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Datasheet for the decision of 7 November 2013

Case Number: T 0072/10 - 3.3.08

Application Number: 01901634.4

Publication Number: 1254258

IPC: C12Q1/68, G01N33/569

Language of the proceedings: EN

Title of invention:
A method for detection of pathogenic organisms

Patent Proprietor:
Herrmann, Björn
Kirsebom, Leif
Stolt, Pelle c/o Kirsebom, Leif

Opponent:
MacLean, Martin Robert

Headword:
Pathogenic organisms/BJÖRN

Relevant legal provisions:
EPC Art. 54(2), 56, 83
RPBA Art. 13(1)

Keyword:
Main request - justification for filing at the oral proceedings (yes)
Sufficiency of disclosure - (yes)
Novelty - (yes)
Inventive step - (yes)

Decisions cited:

Catchword:

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Case Number: T 0072/10 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 7 November 2013

Appellant: (Patent Proprietor 1)	Herrmann, Björn Skrindvägen 21 756 47 Uppsala (SE)
Appellant: (Patent Proprietor 2)	Kirsebom, Leif Vreta Strandväg 20 755 91 Uppsala (SE)
Appellant: (Patent Proprietor 3)	Stolt, Pelle c/o Leif Kirsebom Vreta Strandväg 20 755 91 Uppsala (SE)
Representative:	Brann AB P.O. Box 12246 102 26 Stockholm (SE)
Respondent: (Opponent)	MacLean, Martin Robert Mathys & Squire LLP 120 Holborn London EC1N 2SQ (GB)
Representative:	MacLean, Martin Robert Mathys & Squire LLP 120 Holborn London EC1N 2SQ (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 13 November 2009 revoking European patent No. 1254258 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman:	M. Wieser
Members:	T. J. H. Mennessier
	C. Heath

Summary of Facts and Submissions

I. The patent proprietors (appellants) lodged an appeal against the decision of the opposition division dated 13 November 2009, whereby the European patent No. 1 254 258, granted on European patent application No. 01901634.4 (published as the international application WO 01/51662), was revoked. Basis for the revocation was the main request corresponding to the claims as granted and the first and second auxiliary requests filed with the letter of 14 September 2009.

II. The main and the first auxiliary requests were refused for lack of novelty (Article 54 EPC), and the second auxiliary request for lack of novelty and inventive step (Articles 54 and 56 EPC).

III. The patent has been opposed by one opponent (respondent) on the grounds as set forth in (i) Article 100(a) EPC that the invention was neither new nor inventive, and (ii) in Article 100(b) EPC that the invention was insufficiently disclosed.

IV. The appellants filed their statement setting out the grounds of appeal. The requests on which the decision under appeal is based were maintained.

V. The respondent filed submissions in reply to the statement of grounds.

VI. On 24 May 2013, the Board issued a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) expressing its preliminary and non-binding views.

VII. On 7 October 2013, the appellants replied to the Board's communication and filed a main and three auxiliary requests to replace the requests then on file. The main request and auxiliary requests 1 and 2 were new. Auxiliary request 3 was identical to the second auxiliary request underlying the decision under appeal (and of the statement of grounds). Two new documents accompanied the appellants' submissions.

VIII. The respondent did not file any substantial submissions in reply to the Board's communication.

IX. Oral proceedings took place on 7 November 2013. As announced in its letter of 4 June 2013, the respondent did not attend.

X. In the course of the oral proceedings, the appellants filed a new main request.

XI. This main request consists of seven claims of which claims 1 and 4 read:

"1. A method for interspecies differentiation of pathogenic organisms, comprising analysis of the P3 hypervariable region of the RNase P RNA gene, wherein the pathogens are mycobacteria or chlamydia."

"4. A method for detection of pathogenic organisms including interspecies differentiation comprising an interspecies differentiation step according to claim 1, wherein the analysis comprises amplification of nucleic acids of the hypervariable region P3 of the RNase P RNA gene from the pathogens; forming a heteroduplex with related nucleic acids; and analysis thereof."

Claims 2, 3 and 5 to 7 are dependent on claim 1.

XII. The following documents are referred to in the present decision:

(D1) B. Herrmann et al., Journal of Clinical Microbiology, Vol. 34, No. 8, August 1996, pages 1897 to 1902

(D2) M. Cho et al., International Journal of Systematic Bacteriology, Vol. 48, 1998, pages 1223 to 1230

(D3) E. S. Haas and J. W. Brown, Nucleic Acids Research, Vol. 26, No. 18, 1998, pages 4093 to 4099

(D5) J. W. Brown, Nucleic Acids Research, Vol. 26, No. 1, 1998, pages 351 to 352

(D6) Home page of the internet site "http://www.mbio.ncsu.edu/RNaseP/home.html" retrieved on 5 December 2007

(D7) B. D. James et al., Cell, Vol. 52, 15 January 1988, pages 19 to 26

(D8) C. Massire et al., Journal of Molecular Biology, Vol. 279, 1998, pages 773 to 793

XIII. The submissions made by the appellants, insofar as they are relevant to the present decision, may be summarized as follows:

The subject-matter of the claims was sufficiently disclosed according to the requirements of Article 83 EPC.

