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Datasheet for the decision of 21 May 2015

Case Number: T 2417/11 - 3.5.05
Application Number: 06826464.7
Publication Number: 1941414
IPC: G06F19/00
Language of the proceedings: EN

Title of invention:
SELECTION OF GENOTYPED TRANSFUSION DONORS BY CROSS-MATCHING TO GENOTYPED RECIPIENTS

Applicant:
BioArray Solutions Ltd.

Headword:
GENOTYPED TRANSFUSION DONORS BY CROSS-MATCHING TO GENOTYPED RECIPIENTS/BIOARRAY

Relevant legal provisions:
EPÜ 1973 Art. 56

Keyword:
Inventive step - (no)

Decisions cited:

Catchword:
Case Number: T 2417/11 - 3.5.05

DECISION
of Technical Board of Appeal 3.5.05
of 21 May 2015

Appellant: BioArray Solutions Ltd.
(Applicant)
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Decision under appeal: Decision of the Examining Division of the European Patent Office posted on 29 June 2011 refusing European patent application No. 06826464.7 pursuant to Article 97(2) EPC.

Composition of the Board:
Chair A. Ritzka
Members: M. Höhn
G. Weiss
Summary of Facts and Submissions

I. This appeal is against the decision of the examining division, posted on 29 June 2011, refusing European patent application No. 06826464.7 on the ground of lack of inventive step (Article 56 EPC 1973) with regard to prior-art publications:


D2: AMBRUSO D.R. ET AL.: "Experience with donors matched for minor blood group antigens in patients with sickle cell anemia who are receiving chronic transfusion therapy", TRANSFUSION, vol. 27, no. 1, 1987, pages 94-98,


D5: US 2005 143928 A1 (Moser et al.) and


II. The notice of appeal was received on 29 August 2011. The appeal fee was paid on the same day. The statement setting out the grounds of appeal was received on 9 November 2011. The appellant requested that the appealed decision be set aside and that a patent be
granted on the basis of the main request or first to
fourth auxiliary requests, all filed with the statement
setting out the grounds of appeal. Oral proceedings
were requested on an auxiliary basis.

III. With a communication dated 26 January 2015 the board
summoned the appellant to oral proceedings on 21 May
2015. In an annex to the summons the board expressed
its preliminary opinion that all requests lacked
inventive step (Article 56 EPC 1973). Furthermore, it
appeared that the second, third and fourth auxiliary
requests did not fulfil the requirements of Article
123(2) EPC.

IV. By letter dated 20 April 2015 the appellant submitted a
set of claims according to an amended main request,
replacing all other requests on file, supported by
arguments in favour of inventive step.

V. Independent claim 1 according to the main request reads
as follows:

"1. A method of identifying blood product donors
transfusion compatible with a particular recipient or
multiple recipients on the basis of cross-matching
transfusion antigen genotypes, comprising:
representing candidate donor and recipient minor blood
types as bit strings, where one value of a bit
represents that a particular blood type antigen is
present and another value represents that said antigen
is not present, and where the bit strings comprise a
unit of at least two bits representing an antigen
configuration of a specific phenotype;
matching the candidate donor and recipient bit strings
by respectively forming a Boolean expression between
corresponding bits of said candidate donor and
recipient bit strings, said Boolean expression being given by \{ [\beta_d ]_i \text{ AND NOT } [\beta_r ]_i \} \text{ EQ } 0, \text{ wherein } [\beta_d ]_i \text{ is the candidate donor bit for the } i\text{-th antigen and } [\beta_r ]_i \text{ is the recipient bit for the } i\text{-th antigen, wherein the Boolean expression yields a first value in the event of a match, indicating compatibility, and a second value in the event of a mismatch, indicating incompatibility; and recording results of the Boolean expression."

VI. Oral proceedings were held on 21 May 2015.

The appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed with letter dated 20 April 2015.

VII. After due consideration of the appellant's arguments the chair announced the decision.

**Reasons for the Decision**

1. **Admissibility**

The appeal complies with Articles 106 to 108 EPC (see Facts and Submissions, point II above). It is therefore admissible.

2. **Article 123(2) EPC**

2.1 The amendments made to claim 1 are supported by the formula as disclosed on page 11, line 1 as filed and in figure 2 at the bottom of the middle embodiment ("Restricted match").
Claim 1 therefore fulfils the requirements of Article 123(2) EPC.

