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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:

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Case Number: **T 2417/11 - 3.5.05**

D E C I S I O N
of Technical Board of Appeal 3.5.05
of 21 May 2015

Appellant: (Applicant)	BioArray Solutions Ltd. 35 Technology Drive, Suite 100 Warren, NJ 07059 (US)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
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:

        D1:   LAU F.Y. ET AL.: "Provision of phenotype-
        matched blood units: no need for pre-transfusion
        antibody screening", HAEMATOLOGICA, vol. 86, no. 7,
        July 2001 (2001-07), pages 742-748,
        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,
        D3:   WORKING PARTY OF THE BCSH: "Guidelines for
        compatibility procedures in blood transfusion
        laboratories", TRANSFUSION MEDICINE, vol. 14, 2004,
        pages 59-73,
        D4:   SIMON R.: "Application of Optimization Methods
        to the Hematological Support of Patients with
        Disseminated Malignancies", MATHEMATICAL BIOSCIENCES,
        vol. 25, 1975, pages 125-138,
        D5:   US 2005 143928 A1 (Moser et al.) and
        D6:   HASHMI GHAZALA ET AL.: "A flexible array format
        for large-scale, rapid blood group DNA typing",
        TRANSFUSION, vol. 45, no. 5, 1 May 2005 (2005-05-01),
        pages 680-688.

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 { $[\beta_d]_i$ AND NOT $[\beta_r]_i$ } EQ 0, wherein $[\beta_d]_i$ is the candidate donor bit for the i-th antigen and $[\beta_r]_i$ is the recipient bit for the i-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
        $\{ [\beta_d]_i \text{ AND NOT } [\beta_r]_i \} \text{ EQ } 0$, wherein $[\beta_d]_i$ is the
        candidate donor bit for the i-th antigen and $[\beta_r]_i$ 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