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Datasheet for the decision of 9 September 2013

Case Number: T 0018/10 - 3.3.08

Application Number: 04758774.6

Publication Number: 1616035

IPC: C12Q 1/68

Language of the proceedings: EN

Title of invention:
Caries risk test for predicting and assessing the risk of disease

Applicant:
UNIVERSITY OF SOUTHERN CALIFORNIA
Proactive Oral Solutions, Inc.

Headword:
Caries Lectin detection/UNIVERSITY SOUTHERN CALIFORNIA

Relevant legal provisions:
EPC Art. 83, 84

Keyword:
"Main and Auxiliary Requests I-II: clarity and support (no)"

Decisions cited:
G 0010/93

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0018/10 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 9 September 2013

Appellants: (Applicant 1)
UNIVERSITY OF SOUTHERN CALIFORNIA
3716 South Hope Street
Suite 313
Los Angeles, CA 90007—4344 (US)

(Applicant 2)
Proactive Oral Solutions, Inc.
2921 St. Albans Drive
Los Alamitos, CA 90720 (US)

Representative:
Scott, Susan Margaret
Abel & Imray
20 Red Lion Street
London WC1R 4PQ (GB)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted on 6 July 2009 refusing European patent application No. 04758774 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman: M. Wieser
Members: P. Julià
D. S. Rogers

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse the European patent application no. 04 758 774.6, published as International patent application WO 2004/089187 (hereinafter "*the application*").

II. The examining division considered the sole claim request filed by the applicant on 20 May 2009 not to fulfil the requirements of Articles 84, 54, 56 and 82 EPC. Claims 1, 5, 14-15, 18 and 27 of this request read as follows:

"1. A method for predicting the risk of dental caries in a subject, said method comprising:
contacting an aliquot of an unfractionated saliva sample obtained from said subject with more than one lectin under conditions that allow said more than one lectin to bind to more than one respective lectin-binding components of saliva;
detecting the amounts of the bound lectins; and
comparing the amounts of the bound lectins to the amounts known to bind a saliva sample from a control subject, wherein the amounts of bound lectins are indicative of the risk of dental caries in the subject."

"5. The method of any one of claims 1 to 4, wherein each of the more than one lectin is selected from the group consisting of DSL, ECL, PSA, WGA, UEA, MAL I, MAA, PNA, AAL, LTL, MAL II, JAC, LEL, SNA, PTL I, ACL, GSL II, VVA, BPL, WFL, SJA, MPL, GNL, HHL, CCA, NPL, STL, PHA-L, PHA-E, GSL I, DBA, HMA, EEA, LPA, and PTL II."

"14. Use of a therapeutic reagent effective for dental caries for the preparation of a pharmaceutical composition for preventing or reducing the risk of dental caries in a subject, wherein the pharmaceutical composition is to be administered to said subject when the content of a lectin-binding component in saliva, which has been determined according to the method of claim 1, is above or below the level in a normal control."

"15. A kit for detecting dental caries, the kit comprising:
means for collecting a saliva sample;
means for measuring the amounts of more than one lectin-binding components in said sample; and
an oral fluid standard for comparing with the amounts of said components in said sample."

"18. An assay device for detecting the presence of more than one lectin-binding component in a saliva sample, said device comprising:
a sample receiving zone comprising a first matrix material and more than one lectin bound to said matrix material; and
a control zone comprising a second matrix material and having at least one control saliva sample of a known concentration."

"27. The method of claim 26, wherein said first set of lectins comprises two or more lectins that are positively correlated with one or more of DFS, DFT, DMFT, DMFS, dfs, dft, dmft, dmfs, and dfs/t, and said second set of lectins comprises two or more lectins

that are respectively negatively correlated with DFS, DFT, DMFT, DMFS, dfs, dft, dmft, dmfs, and dfs/t."

III. The examining division considered claims 1-5 not to fulfil the requirements of Article 84 EPC, since the application and supplementary evidence (Appendix filed by the applicant on 20 October 2008) only provided support for a specific choice of lectins but not for any combination of more than one lectin. Claim 27 was also objected under Article 84 EPC, since its subject-matter encompassed lectins defined only by their desired function and undue experimentation was required to screen lectins randomly. Claims 1-5 and 8-9 were considered not to be novel and/or inventive over the disclosure of document D1 (R. Seemann et al., Caries Res. 2001, Vol. 35, pages 156 to 161) (Articles 54 and 56 EPC). The combination of documents D1 and D3 (US 5,356,782, published on 18 October 1994) was considered to render the subject-matter of claims 15 to 21 not inventive (Article 56 EPC). In the light of document D1, the applicant's claim request was also considered by the examining division not to fulfil the requirements of Article 82 EPC.