3. Article 56 EPC 1973 - Inventive step

3.1 The board agrees that D1 can be regarded as the closest prior art which discloses a method of identifying blood product donors compatible with a particular recipient comprising matching the candidate donor and recipient minor blood group antigens (see reference made to page 743, left-hand column, line 14 to right-hand column, line 12). It is regarded as implicit in D1 that compatibility check results are recorded. Since D1 is based on phenotype-matched blood units it can be assumed that for each unit the specific phenotype is stored what requires two or more bits in its digital representation.

3.2 In the board's view the subject-matter of claim 1 differs from the method known from D1 in that:

(a) the blood group types in claim 1 are determined by first genotyping the individuals concerned for selected genes encoding blood type antigens, and consequently inferring the blood group types of the individuals from the determined genotypes ("transfusion antigen genotypes"), whereas in D1 the blood group types are determined by using serological methods;
(b1) the cross-matching of the blood group profiles is performed by evaluating the Boolean expression given by \{ [β_d]_i AND NOT [β_r]_i \} EQ 0, wherein [β_d]_i is the candidate donor bit for the i-th antigen and [β_r]_i is the recipient bit for the i-th antigen; and
(b2) the minor blood group profiles of patients and donors are represented by bit strings, wherein the Boolean expression yields a first value in the event of
a match, indicating compatibility, and a second value in the event of a mismatch, indicating incompatibility.

4. As far as feature (a) is concerned, the board concurs with the decision under appeal (see point 11.2.4 of the decision) that it does not involve an inventive step, because blood-group DNA typing was generally known at the priority date of the application (reference was made to D6, abstract).

Using the typing method of D6 instead of the serological method used in D1 solves the problem of using an alternative blood typing method.

The choice of the alternative method of D6 does not involve an inventive step, because the advantages thus achieved could be readily contemplated in advance, e.g. addressing clinical problems that cannot be addressed by serological techniques, such as the determination of antigens for which the available antibodies are only weakly reactive.

Distinguishing feature (a) is therefore considered to be obvious in view of the teaching of D6.

5. Distinguishing feature (b1) specifies a mathematical representation of the so called "Relaxed Cross-matching Rule" referred to by the appellant (see e.g. page 5 of the statement setting out the grounds of appeal). This particular cross-matching rule is described in words as "Donor Does NOT Express Antigens Not Expressed by Recipient" (see e.g. figure 2 of the present application, middle embodiment).

5.1 According to the appellant, the effect is to be regarded as avoiding the risk of allo-immunisation and
the resulting reduction of the pool of compatible donors (see e.g. point 4 of the letter dated 20 April 2015).

In accordance with the appellant (see e.g. page 5, second paragraph of the letter dated 20 April 2015), the underlying problem is therefore considered to be to identify compatible donors for blood transfusion without thereby reducing the pool of potential donors.

5.2 The provision of the particular cross-matching rule according to feature (b1) does not provide for an inventive technical contribution for the following reasons.

5.3 D4 is concerned with the application of optimization methods to the hematological support of patients and discloses several approaches for selecting donors for blood transfusion. In particular, D4 also deals with the problem of allo-immunisation, i.e. the formation of allo-antibodies in the recipient caused by so called "foreign antigens".

D4 especially discloses (see D4, page 126, third paragraph):

"There are alternative approaches, however. A patient not previously transfused will initially receive as compatible the platelets of any donor. After a period ranging from days to several weeks of retransfusions with the same foreign antigens, the patient will develop antibodies and will not respond to transfusions from donors whose platelets contain these antigens. The antibodies developed are specific for the foreign antigens which have been transfused, and the patient
will still respond well to donors containing different and new foreign antigens."

The skilled reader of D4 thereby learns that the risk of allo-immunisation is caused by donors' foreign antigens, with the effect that the pool of potential donors is constantly reduced.

The skilled person trying to solve the above-mentioned objective problem to identify compatible donors for blood transfusion without thereby reducing the pool of potential donors would therefore learn from D4 that allo-immunisation has to be avoided by not using foreign antigens.

5.4 Foreign antigens in D4 are interpreted by the board as antigens which a potential donor has, but the recipient does not have, as is clear from the use of the term "foreign". In order to identify an antigen in the donor's blood to be "foreign", knowledge about the recipient's antigens is additionally required.

In other words, the obvious conclusion from the disclosure of D4 to avoid foreign antigens for solving the objective problem amounts to no more than the relaxed cross-matching rule according to the present application expressed in different wording (with double negation) as "Donor Does NOT Express Antigens Not Expressed by Recipient" (see e.g. figure 2 of the present application, middle embodiment). The board therefore judges that the cross-matching rule underlying the mathematical expression in distinguishing feature (b1) is rendered obvious by D4.