The claimed subject-matter was novel as none of documents D1, D2 and D3 disclosed that the P3 loop of the RNase P RNA gene allowed species differentiation in chlamydia or mycobacteria.

Starting from document D1 taken as the closest prior art, the technical problem to be solved was how to provide a rapid and inexpensive method for interspecies differentiation in chlamydia and mycobacteria. The solution was the analysis of only one hypervariable region of the RNase P RNA gene, namely the P3 region. Documents D5 to D8 did not relate to a method for interspecies differentiation in chlamydia or mycobacteria. The skilled person would have had no reasonable expectation of success in analysing the P3 region.

XIV. The submissions made in writing by the respondent may be summarized as follows:

In its only submission, dated 15 July 2010, the respondent referred to appellant's main request and auxiliary requests 1 and 2 then on file. The main request, i.e. the claims as granted, related to pathogenic organisms in general, and the P3 and P19 hypervariable loop. Auxiliary request 1 was restricted to the P3 loop and auxiliary request 2 to mycobacteria and the P3 loop.

With regard to Article 83 EPC the respondent did not submit any substantial argument but referred only to its reasons presented before the Opposition Division.

With regard to Article 54 EPC the respondent agreed with the Opposition Division and stated that the main request

and auxiliary request 1 lacked novelty over the disclosure in documents D1, D2 and D3.

Finally, the respondent considered that auxiliary request 2 did not meet the requirements of Article 56 EPC as the claimed subject-matter was obvious in the light of document D1 when read alone or in combination with any of documents D5, D6, D7 or D8.

XV. The appellants (patent proprietors) request that the decision under appeal be set aside and the patent be maintained on the basis of the new main request filed at the oral proceedings.

XVI. The respondent has requested in writing that the appeal be dismissed.

Reasons for the Decision

Admissibility of the main request

1. The main request, filed at the oral proceedings, differs from auxiliary request 2, filed with the letter of 7 October 2013 in reply to the Board's communication, only by an amendment in claim 4, wherein a reference to hypervariable region P19 has been deleted. The claims correspond to the claims as granted with the only exceptions that the reference to hypervariable region P19 in claims 1 and 4 has been deleted and the subject-matter of dependent claim 5 as granted has been introduced into claim 1.

2. The newly filed claims are a straightforward response to the Board's communication and do not give rise to any new objection.

3. Therefore, the Board in exercising the discretion conferred to it by Article 13(1) RPBA, decides to admit the main request into the proceedings.

Article 123 EPC

4. As Article 100(c) EPC was not a ground for opposition and as the amendments carried out in the appeal procedure do not give rise to an objection in this respect (see point 1 above), the requirements of Article 123(2) EPC are met.

5. The scope of protection has been restricted with regard to the claims as granted, so that also the requirements of Article 123(3) EPC are met.

Article 84 EPC

6. The Board is satisfied that, owing to the amendments carried out to define the claimed subject-matter, the main request complies with the requirements of Article 84 EPC.

Article 83 EPC

7. In the written phase of the appeal proceedings the respondent did not provide any substantial submissions in support of its contention that the patent should be revoked for reasons of lack of sufficiency.

8. In the absence of any verifiable facts and in view of the disclosure in the patent under appeal (see specification paragraphs [0029], [0034] and [0035] with respect to mycobacteria and paragraph [0056] with

respect to chlamydia), the Board is satisfied that the main request meets the requirements of Article 83 EPC.

Article 54 EPC

9. An essential technical feature of the method according to claim 1 (and of claim 4) is the analysis of the P3 hypervariable region of the RNase P RNA gene of the mycobacteria or chlamydia to be tested.

10. Document D1 characterises the RNase P RNA genes of *Chlamydia trachomatis*, *Chlamydia pneumoniae*, and *Chlamydia psittaci* and shows that they have heterologous sequences which can be used for differentiation of species on the basis of restriction fragment length polymorphisms (RFLPs) (see page 1901, right-hand column, last paragraph). This sequence heterology is specifically referred to on page 1898, right-hand column, first paragraph, last sentence which reads "*The heterologous base positions that differentiated the three Chlamydia species were found in several regions of the gene, but particularly in the* ***P12*** *domain [...], in loop* ***P17*** *[...], and in the* ***P19*** *stem-loop structure [...]).*" (emphasis by the Board).

11. The P3 hypervariable region is referred to in document D1 only in Figure 2 on page 1899, where the suggested secondary structures of RNase P RNA in *Chlamydia trachomatis* are represented. In this figure most of the nucleotides of the P3 region are not identified as the usual nucleotides A, U, C and G but are designated by the capital letter "N" which according to the legend of the figure "*denotes tentative nucleotide in the flanking regions of the primers based on M1 RNA*".

12. In the decision under appeal (see the first paragraph on page 8), the Opposition Division took the view that the P3 hypervariable region was also represented in Figure 3 on page 1900, where sequences of RNase P genes from *C. trachomatis*, *C. pneumoniae* and *C. psittaci* are aligned for comparison, starting from nucleotide 17 of the *C. trachomatis* sequence.