IV. The applicant (appellant) filed a notice of appeal and a statement setting out the Grounds of Appeal. With the Grounds of Appeal, the appellant filed a Main Request, essentially identical to the request considered by the examining division, and Auxiliary Requests I and II. Oral proceedings were requested in case the board were not willing to grant a patent on the basis of any of these requests.

V. As regards Article 84 EPC, the appellant argued that the application provided for the first time a method to predict the risk of caries. This method was fully supported and defined in the claims, and there was no reason to limit the scope of protection unduly. The supplementary evidence filed on 20 October 2008 supported the view that the method was not restricted to lectin MAL I and that individually tested lectins, that were found not to be suitable in document D1 (*supra*) (e.g. VVA and GNL), could indeed be encompassed by the method of claim 1 in the form of lectin mixes. Furthermore, the application provided not only examples with more than two lectins but also examples with two lectins (e.g. Table 3 on page 52). Contrary to the assessment of the examining division, claim 27 was not defining the claimed subject-matter by the result to be achieved. The expression "lectins that are positively correlated" was a functional feature in accordance with the requirements laid down in the case law of the Boards of Appeal. Undue burden was not required, only reasonable experimentation was necessary to reduce claim 27 to practice in accordance with the instructions given in the application.

The appellant put forward further arguments in order to support novelty and inventiveness of the claimed subject-matter as well as unity of the invention (Articles 54, 56 and 82 EPC).

VI. Summons to oral proceedings were issued on 26 April 2013. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA annexed thereto, the appellant was informed of the board's preliminary opinion on the substantive issues

of the case. In particular, the board referred to the admissibility of the appellant's claim requests and objected to the subject-matter of claims 1, 5, 9, 14-15, 18 and 27 of the Main Request under Article 84 EPC alone and/or in combination with Article 83 EPC. In view thereof, the board refrained from an analysis of the appellant's arguments put forward under Articles 54, 56 and 82 EPC.

VII. On 27 August 2013, the appellant withdrew its request for oral proceedings. No comments or substantive reply to the objections raised by the board in its communication pursuant to Article 15(1) RPBA were provided by the appellant.

VIII. On 3 September 2013, the board cancelled the oral proceedings.

IX. The appellant (applicant) requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of its Main Request or Auxiliary Requests I and II, all filed with its statement of Grounds of Appeal on 16 November 2009.

Reasons for the Decision

Admissibility of the Main Request

1. Except for a clerical correction in claim 5, namely to define lectin UEA as UEA I, the Main Request filed with the appellant's statement of Grounds of Appeal on 16 November 2009 is identical to the request filed on 20 May 2009, the sole claim request considered by the

examining division in the decision under appeal. The Main Request is thus admitted into the appeal proceedings.

Procedural issues

2. According to decision G 10/93 (OJ EPO 1995, page 172, Headnote) "*In an appeal from a decision of an examining division in which a European patent application was refused the board of appeal has the power to examine whether the application or the invention to which it relates meets the requirements of the EPC. The same is true for requirements which the examining division did not take into consideration in the examination proceedings or which it regarded as having been met. If there is reason to believe that such a requirement has not been met, the board shall include this ground in the proceedings*".

In the present case, the board considers that such additional grounds exist and therefore, in its communication pursuant to Article 15(1) RPBA, informed the appellant of these additional grounds (cf. Section VI *supra*). In view of the fact that the appellant has not provided any substantive reply to these grounds (cf. Section VII *supra*), the present decision is essentially based on the board's objections raised in this communication.

Main Request

Article 84 EPC; Articles 84 and 83 EPC

3. According to the established case law of the Boards of Appeal, there is no reason to interpret an excessively

broad claim more narrowly, if it is a question not of understanding concepts that require explanation but rather a question of examining an excessively broad request in relation to the state of the art (cf. "Case Law of the Boards of Appeal of the EPO", 6th edition 2010, I.C.2.9, page 105). The claims must also reflect the actual contribution to the art in such a way that the skilled person is able to perform the invention over the entire range claimed (cf. "Case Law", *supra*, II.B.4.1, page 275). In view of this case law, the board considers that some claims do not fulfil the requirements of Article 84 EPC, in particular as regards clarity and support by the description.

