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Datasheet for the decision of 25 April 2019

Case Number: T 1759/12 - 3.3.08

Application Number: 98910143.1

Publication Number: 0975810

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Language of the proceedings: EN

Title of invention:
Method of PCR testing of pooled blood samples

Patent Proprietor:
Baxalta Incorporated
Baxalta GmbH

Opponent:
Octapharma AG

Headword:
Blood sample testing/BAXALTA

Relevant legal provisions:
EPC Art. 54, 56, 83, 84, 99, 117(1), 123(2)
EPC R. 76, 77, 115(2)
RPBA Art. 12(4), 15(3)

Keyword:
Admissibility of opposition - yes
Admission of auxiliary request 3 - yes
Hearing of witnesses - no
Main request and auxiliary requests 1 to 3 - inventive step - no
Auxiliary request 4 - requirements of the EPC met - yes

Decisions cited:
T 1422/12

Catchword:

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 1759/12 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 25 April 2019

Appellant I: (Patent Proprietor 01)	Baxalta Incorporated 1200 Lakeside Drive Bannockburn, IL 60015 (US)
Appellant I: (Patent Proprietor 02)	Baxalta GmbH Thurgauerstrasse 130 8152 Glattpark, Opfikon (CH)
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Appellant II: (Opponent)	Octapharma AG Seidenstrasse 2 8853 Lachen (CH)
Representative:	Diepholz, Meikel Patent- und Rechtsanwälte Ullrich & Naumann PartG mbB Schneidmühlstrasse 21 69115 Heidelberg (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 22 May 2012 concerning maintenance of the European Patent No. 0975810 in amended form.**

Composition of the Board:

Chairman	B. Stolz
Members:	M. Montrone
	R. Winkelhofer

Summary of Facts and Submissions

I. Appeals were lodged by the patent proprietors (hereinafter "appellant I") and the opponent (hereinafter "appellant II") against the decision of an opposition division to maintain the European patent No. 0 975 810 in amended form, which was filed as an international application and published as WO 98/30723 (hereinafter the "patent application").

II. In the decision under appeal, the opposition division held that the main request (claims as granted) and auxiliary requests 1 and 4 contravened Article 123(2) EPC, while auxiliary requests 2 and 3 contravened Article 56 EPC. It further took the view that auxiliary request 5 and pages of the description adapted thereto complied with the requirements of the EPC.

III. With its statement of grounds of appeal, appellant I submitted nine auxiliary requests. Present auxiliary requests 1, 2, 4, 5, 7 and 8 correspond to auxiliary requests 2, 3, 5, 6, 8 and 9 respectively, in the decision under appeal. Present auxiliary requests 3, 6 and 9 are new to the proceedings.

IV. With its statement of grounds of appeal, appellant II submitted arguments as to why the subject-matter of auxiliary request 5 as maintained by the opposition division (i.e. auxiliary request 4 in the appeal proceedings) comprised added subject-matter, lacked clarity and inventive step, and was insufficiently disclosed.

V. The board informed the parties that the term of the patent in suit pursuant to Article 63(1) EPC had expired and asked whether or not the appeal proceedings

should be continued. In reply, appellant I requested that the proceedings be continued.

VI. The parties were summoned to oral proceedings. In a communication pursuant to Article 15(1) RPBA, the parties were informed of the board's provisional, non-binding opinion on some of the legal and substantive matters of the case. In reply thereto, appellant II announced that it would not be attending the oral proceedings, without however, submitting substantive arguments in response to any of the issues raised in the board's communication.

VII. Oral proceedings before the board were held on 25 April 2019, in the absence of appellant II.

VIII. Claim 1 of the main request reads:

"1. A method for uniquely identifying viral positive biological fluid donations, the method comprising:
providing a multiplicity of biological fluid donations;
defining an n-dimensional matrix, where n is an integer, the matrix further comprising a multiplicity of internal elements, each element defined by an intersection of the n-dimensions of the matrix, each individual element identified by a respective matrix notation, the matrix notation comprising an index for each dimension of the array;

taking a sample from each of the biological fluid donations;
mapping each sample to a respective particular one of each element of the matrix, each individual sample identified by its corresponding element’s respective matrix notation; taking aliquots from each sample, the

number of aliquots taken from each sample defined by the number of dimensions characterizing the matrix;
forming subpools from the aliquots of each sample, each subpool containing an aliquot from all samples identified by a matrix notation in which one dimensional index is fixed, each respective subpool identified by said fixed dimensional index;
testing each subpool via a PCR test for viral indication;
determining the respective dimensional indices of subpools which return a positive viral indication; and
combining said dimensional indices into a matrix notation thereby unambiguously identifying a unique matrix element defined by the matrix notation, thus unambiguously identifying a uniquely viral positive sample."