The appellant argued that, although D4 admittedly mentioned the problem of reduction of the pool of
compatible donors caused by allo-immunisation, D4 taught an entirely different solution to this problem from that suggested by the claimed subject-matter, and that the board's interpretation of D4 and findings were based on hindsight. The board is not convinced by this argument because D4 (see p. 126, third paragraph) teaches that patients will still respond well to donors containing different and new foreign antigens, if the patient has developed antibodies in reaction to re-transfusions with the same foreign antigens, i.e. if allo-immunisation has occurred, this teaching implying in the board's view that blood transfusions with foreign antigens should be avoided at any time.

5.5 An inventive technical contribution therefore could only be achieved by an efficient implementation on a computer, of a method of identifying blood product donors' transfusion compatible with a particular recipient on the basis of the cross-matching rule according to distinguishing features (b1) and (b2) of claim 1.

5.6 The board agrees with the problem solved by distinguishing feature (b2) as set out in the decision under appeal to be that of how to represent the blood type profile of patients and prospective donors for using this representation in the patient-donor cross-matching on a computer.

5.7 In the decision under appeal the proposed solution, namely the use of bit strings and a Boolean expression, was not considered to involve an inventive step.

5.8 D4 uses a different cross-matching rule, but discloses implementing a matching rule using binary variables (see page 130, first paragraph). D4 further discloses
that a cross-matching rule for being implemented on a computer can be expressed by a mathematical formula (see e.g. equation (5) on page 135). The skilled reader of D4 would therefore consider implementing the cross-matching rule to "avoid foreign antigens" also by translation into a corresponding mathematical equation, which is considered to be a routine operation of a software programmer with ordinary skills in the art.

5.9 The appellant essentially counter-argued that qk probabilities in D4 did not refer to strings of binary values, but to strings of real values. According to the appellant, D4 did not teach a Boolean expression but an arithmetic expression with regard to equation (5) on page 135. Furthermore, recipient bit strings were donor-dependent because they showed only the presence of donors' antigens, whereas according to feature (b2) bit strings indicated both their presence and absence of a respective antigen (see e.g. page 3, 2nd par. from the bottom and page 8, 1st par. of the statement setting out the grounds of appeal).

5.10 The board notes that it considers an implementation using binary representations of data and Boolean expressions to be an obvious implementation option in view of the skilled person's general knowledge of computer implementations in the field of medicine and genetic engineering (reference is made by way of example to prior-art publication D5, paragraphs [0028] and [0029], disclosing that it was known also in the medical field to identify patterns in binary sequences of "1"s and "0"s and to use Boolean AND operations for this purpose; see also paragraph [0197] explicitly mentioning the use of binary strings). The board is convinced that those notorious programming techniques were also known in computer-implemented analysis
methods in the field of medicine and genetic engineering.

In order to identify an antigen in the donor's blood as "foreign", knowledge about the donor's and the recipient's antigens is required (see point 5.5 above). For this reason the skilled software programmer would consider also using a string for representing the recipient's antigens, i.e. to use separate strings for both the donor's and the recipient's antigens, and to compare corresponding binary values of those strings representing single antigens in order to analyse whether foreign antigens exist, indicating incompatibility. The board does not see any unexpected or surprising effect resulting from the particular implementation according to feature (b2), and in particular there are no technical hurdles to be overcome. The board therefore judges that the skilled person would have considered a respective implementation of the cross-matching rule according to feature (b1) on a computer without the need for inventive skills in view of the disclosure of D4 with regard to the common general knowledge in the art.

5.11 The appellant's arguments presented with the statement setting out the grounds of appeal and during the oral proceedings therefore did not convince the board.

5.12 Since both D1 and D4 are concerned with estimating the compatibility between recipients and donors, the board agrees with the decision under appeal that the skilled person would combine their teaching without any inventive effort. Distinguishing features (b1) and (b2) are therefore rendered obvious by a combination of D1 and D4 in view of the skilled person's common general knowledge.
6. The board furthermore agrees with the decision under appeal that no combined synergistic effect is produced by distinguishing features (a) and (b) going beyond their respective effects, which are therefore considered to be a mere juxtaposition.

6.1 In the board's judgement, the appellant has not overcome the objection under Article 56 EPC 1973 for lack of inventive step against the subject-matter of claim 1 in the decision under appeal.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: 

The Chair:

K. Götz-Wein 

A. Ritzka

Decision electronically authenticated