4. The method of **claim 1** for predicting the risk of dental caries in a subject comprises three steps, namely: 1) contacting an aliquot of an unfractionated saliva sample - containing more than one lectin-binding component - with more than one lectin, under conditions that allow the binding of the lectins to the respective lectin-binding component, 2) detecting the amounts of lectins bound, and 3) comparing these amounts to the amounts known to bind a saliva sample from a control subject, wherein the amounts of bound lectins are indicative of the risk of dental caries in the subject (cf. Section II *supra*).

4.1 The method of claim 1 embraces embodiments which rely on the combination of two lectins only, without a limitation to any particular type of lectin. In view of the actual disclosure of the application, the board considers that there is no technical support for these embodiments.

4.1.1 In Example I of the application, the most predictive lectins related to the MUC7 and MUC5B mucin concentrations (known in the art to have the best association with the forecast of decay and filled permanent teeth, DFT) are identified (cf. page 49, lines 3-6). **MAL I** (Maackia Amurensis Lectin I; for α-2,3 linked sialic acid) has the highest individual correlation with DFT (cf. page 50, Table 1 and page 52, lines 15-17) and, in view of the results obtained, **ACL** (Amaranthus Caudatus Lectin; for different configurations of sialylated T-antigen) was dropped from the lectin panel (cf. page 50, lines 21-22). The prominence of sialic acid is further supported by the results obtained with SNA (Sanbucus Nigra Lectin; primarily for α-2,6 linked sialic acid). JAC (Jacalin, Jackfruit seed lectin; for a different configuration of sialylated T-antigen) identifies a form of the T-antigen that may be a negative factor (cf. page 50, lines 19-21). AAL and UEA I (Aleuria Aurantia Lectin and Ulex Europaeus Lectin I; for different Lewis antigens, especially the variety with α-1,2 linked fucose) are "*somehow ... interwoven in the relationship between mucin and DFT*" (cf. page 50, lines 17-19). The outcome of the overall relationship of DFT to a panel of lectins containing MAL, JAC and MAA (Maackia Amurensis), after standardizing the contribution of each independent variable, is acknowledged to be complex (cf. page 53, lines 21-27).

4.1.2 In line therewith, the test composition used in Example 2 is based on "*the lectins that have been shown to be contributors to the predictive regression equations*" in Example 1, with reference to three lectins (cf. page 59, lines 4-19). In Example 3, a combination of the three

lectins MAL I, JAC and SNA (disclosed in Table 1 as contributors) is used for assigning tested individuals to four different groups: high, medium, low and zero DFT (cf. page 62, lines 23-26). When combined with other factors (age, ethnicity), it is found that "*MAL I accounts for more than 50% of the regression equation*" (page 63, lines 7-8). In assays with further lectins, only slightly better results are obtained (R^2 improves from 0.926 to 0.990 in the best case, with possible alternatives 0.957 and 0.966, all of them > 0.90). In all these assays, MAL I and JAC (the two lectins identified in Table 1 as having the most relevant results in inverse correlation to MUC5B and MUC7) are used (cf. page 64, lines 15-24).

4.1.3 The results obtained with individual lectins and combinations thereof (cf. page 50-52, Tables 1-3) support the following conclusions: 1) each lectin has a particular DFT correlation, 2) not all lectins have a significant DFT correlation, 3) MAL I provides the strongest link to DFT forecast (cf. page 54, lines 7-8), and 4) certain combinations of lectins do not improve the strength of the relationship (of MAL I) to DFT, only a few combinations improve the DFT correlation (cf. page 52, line 17 to page 53, line 27).

4.2 As regards the Appendix filed by applicant/appellant on 20 October 2008, the following points are of relevance:

4.2.1 The data based on multiple linear regression is obtained with a mixture of at least 12 lectins, except for one example with 9 lectins, in which the number of lectins was lowered by using "*a proprietary data management system*". The formulation date of these

mixtures is sometime in 2005, two years after the priority date of the application.