IX. Claim 1 of auxiliary request 1 differs from that of the main request in that the feature "*where n is an integer*" has been replaced by "*where n is any integer from 2 to N*".

X. Claim 1 of auxiliary request 2 differs from that of the main request in that the feature "*where n is an integer*" has been replaced by "*where n is any integer from 2 to N*", and in that the feature "*wherein the subpools are all tested at once in a single PCR testing cycle*" has been added.

XI. Claim 1 of auxiliary request 3 differs from that of the main request in that the feature "*where n is an integer*" has been replaced by "*where n is any integer from 2 to N*", and in that the feature "*forming a single master pool by combining an aliquot of each sample or an aliquot of each of the subpools, the master pool containing a sample from all of the donations;*

performing a PCR test for viral indication on the master pool, and if the PCR test of the master pool is positive, the following steps are carried out:
testing each subpool via a PCR test for viral indication, wherein the subpools are all tested at once in a single PCR testing cycle;" has been added.

XII. Claim 1 of auxiliary request 4 differs from that of the main request in that the feature "*where n is an integer*" has been replaced by "*where n is any integer from 3 to N*".

Furthermore, claim 10 of auxiliary request 4 reads:

"10. A method for uniquely identifying viral positive biological fluid donations, the method comprising:
providing a multiplicity of biological fluid donations;
defining an n-dimensional matrix, where n is any integer from 3 to N, the matrix further comprising a multiplicity of internal elements, each element defined by an intersection of the n-dimensions of the matrix, where each individual element identified by a respective matrix notation $X_{i...N}$, wherein the subscript of the matrix notation defines the dimensional indices of the array;
taking N aliquots from each sample of each of the biological fluid donations, the number of aliquots taken from each sample defined by the number of dimensional indices comprising the array;
forming subpools from the aliquots of each sample, each subpool comprising an aliquot from all of the samples identified by a matrix notation in which one dimensional index is fixed;
testing each subpool via a PCR test for viral indication; and

evaluating the dimensional indicia of each subpool which returned a viral positive indication in the first PCR test, in accordance with a reduction by the method of minors, the evaluation identifying a unique element defined by the dimensional indicia of each positive subpool if only a single subpool representing each dimensional index returns a positive viral indication, thus unambiguously identifying a viral positive sample".

Claims 2 to 9 and 11 to 19 define preferred embodiments of claims 1 and 10, respectively.

XIII. The following documents are referred to in this decision:

D1: V. Schottstedt *et al.*, Beiträge zur Transfusionsmedizin, 1996, Vol. 12: 13-17;

D2: Conference Program: "International Conference on the Virological Safety of Plasma Derivatives", November 1996, including an attached speech manuscript of V. Schottstedt *et al.*;

D3: V. Schottstedt, "SLT Applikation", dated September 1996, 1-3;

D4: P. M. Rogers *et al.*, Vox Sanguinis, 1997, Vol. 72: 199-206;

D5: Program of the workshop on "Nucleic Acid Amplification Tests for the Detection of Blood Borne Viruses", October 1996, Amsterdam, The Netherlands;

D6: List of Participants: EPFA/NIBSC workshop on NAT,

31 October 1996, Amsterdam, The Netherlands.

XIV. Appellant I's submissions, insofar as relevant to the present decision, may be summarised as follows:

Admissibility of the opposition (Article 99 EPC, Rules 76 and 77 EPC)

The opposition was inadmissible. The grounds for opposition were insufficiently substantiated since, with regard to novelty, the notice of opposition did not indicate the facts, evidence and arguments as required by Rule 76(2)(c) EPC concerning the disclosure of document D1, while documents D2 to D4 lacked relevance.

Admission of auxiliary request 3 into the appeal proceedings

Auxiliary request 3 should be admitted into the appeal proceedings. This request could not have been filed earlier than with the statement of grounds of appeal, because it addressed an objection under Article 123(2) EPC which came up only during the oral proceedings before the opposition division.

Main request (claims as granted)

Inventive step (Article 56 EPC) - claim 1

Document D1 represented the closest prior art. Claim 1 was directed to several embodiments, including a method for uniquely identifying viral positive biological fluid donations in a 2-dimensional matrix. This method differed from that of document D1 in that only two aliquots were taken from each sample instead of three,

which allowed the claimed method to be carried out in less time with a lower number of required disposable tips for pipetting. In other words, the claimed method produced results faster and at significantly reduced costs compared to that of the closest prior art. Furthermore, the claimed method was easier to be upscaled for analysing large sample sizes. Accordingly, the technical problem to be solved was the provision of an improved method for uniquely identifying viral positive biological fluid donations.

