc.," 73 F.3d 1573 (Fed. Cir. 1996), it is not clear whether a range using the term "between" includes the limit values of this range.
- 4.3 However, in the present case, it does not need to be specified whether or not the term "between" is clear, since this term is not contained in claim 1 in isolation, but in a specific context, namely combined with the statement that the additive solution is acidified. Hence, at least in the specific context of the present case, there can be no doubt that the value of 7.0, which implies a neutral rather than an acidic pH, is excluded.

4.4 Claim 1 of the main request therefore meets the requirements of Article 84 EPC.

5. Novelty

The examining division has not raised any novelty objections and the board is convinced that the subject-matter of the claims of the main request is novel.

6. Article 56 EPC

6.1 The aim of the application as filed is to provide a method for enhancing the quality and the survival of red blood cells during storage (abstract of the application as filed). Enhancing red blood cell quality and survival during storage can be evaluated by measuring the 2,3-DPG level in the red blood cell sample. A higher 2,3-DPG level in the red blood cell sample means an enhanced red blood cell quality and survival during storage (paragraph [0018] of the application as filed).

6.2 Closest prior art

D3 (abstract and example, columns 4 and 5) is concerned with a method of improving storage of blood comprising the addition of ACD (acid citrate dextrose) to a blood sample and the depletion of CO₂ with Ca(OH)₂ compounded into silicon rubber blocks inserted in the blood storage bag. The method further comprises a storing step at a temperature of 4°C.

Therefore, in line with the examining division's decision, D3 may be considered a suitable starting point for the assessment of inventive step of the claimed subject-matter.

6.3 Distinguishing features

D3 discloses a method for enhancing red blood cell quality and survival during storage, as required by the preamble of claim 1 of the main request. D3 also discloses a red blood cell sample comprising ACD, which may be considered an acidified additive solution as required by step (a) of claim 1 of the main request. Finally, D3 discloses a step of storing the red blood cell sample in an environment at 4°C, i.e. at a temperature between 1 and 6°C as required by step (c) of claim 1 of the main request.

The distinguishing feature of claim 1 of the main request over the disclosure of D3 is at least the CO₂ depletion of the red blood cell sample **prior to** storage in step (a) of claim 1 of the main request. Contrary to this, D3 discloses CO₂ depletion only **after** transferring the blood sample into the storage bag comprising silicon rubber blocks compounded with Ca(OH)₂. This feature was also considered to be a distinguishing feature by the examining division.

6.4 Objective technical problem

As submitted by the appellants, the declaration by S. Cooker filed on 22 May 2022 provides technical data (figure 3) demonstrating that 2,3-DPG levels are increased when CO₂ is depleted prior to storage (blue curve, according to claim 1 of the main request), in comparison with an experiment in which CO₂ depletion occurs only in a blood bag (red curve, representing the teaching of D3). As set out above, a higher 2,3-DPG level in the red blood cell sample means an enhanced red blood cell quality and survival during storage.

It can thus be concluded that the red blood cell quality and survival are enhanced during storage in comparison with the method disclosed in D3.

The objective technical problem may therefore be considered that of providing a method for storing blood that leads to enhanced red blood cell quality and survival during storage.

In its communication, the board had observed that this technical problem was not solved over the whole scope of claim 1 of the main request. Claim 1 in particular comprised embodiments in which the acidified additive solution in the red blood cell sample was present in excess such that the pH of the blood came close to 5.5, at which pH the red blood cells would have died and thus would not have had any enhanced quality of survival during storage compared with D3; however, in fact, claim 1 refers to a *"method for enhancing red blood cell quality and survival during storage"*. As convincingly set out by the appellants during the oral proceedings, the skilled person, on the basis of their common general knowledge, would know that this excludes overdosing additive solution, which results in the death of the red blood cells. Hence, on the basis of their common general knowledge, the skilled person would not infer this overdosing from claim 1.

6.5 Obviousness

There is no motivation in D3 for how to enhance red blood cell quality and survival during storage. D3, as set out above, teaches the depletion of CO₂ for "maintaining the blood in storage for prolonged periods of time" during the storage of blood, and not before storage.

Hence, the solution proposed in claim 1 of the main request is not obvious in view of D3 alone.

When denying the inventive step, the examining division relied on D1. This document (abstract) teaches the depletion of O₂ from a red blood cell sample for "prolonging the storage life of the deoxygenated blood"; however, D1 does not mention anything regarding how to enhance red blood cell quality and survival during storage as per the method disclosed in D3 and does not teach removing CO₂ from the red blood cell sample before storage.

Hence, the solution proposed in claim 1 of the main request is not obvious in view of D3 in combination with D1.

- 6.6 Therefore, the subject-matter of claim 1 of the main request and, by the same token, of claims 2-10, which are dependent on claim 1, involves an inventive step.
7. The main request is allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the examining division with the order to grant a patent on the basis of the claims according to the main request filed as auxiliary request 4 with the letter of 5 May 2022 and possibly a description to be adapted to these claims.

The Registrar:

The Chairman:



N. Maslin

M. O. Müller

Decision electronically authenticated