4.2.2 The lectins used in the mixtures analyzed by multiple linear regression have different specificities, such as α-2,3 (MAA), α-2,6 (SNA), α-1,2 (AAL), and some of them include the lectin JAC, shown in the application to have an inverse relationship or correlation to other lectins. The presence of ACL, VVA and/or GNL in some of these mixtures does not provide much information, since they all consist of a large number of lectins and thus, their contribution may not be relevant or substantial for the results obtained.

4.2.3 The data based on neural nets have also been obtained in the years 2005-2008 and refer to a "*combination of proprietary data management system and neural net mathematics*" which are not disclosed in the application. Except for the mixtures indicated in point 10 of the Appendix, all other mixtures contain at least 5 lectins and have, *prima facie*, properties (specificity) similar to those used for multiple linear regression. Thus, the presence of VVA in some of them may not be relevant for the results obtained.

4.2.4 Point 10 of the Appendix is the sole source of information on file concerning combinations of two lectins. However, the correlation given for these combinations with the risk of caries in young adults is very low ($p=<0.05$; see for comparison Table 3, page 52 of the application) and no information is provided for each of them separately. Two of these mixtures contain ACL, which was dropped from the lectin panels used in the Examples of the application (*supra*).

4.2.5 The relevance of the information provided in this Appendix is questionable since it is not a complete disclosure. There is no information regarding the methods and parameters used which may be of relevance for achieving the information disclosed, such as, *inter alia*, the proprietary data management and the neural net.

4.3 The results shown in the Appendix are in line with those obtained in the Examples of the application which, as stated in point 4.1.3 *supra*, allow the following conclusions: 1) the contribution of MAL I and JAC to the DFT correlation is substantial and highly relevant, 2) the presence of additional lectins with different specificities may optimize this correlation; however 3) the contribution of other lectins may be irrelevant. In view thereof, the board considers that a generalization to use any possible combination of whatever lectins (more than one, at least two) in a method for predicting the risk of dental caries is not supported by the disclosure of the application.

4.4 It is arguable whether, in the method of claim 1, the lectins have to be used simultaneously (as a mixture) (as argued by the appellant) or whether they may be used spatially and/or temporally separated (as argued by the examining division). This interpretation is of relevance for defining the characteristics and properties of the assay device of claims 18-21 (cf. Section II *supra*). The references found in the application, such as on page 23, line 31 to page 24, line 1 and on page 28, lines 21-23 and the fact that, for a mixture of three lectins (MAL I, JAC and SNA),

three different Western blots were used (cf. paragraph bridging pages 63 and 64), are considered by the board to support the interpretation of the examining division.

4.5 The definition of the term "*control subject*" given in the description introduces a certain degree of ambiguity in claim 1. On the one hand, a control subject is merely a subject without the disease (dental caries), such as indicated on page 19, lines 10-12, page 20, lines 14-15 and page 26, lines 19-21, on the other hand, a control subject is also defined as a subject with a known disease level, in particular a subject classified - by an alternative method (number of cavities) - as belonging to a very low risk group, such as indicated in the paragraph bridging pages 23-24 and page 44, lines 22-29. It is noted that in Examples 1 and 2, control subjects are identified by their levels of MUC7 and MUC5B mucin concentrations.

4.6 Likewise, in view of the different definitions given to the term "*control subject*", the reference in claim 1 to the amounts of bound lectins as being indicative of the risk of dental caries is ambiguous. The more so in the light of claim 2, which implies that the amounts indicated in claim 1 may be neither above nor below those of a control subject.

4.7 In view of the sheer number of possible lectin combinations and the scarce information provided by the application, the board considers that claim 1 is drafted in terms of the result desired to be achieved (an objection raised by the examining division against the subject-matter of claim 27, see page 4, point 5.3 of the decision under appeal) and that the application

does not provide sufficient technical support to perform the invention over the entire scope of claim 1 (cf. point 4.3 *supra*).

5. The subject-matter of **claim 5** includes the lectin ACL which, according to Example 1 of the application, is not significant and was thus dropped from all lectin panels used (cf. page 50, lines 21-22 and Table 1). Apart from the Appendix filed on 20 October 2008, whose deficiencies are discussed in point 4.2 *supra*, there is no support on file for combinations of two lectins, one of them being ACL.