The skilled person starting from the method of document D1 would not have arrived at the method according to claim 1 in an obvious manner, since the use of a reduced number of sample aliquots was not pointed at or otherwise suggested in document D1. Furthermore, Figure 1 in document D1 disclosed an assay wherein 600 blood samples were analysed by three PCR tests, i.e. a multi-step approach. Thus, single PCRs of the whole assay could not be picked out in isolation, in particular not the third one which analysed 96 samples only, a capacity too low for analysing 600 samples. The skilled person would also not have used the PCR assay disclosed in document D1 for analysing less than 600 samples, because the assay was developed for the large sample sizes commonly encountered by services handling blood donations. Even if the skilled person would have considered its use for smaller sample sizes, he or she would have performed the complete three step approach disclosed in document D1 using microtiter plates of a reduced array size, because the total number of required PCR reactions was smaller in an assay based on three PCRs compared to one or two PCRs.

Auxiliary requests 1 to 3

Inventive step (Article 56 EPC) - claim 1

The method according to claims 1 of auxiliary requests 2 and 3 required *inter alia* that the "*subpools are all tested at once in a single PCR testing cycle*". Such a test concept was fundamentally different from that disclosed in document D1, which was based on a multi-step approach. This concept had the effect that the number of required PCR test cycles was reduced and that virus loss during storage of the subpools was avoided. Thus, the claimed methods were inventive.

Auxiliary request 4

Articles 123(2) EPC - claims 1 and 10

The feature "*where n is any integer from 3 to N*" in claims 1 and 10 had a basis in claim 2 as originally filed in conjunction with the disclosure on page 30, lines 1 and 2 of the patent application, since the terms "*grid*" and "*matrix*" were used interchangeably (see e.g. page 29, line 38 of the patent application).

Article 84 EPC - claims 1 and 10

The range "*from 3 to N*" as recited in claims 1 and 10 was clear, since the "to" in this range necessarily implied that the variable "*N*" related to a value higher than three. Furthermore, a skilled person willing to understand the subject-matter of the claims would have immediately realised that a counting down from three to a smaller value was in the present case technically not sensible. In particular, since this was in conflict with the need to identify the elements at a dimensional

"*intersection*", which however was lacking in matrices characterised by "*N*" being 1 or 0.

Article 83 EPC - claims 1 and 10

The concept of using matrices encompassing dimensions higher than three as referred to in claims 1 and 10 was mathematically defined by specific variables assigned to any dimension of the matrix, and hence, not restricted to matrices consisting of two or three dimensions only, i.e. spatial dimensions. Therefore, the inventions defined in claims 1 and 10 were sufficiently disclosed.

Inventive step (Article 56 EPC) - claims 1 and 10

Document D1 represented the closest prior art. The methods of claims 1 and 10 differed from that of document D1 in a matrix having at least three dimensions instead of two. This had the effect that the number of required PCR tests to be carried out for analysing large numbers of samples was reduced. Consequently, the technical problem was defined as the provision of a process for testing a large number of blood or plasma samples by using a small number of PCR tests only. The subject-matter of claims 1 and 10 provided a non-obvious solution to this problem, since none of the available prior art documents suggested the advantageous effects obtained by using a matrix as referred to in claim 1.

XV. Appellant II's submissions, insofar as relevant to the present decision, may be summarised as follows:

Admissibility of the opposition (Article 99 EPC, Rules 76 and 77 EPC)

The opposition was admissible.

Admission of auxiliary request 3 into the appeal proceedings

Auxiliary request 3 should not be admitted into the appeal proceedings because it could have been filed in the first instance proceedings to overcome the objection under Article 123(2) EPC raised against the then auxiliary request 4 (Article 12(4) RPBA).

Witness hearings (Article 117(1) EPC)

Mr. V. Schottstedt and Dr. T. Gärtner should be heard as witnesses to provide evidence that the methods of claims 1 and 10 were anticipated by the disclosure of documents D2 and D4 to D6.

Auxiliary request 4

Article 123(2) EPC - claims 1 and 10

Claims 1 and 10 comprised added subject-matter because the feature "*where n is any integer from 3 to N*" had no literal basis in the patent application. Moreover this feature encompassed any matrix with at least 3-dimensions irrespective of its structure, while the patent application disclosed in the paragraph bridging pages 29 and 30 for such a matrix a "*square*" form only. A basis for the generic term "*matrix*" in claims 1 and 10 was also not derivable from claim 2 as originally filed, which disclosed a "*grid*", i.e. a specific embodiment of a matrix.