5.1 It is also noted that none of the lectins referred to in claim 5 or in any of the other dependent claims is designated with a complete name but only in abbreviated form. It is questionable whether each and every one of these abbreviations may be clearly understood by a skilled person as being standard and well-known in the field, i.e. without introducing any ambiguity into the claims. Likewise, a similar objection applies to abbreviations concerning dental diseases, such as those referred to in claim 27 (cf. Section II *supra*).

6. The use of **claim 14** relies on a therapeutic reagent which is defined as being "*effective for dental caries*" (cf. Section II *supra*). In view thereof, the following questions arise:

6.1 It is questionable whether all therapeutic reagents effective for the treatment or reduction of dental caries are also efficient in the prevention of dental caries (see page 41, "Anti-Caries Reagents").

6.2 In view of the references in the application to the "identification of population risk" when using other methods, such as on page 23, lines 14-18 and page 44, lines 22-29, the question arises whether the population group identified by the method of claim 1 is actually a new subpopulation and whether this subpopulation essentially overlaps, completely or partially, with those identified with these other methods known in the art. In other words, does the scope of claim 14 embrace a known use (preventing/reducing the risk of dental caries) for known products (anti-caries reagents) in a subpopulation which is also known in the art (medium and high risk) but which is now only identified by a different method?

6.3 Since the appellant has failed to provide a substantive reply to these questions (cf. Section VII *supra*), the board is not in a position to acknowledge claim 14 to fulfil the requirements of Article 84 EPC alone and/or in combination with Article 83 EPC.

7. The subject-matter of **claim 15** does not relate to the prevention or reduction of dental caries risk. The purpose-limited kit is explicitly stated to be "*for detecting dental caries*" (cf. Section II *supra*). In view thereof, the following issues are of relevance:

7.1 The claimed kit is required to comprise "*means for measuring the amounts of more than one lectin-binding components*". However, the means are not - necessarily and exclusively - those referred to in the method of claim 1, i.e. "*more than one lectin under conditions ...*". They may well be completely different and not rely on binding but on other techniques which

are not suggested, let alone disclosed, in the application. Moreover, it is not evident whether means useful for predicting the risk of dental caries must, always and necessarily, be identical to those useful for detecting dental caries.

7.2 Indeed, the term "*means*" itself is ambiguous, since it may refer to a technical device for carrying out a measure (cf. page 20, lines 19-22) or else to the products required for identifying and measuring the lectin-binding components. The nature and composition of the "*oral fluid standard*" is also ambiguous in view of the definition given in the application which, as stated on page 25, lines 22-31 may include a spiked surrogate and may be dependent on the context (cf. page 39).

8. Likewise, the subject-matter of **claim 18** and dependent claims 19-21 neither relates to the prediction of dental caries nor to the detection of dental caries, but only to a mere detection of the presence of (whatever) "*more than one lectin-binding component in a saliva sample*" (cf. Section II *supra*). There is no requirement that the (more than one) lectins bound to a first matrix material in the receiving zone have to be of relevance for the prediction and/or detection of dental caries. In the absence of such a requirement, the nature and composition of the (at least one) "*control saliva sample of a known concentration*" in the control zone is also considered to be completely ambiguous.

9. The subject-matter of **claim 27** refers to a first and a second set of (two or more) lectins that are positively

and negatively correlated with one or more of several dental prognosis, respectively. In view of the comments made above and the scarce information provided by the application (Tables 1-3), the board, as stated in point 4.7 *supra*, considers that the objection raised by the examining division on page 4, point 5.3 of the decision under appeal is justified (cf. Section III *supra*).

10. In view of all the foregoing observations and objections, the board considers the Main Request not to fulfil the requirements of Article 84 EPC alone and/or in combination with Article 83 EPC.

Auxiliary Requests I and II

11. Auxiliary Request I filed with the appellant's statement of Grounds of Appeal differs from the Main Request by the deletion of claim 27. Auxiliary Request II also filed with the appellant's statement of Grounds of Appeal differs from the Main Request in that the subject-matter of claim 5 of the Main Request has been incorporated in claim 1. In view of the findings below, it is not necessary to assess the admissibility of these requests in the appeal proceedings.

12. Many of the objections raised above for the Main Request under Article 84 EPC alone and/or in combination with Article 83 EPC apply also to Auxiliary Requests I and II. Therefore, Auxiliary Requests I and II do not fulfil *prima facie* the requirements of the EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski M. Wieser