Article 84 EPC - claims 1 and 10

The feature "*3 to N*" in claims 1 and 10 lacked clarity and support. The variable "*N*" in that range might relate to a value smaller than three, since it was common in the art to count backwards, for example, in "*Count-down*" situations. Furthermore, the feature "*where n is any integer from 3 to N*" lacked support in the description.

Article 83 EPC - claims 1 and 10

The methods of claims 1 and 10 were characterised by mapping sample aliquots to elements in matrices comprising *inter alia* more than three dimensions. However, the patent application did neither disclose a matrix having more than three dimensions nor contained information how such a mapping of samples to elements in matrices exceeding three dimensions could be achieved. Consequently, the inventions defined in claims 1 and 10 were insufficiently disclosed.

Inventive step (Article 56 EPC) - claims 1 and 10

Document D1 represented the closest prior art. The subject-matter of claims 1 and 10 differed therefrom in that the matrix was at least 3-dimensional, contrary to a 2-dimensional matrix. The technical problem to be solved was considered as the provision of a method for identifying viral positive blood donations wherein the sample aliquots were arranged in an alternative manner. Starting from a 2-dimensional sample arrangement disclosed in document D1, the skilled person arrived in an obvious manner at a 3-dimensional sample arrangement because this required a mere stacking of microtiter

plates on top of each other. Further, the problem was not solved across the whole scope of the claims, since a mapping of samples to elements in matrices exceeding three dimensions was not enabled.

XVI. Appellant I requested that the decision under appeal be set aside and that the opposition be rejected as inadmissible, or that the patent be maintained either on the basis of the main request, i.e. the claims as granted, or in the alternative, on the basis of one of auxiliary requests 1 to 9.

XVII. Appellant II requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

Reasons for the Decision

1. The duly summoned appellant II did not attend the oral proceedings, which in accordance with Rule 115(2) EPC and Article 15(3) RPBA took place in its absence.

Admissibility of the opposition (Article 99 EPC, Rules 76 and 77 EPC)

2. Appellant I submitted that the opposition was not admissible because the opponent (appellant II) did not sufficiently substantiate its novelty objection therein.

3. The notice of opposition objects to the patent in suit not only on the ground of Article 100(a) EPC for lack of novelty (Article 54 EPC), but also on lack of inventive step (Article 56 EPC) and insufficiency of disclosure (Article 100(b) EPC) (see page 2, first two

paragraphs). It is established case law that an opposition is admissible if at least one of the grounds of opposition is sufficiently substantiated in the notice of opposition (see Case Law of the Boards of Appeal, 2016, 8th edition (hereinafter "CLBA"), IV.D. 2.2.7). Since appellant I has not objected to the opponent's (appellant II) substantiation as being insufficient with regard to all of the grounds, except for novelty, already from the outset it cannot succeed.

4. Thus, the opposition is admissible.

Admission of auxiliary request 3 into the appeal proceedings (Article 12(4) RPBA)

5. Auxiliary request 3 was filed by appellant I with its statement of grounds of appeal (see section III above). According to Article 12(1) and (4) RPBA, the request would therefore normally be, as a rule, part of the appeal proceedings. With reference to Article 12(4) RPBA, however, this rule does not apply under all circumstances, since the provision refers to the power of the boards of appeal to hold inadmissible, i.e. exclude, *inter alia* requests filed for the first time with the statement of grounds of appeal which could have been filed during the first instance proceedings.

6. In its communication in preparation of the oral proceedings, the board explicitly addressed the issue of admission of auxiliary request 3 into the appeal proceedings. In this context it was observed that the amendments in claims 1 and 10 of present auxiliary request 3 directly addressed an issue under Article 123(2) EPC that was raised by the opponent against the corresponding claims in auxiliary requests 1 and 4 during the first instance proceedings. This issue came

up only during the oral proceedings before the opposition division, although the opponent was aware of these sets of claims from the onset of the opposition proceedings (see points 18 and 19 of the board's communication).

7. Appellant II neither provided any substantive comments or arguments in reply to the board's positive provisional opinion on the admission of auxiliary request 3, nor attended the oral proceedings (see point VII supra).

8. In these circumstances, auxiliary request 3 is admitted into the appeal proceedings.

Witness hearings (Article 117(1) EPC)

9. Appellant II requested the hearing of witnesses for providing evidence that (i) documents D2 to D4 were publicly available before the claimed priority date of the patent, and (ii) that the claimed subject-matter was anticipated by the disclosure of documents D2, D5 and D6.

10. In its communication in preparation of the oral proceedings, the board addressed the issue of witness hearings. In this context, the opinion was expressed that the disclosure of documents D2 to D6 did not add any information that went beyond the disclosure of document D1, and that in these circumstances the hearing of witnesses on the issues of the documents' public availability and disclosure was not necessary.

11. Despite the board's negative opinion on hearing witnesses, appellant II neither provided substantive comments or arguments nor attended the oral

proceedings. Accordingly, for the reasons given therein, witnesses were not heard.

Main request (claims as granted)

Claim interpretation - claim 1

12. Claim 1 is directed to a method for uniquely identifying viral positive biological fluid donations, which encompasses blood donation samples. The method **comprises** various process steps. In other words, the claim is openly defined and allows for the presence of other process steps in addition to those explicitly recited in the claim.

12.1 The method **comprises** the steps of, firstly, defining an n-dimensional matrix comprising a multiplicity of elements. Each element is defined by its position at a dimensional intersection in the matrix and a notation, while the matrix itself is defined by an index for each dimension. In other words, in a 2-dimensional matrix, for example, consisting of columns (first dimension) and rows (second dimension) each element is uniquely identified at the intersection (crossing) of the column and the row to which different letters and/or numbers ("indexes") have been allocated.

12.2 In a second step, each sample from a multiplicity of fluid donations is mapped to a particular element in the matrix which allows its unique identification. Then aliquots of these samples, i.e. sub-samples are taken. Their number is defined by the number of dimensions characterising the matrix, for example, two in a 2-dimensional matrix.

12.3 In a further step, all sample aliquots belonging to a single notation and a single dimensional index of the matrix are pooled, for example, in a 2-dimensional matrix all samples of the same row and the same column.

12.4 Each of the pooled samples are then tested by PCR for detecting a potential viral contamination. In case one of the pools is tested viral positive, the unique indexing of the pools in the elements of the matrix allows the identification of the single virus-positive sample donor.

13. The term "*n-dimensional matrix*" referred to in claim 1 is not defined and, hence, encompasses any number of dimensions. In the board's opinion, the skilled person would construe this term to relate to an abstract concept that is mathematically defined by variables, such as integers, notations and indexes. Thus, an n-dimensional matrix according to claim 1 is not confined to the physical space of two dimensions (N=2, e.g. a microtiter plate), or three dimensions (N=3, e.g. a cube), but encompasses an undefined number of higher dimensions, such as N=4 (e.g. a row of cubes), N=5 (e.g. rows of cubes on a table), N=6 (e.g. rows of cubes on tables in different rooms) etc. The indexing of each dimension allows the unique identification of samples/elements in the matrix.

14. Furthermore, the term "*multiplicity*" in relation to biological fluid donations and internal matrix elements as referred to in claim 1 has a relative meaning. In the board's view, this term means at least two or more. Thus, claim 1 encompasses the provision of fluid donation samples to be tested and matrices with internal elements in any number exceeding one.

Inventive step (Article 56 EPC) - claim 1

Closest prior art

15. It is uncontested that document D1 represents the closest prior art for the method according to claim 1.

16. Document D1 discloses a PCR-based method for uniquely identifying virus-contaminated samples of blood donations, which requires that up to three separate PCR tests are performed on different pools of samples. In order to identify virus-positive blood samples, aliquots of each sample are filled in wells of three sets of identical microtiter plates containing 96 sample wells, i.e. one set of plates for each of the three PCR tests (see page 13, column 2, first and second paragraphs, Figure 1 on page 17).

16.1 In a first PCR test, a **single** so-called master pool sample containing aliquots from **all** the blood samples to be tested (**maximum of 600**) is examined for the presence of a potential virus contamination (see page 13, column 2, second paragraph, Figure 1, left part). In case the sample of the master pool is virus-positive, two additional PCR tests are required for identifying the contaminated donor sample(s).

16.2 The second PCR test aims at the identification of the one or more microtiter plates containing a virus-positive sample. For this purpose pools of samples derived from **one** microtiter plate only are generated, i.e. each pool contains a **maximum of 96** samples (see page 13, column 2, last paragraph to page 14, column 1, first paragraph and Figure 1, middle part).

16.3 The third PCR test serves the identification of a single virus-positive sample. This is achieved by forming subpools of samples derived from each column (indexed as "*1 - 12*") and row (indexed as A to H ("*A bis H*")) of the microtiter plate previously tested virus-positive. All of these subpools are analysed in a single PCR test cycle at the same time. The virus-positive sample(s) is/are located in the well positioned at the crossing, i.e. the intersection, of a virus-positive "row" and "column" sample pool (see page 14, column 1, first paragraph and Figure 1, right part).

16.4 It is uncontested that the microtiter plates of Figure 1 in document D1 represent 2-dimensional matrices with 96 internal elements.

17. As set out above (see points 13 and 14), the method according to claim 1 encompasses various embodiments, including a method wherein the matrix may consist of two dimensions (N=2) and contains 96 sample elements - like the microtiter plate disclosed in document D1. This embodiment of claim 1 will be considered in the following.

18. As likewise set out above (see point 12), the method of claim 1, and accordingly the embodiment under consideration, is openly defined and allows for the presence of further unspecified process steps, for example the first and the second PCR test reported in document D1 (see above). Thus, the claimed embodiment differs from the method disclosed in Figure 1 of document D1 only in that two aliquots are taken from each sample, instead of three.

19. Appellant I argued that the technical effects ascribed to this difference were a faster and cheaper method, in particular in situations with large sample numbers. Hence the technical problem underlying the claimed method consisted in providing an improved method for uniquely identifying viral positive biological fluid donations.

20. According to established case law, only the effects actually achieved vis-à-vis the closest prior art are to be be taken into account for the determination of the technical problem. Furthermore, the effect has to be attained throughout the entire range covered by the claim (see Case Law of the Boards of Appeal, I.D.4.1, including T 1422/12 of 11 April 2013 cited therein, and I.D.4.3).

21. As set out above, the claimed method is not limited to the analysis of "large" sample numbers, due to the relative meaning of the term "*multiplicity*", which may encompass any number exceeding one. In the board's opinion, and contrary to appellant I's view, the same applies to the teaching of document D1 for the following reasons:

22. The board agrees with appellant I that the PCR-based assay reported in document D1 was developed to overcome technical problems and high costs associated with a PCR testing of single blood samples (see page 13, second column, line 1 *et seq*. which reads as follows: "*Die PCR (Polymerase-Ketten-Reaktion = Virusdirektnachweis durch Suche nach Viruserbinformation) als theoretisch geeignetes Tool ist derzeit aus technischen und Kostengründen noch nicht routinemäßig für das separate Screening jeder Einzelspende bei großen Blutspendediensten einzusetzen. Um dennoch die*

unbestrittenen Vorteile der PCR nutzen und Erfahrungen sammeln zu können..." (emphasis added)).

23. However, since already the pooling of some samples compared to a single sample to be tested by PCR provides cost and logistic advantages, the skilled person would rather derive from this passage in document D1, that pools containing far less than the 600 samples explicitly mentioned in document D1 likewise benefit from these advantages.

24. This view is further supported by the mentioning of a pool of "*maximal 600*" or a "*max. 600er Pool*" of single samples in document D1 (see page 13, column 2, second paragraph, Figure 1, left part). The term "*maximal*" in this context explicitly teaches the skilled person that the assay may be used for pools of samples well below that number, because it defines solely the upper limit.

25. There are also no technical reasons indicated in document D1 that would deter the skilled person from applying the PCR test to pools of samples of lower numbers. On the contrary, the document teaches that pools of 600 samples are defined as maximum, because at this size the sensitivity of the PCR still equals that of the available commercial kits for testing single blood samples (see page 14, column 2, first and second paragraph reading as follows: "*Die in der täglichen Routine erreichbare Testsensitivität (Virus-konzentration bei einem positiven Spender in einem Pool von 599 virusfreien Spenden) liegt bei [...]. Damit wird mindestens die gleiche Nachweisempfindlichkeit wie bei Testung von Einzelspenden mit den heute verfügbaren kommerziellen Testkits erreicht*", emphasis added). In other words, the reliability of the PCR to detect a single virus contamination in a pool of 600 blood

samples equals that of analysing samples individually, or pools containing up to 600 samples do not negatively affect the PCR sensitivity under the experimental conditions disclosed in document D1.

26. Likewise the mentioning of about "*3000*" blood samples as the daily workload of the German Red Cross in a specific federal state in Germany (see paragraph bridging page 14 and 15 of document D1) does not teach the skilled person that the assay cannot be used for smaller numbers of blood samples. The skilled person is aware that the number of blood donations varies since the donation is voluntary, and that a need exists for testing them quickly, irrespective of their numbers, because donated blood has a limited storage stability.

27. In view of the considerations above, the skilled person would use the PCR assay disclosed in document D1 to test for potential virus contaminations in blood samples where the total number of blood samples does not exceed 96, i.e. the number of wells found on a single microtiter plate.

28. In these circumstances, the skilled person would further derive from Figure 1 in document D1 that three separate PCR tests for identifying a virus-positive sample are not necessary - but only two, because the sample pool to be examined by the first and the second PCR test is identical. As a consequence thereof, the skilled person would recognise that there is no need for taking three sample aliquots from each sample - but only two, because the number of aliquots equals the maximum number of PCR tests in the assay.

29. Appellant I argued that the skilled person in the light of the teaching of document D1 would strictly follow

the complete three-step PCR approach disclosed in Figure 1, since the overall amount of required PCR reactions was lower compared to a single or a two-step PCR test. However, as set out above in situations with up to 96 samples the first PCR test is superfluous and document D1 does solely disclose microtiter plates with 96 wells. Hence, this argument is not convincing.

30. In view of the considerations above, the board concludes that the claimed embodiment under consideration does not achieve the technical advantages asserted by appellant I when compared to the closest prior art method. Thus, in line with the case law (see above), the technical problem is defined as the provision of an alternative method for uniquely identifying viral positive biological fluid donation samples.

31. The method according to claim 1 solves this problem.

Obviousness

32. As set out above, in situations where the sample size to be pooled does not exceed the number of wells on a single microtiter plate, the skilled person starting from the closest prior art method would immediately recognise that the taking of three sample aliquots instead of two is superfluous, because the pools to be tested for a potential virus contamination by the first and the second PCR test as disclosed in Figure 1 of document D1 are identical.

33. In these circumstances, the skilled person starting from the closest prior art method and faced with the above mentioned problem, would arrive in an obvious manner at the embodiment under consideration.

34. Thus, the method according to claim 1 of the main request contravenes Article 56 EPC.

Auxiliary requests 1 to 3

Inventive step (Article 56 EPC) - claim 1

35. Claim 1 of **auxiliary request 1** embraces the embodiment considered above with regard to the main request (see section X above).

36. This embodiment is also encompassed by the method of claim 1 of **auxiliary request 2** which differs from that of auxiliary request 1 in that the feature "*wherein the subpools are all tested at once in a single PCR testing cycle*" has been added.

36.1 As set out above (see point 16.3), the third PCR test disclosed in Figure 1 of document D1 tests all subpools at the same time in a single cycle.

36.2 Furthermore, like claim 1 of the main request, claim 1 of auxiliary request 2 defines the method "openly", i.e. the claimed method may comprise further process steps in addition to the ones explicitly cited (see above). In view of these considerations, the feature "*wherein the subpools are all tested at once in a single PCR testing cycle*" cannot be construed to relate to all process steps that may be present in claim 1, but only to those explicitly cited. Thus, contrary to appellant I's view, claim 1 of auxiliary request 2 does not relate to a concept fundamentally different from that disclosed in document D1.

37. Claim 1 of **auxiliary request 3** differs from that of auxiliary request 1 in that the feature "*forming a single master pool by combining an aliquot of each sample or an aliquot of each of the subpools, the master pool containing a sample from all of the donations;*
performing a PCR test for viral indication on the master pool, and if the PCR test of the master pool is positive, the following steps are carried out:
testing each subpool via a PCR test for viral indication, wherein the subpools are all tested at once in a single PCR testing cycle;" has been added.

38. This feature in claim 1 of auxiliary request 3 is identical to the formation of a master pool that contains aliquots of all samples to be examined by PCR for a potential virus contamination as disclosed in document D1 (see point 16.1, above). Thus, the reasons set out above for the embodiment under consideration of claim 1 of the main request and auxiliary request 2, likewise apply to the method according to claim 1 of auxiliary request 3.

39. Consequently, the arguments set out above for the embodiment under consideration of claim 1 of the main request likewise apply to the method of claims 1 of auxiliary requests 1 to 3, which likewise contravene Article 56 EPC.

Auxiliary request 4

Article 123(2) EPC - claims 1 and 10

40. The issue to be assessed with regard to Article 123(2) EPC in relation to the subject-matter of claims 1 and 10 of auxiliary request 4 is whether or not the feature

"*where n is any integer from 3 to N*" can be directly and unambiguously derived by the skilled person, using common general knowledge, from the patent application as a whole.

41. Claim 2 as originally filed read as follows: "*The method according to claim 1, wherein the n-dimensional grid is at least a 3-dimensional grid*" (emphasis added). Moreover, page 29, line 38 to page 30, line 2 of the patent application discloses that "*The method begins in block 301 by defining an N-dimensional sample matrix or grid. The matrix may be of any size and comprise any number of dimensions from 2 to N, but preferably is a 3-dimensional regular matrix, organized as a square*" (emphasis added).

42. Claim 2 as originally filed discloses literally the contested feature of present claims 1 and 10, except for the term "*matrix*", for which the term "*grid*" is used. However, page 29, line 38 of the patent application discloses that the method either defines a "*N-dimensional sample matrix or grid*". In other words, the terms matrix and grid are used interchangeably in the patent application, i.e. a "*grid*" is not a specific embodiment of a "*matrix*". In view of these passages in the patent application, and contrary to appellant II's view, the method of claims 1 and 10 finds a direct and unambiguous basis in the patent application.

43. Accordingly, Article 123(2) EPC is complied with.

Article 84 EPC - claims 1 and 10

44. Appellant II submitted that the feature "*3 to N*" in present claims 1 and 10 lacked clarity and support in the patent application, because the variable "*N*" might

relate to values smaller than three, like in a "*count-down*" situation.

45. The board is not convinced by this argument. In line with the opposition division's finding in the decision under appeal, the variable "*N*" in the range "*3 to N*" recited in claims 1 and 10 can only be construed to relate to values higher than three (see point 13 above). There are also no indications for a "*count-down*" situation derivable from the patent application as a whole, which rather on the contrary specifies, for example, in claim 2 as originally filed that the grid (i.e. the matrix) is "*at least*" 3-dimensional (emphasis added). In other words, the value "*3*" defines the lower limit of the range indicated in claims 1 and 10. Furthermore, the range "*3 to N*" finds support on page 30, lines 1 and 2 of the description of the patent application.

46. Thus, the subject-matter of claims 1 and 10 is clear and supported, and hence, auxiliary request 4 complies with the requirements of Article 84 EPC.

Article 83 EPC - claims 1 and 10

47. Appellant II submitted in the context of sufficiency of disclosure and inventive step that the mapping of samples to elements in the matrices exceeding three dimensions falling within the scope of claims 1 and 10 were insufficiently disclosed.

48. The board is not persuaded by this argument, since as set out in point 13 above, the term "*n-dimensional matrix*" in claims 1 and 10 relates to an abstract concept that is mathematically defined by variables. It is thus not confined to the physical space of two or

three dimensions. Since the concept allows for a unique mapping of fluid samples to elements in matrices of any dimension including their subsequent identification, the patent application discloses the invention in a manner sufficiently clear and complete to be carried out by the skilled person.

49. The requirements of Article 83 EPC are therefore complied with.

Article 56 EPC - claims 1 and 10

Closest prior art

50. It is common ground between the parties that document D1 represents the closest prior art for the subject-matter of claims 1 and 10.

51. The claimed methods differ from that disclosed in document D1 in that the matrix has at least three dimensions instead of two, and that subpools are formed "*from all samples identified by a matrix notation in which one dimensional index is fixed*", i.e. from all samples along the axes of all three (or more) dimensions. The use of such a matrix has the effect that the overall number of PCR reactions required for uniquely identifying a virus-positive sample is reduced compared to the method described in document D1. This results in significant time and cost savings.

52. Appellant II submitted that the technical problem was the provision of a method for identifying viral positive blood donations wherein the samples are arranged in an alternative manner. However, as set out above, since the use of an at least 3-dimensional matrix instead of a 2-dimensional improves the claimed

method vis-à-vis that of the closest prior art, the board does not concur with appellant II's view.

53. Thus, the technical problem underlying the subject-matter of claims 1 and 10 is defined as the provision of an improved method for uniquely identifying virus-positive biological fluid donations.

54. The methods according to claims 1 and 10 solve this problem across the whole scope of the claims for the reasons set out above in the context of sufficiency of disclosure.

Obviousness

55. It remains to be assessed whether or not the skilled person starting from the closest prior art method and faced with the problem defined above, would have arrived at the methods of claims 1 and 10 in an obvious manner.

56. Document D1 discloses solely the mapping of potentially viral-positive blood donations by pooling samples in 2 dimensions. Since the teaching of document D1 is limited to the use of microtiter plates, and subpools are only formed from samples from the columns and rows of individual plates, the document provides no suggestions how to further reduce the number of PCR reactions required for identifying potentially virus contaminated blood sample(s), let alone by pooling samples along the axes of further dimensions.

57. Appellant II submitted that the skilled person in the light of the teaching of document D1 merely had to stack the microtiter plates disclosed therein on top of

each other to arrive at the methods according to claims 1 and 10 in an obvious manner.

58. The board does not share this view because document D1 neither mentions the stacking of microtiter plates nor solves the mere stacking of microtiter plates alone the underlying technical problem. Document D1 provides no suggestions or hints that such a stacking could be used for the formation of further subpools along the axes of the third or any higher dimension thereby reducing the number of PCR tests required for identifying virus-positive blood samples. Nor is the formation of additional subpools rendered obvious by any of the other prior art documents on file, either alone or in combination with document D1.

59. Hence, auxiliary request 4 meets the requirements of Article 56 EPC.

60. Since auxiliary request 4 corresponds to auxiliary request 5 upon the basis of which the opposition division decided that the patent could be maintained, both appeals have to be dismissed.

Order

For these reasons it is decided that:

The appeals are dismissed

The Registrar: The Chairman:

B. ter Heijden B. Stolz

Decision electronically authenticated