13. However, the nucleotide sequence CGGACTTTATAAGAAAAGATGCTGGAGAAATTCC, shown in figure 3 of document D1 between positions 16 and 51, corresponds to the sequence starting at position 64 and ending at position 97 of *the C. trachomatis* sequence disclosed in Figure 6 of the patent in suit and is not, therefore, part of the P3 hypervariable loop. Consequently, the alignment shown in Figure 3 of document 1 is not concerned with the P3 hypervariable loop. Therefore, in contrast to the view expressed in the decision under appeal, the Board concludes that document D1 is not anticipating the subject-matter of claim 1.

14. In document D2, a classification of *Saccharomyces* strains based on the sequence of the RNase P RNA gene used as a phylogenetic marker is presented. Thus, the disclosure in document D2 is not concerned with species differentiation of mycobacteria or chlamydia.

15. Document D3 describes insights into the extent and patterns of evolutionary variation in RNase P RNA sequence and structure in bacteria. The study includes considerations with regard to one strain of *Chlamydia psittaci* and one strain of *Chlamydia trachomatis* (see Table 1 on page 4093). The P3 helix is referred to on page 4096 in a statement referring to the conservation of its distal portion in bacteria. Document D3 does not disclose the use of the P3 region of the RNase P RNA

gene in a method for interspecies differentiation of any pathogenic bacteria, let alone chlamydia or mycobacteria.

16. In conclusion, the subject-matter of claim 1 is new over any of documents D1, D2 and D3 and therefore meets the requirements of Article 54 EPC. The same applies to claims 2 to 7 (see Section XI, *supra*).

Article 56 EPC

17. In the decision under appeal document D1 has been considered to represent the closest state of the art. The Board agrees. As noted at point 10 above, D1 describes that the P12 domain, the P17 loop and the P19 stem-loop structure of the RNase P RNA gene allow to differentiate three chlamydia species, namely *C. trachomatis*, *C. pneumoniae* and *C. psittaci*. Based on this disclosure, the authors speculate that (i) sequencing of the RNase P RNA gene may be used for strain differentiation in studies of molecular epidemiology (see page 1897, right-hand column, first paragraph), and (ii) analysing the RNase P RNA genes may provide an alternative target for the detection and typing of chlamydia species. They allege that their results point to a possible general applicability of their disclosure in clinical bacteriology (see page 1901, right-hand column, last paragraph).

18. The technical problem underlying the patent in suit in the light of the disclosure in document D1 is seen in the provision of a method for interspecies differentiation of mycobacteria or chlamydia. As a solution to this problem, the patent proposes the method according to claim 1, which relies on the analysis of the P3 hypervariable region of the RNase P

RNA gene. In view of the results and observations presented in Example 1 (see in particular, paragraphs [0034] and [0035] and Figure 4B in the patent specification) with respect to the interspecies differentiation of mycobacteria and Example 2 (see in particular, paragraph [0056] and Figure 6 in the patent specification) with respect to the interspecies differentiation of chlamydia, the technical problem is considered to be credibly solved over the whole scope of claim 1.

19. The respondent's argument that the claimed subject-matter does not involve an inventive step in view of document D1 alone is not convincing, as D1 does not refer to the P3 hypervariable region of RNase P RNA gene.

20. It remains to be answered whether a skilled person, in the light of document D1 in combination with any of documents D5, D6, D7 and D8, would have arrived at the claimed solution in an obvious way.

21. Document D5 is a short article introducing the ribonuclease P database which is a compilation of RNase P (RNA and protein) sequences, sequence alignments, and secondary structures, available via the world wide web. D5 does not deliver any information regarding the P3 hypervariable region of the RNase P RNA. As a supplement to document D5, the respondent has relied on document D6. However, this latter document, which merely provides a list of the genera whose data is contained in the database, was retrieved on 5 December 2007 from the web site of the RNase P database and does not belong to the prior art.

22. Document D7 describes a comparative analysis resulting in the identification of a common core of primary and secondary structure, in the RNase P RNAs of the bacterial species *Bacillus subtilis* and *Escherichia coli)*, two bacterial species which are unrelated to chlamydia or mycobacteria. Although the sequences for the RNase P RNA sequences of four Bacillus species are aligned in Figure 1 (see page 20), no reference is made to the P3 region of the secondary structure models represented in Figure 2 (see page 22) as being a possible tool for interspecies differentiation.

23. Document D8 describes 3D models for the two main structural types of RNase P RNA of bacteria. Figures 3 and 6 (see page 779 and 781, respectively) provide alignment of regions - other than the P3 hypervariable region - for 18 bacterial species, none of them being related to chlamydia or mycobacteria (note that in both figures "M." stands for "Mycoplasma" and in Figure 3 "C." stands for "Clostridium"). Figure 7 (see page 783) provides alignments of the P4, P5, P7 and P8 regions of the RNase P RNA of eight bacterial species, one of them (*Chlamydia trachomatis)* being classified as a chlamydia and none of them being classified as a mycobacteria. Thus, document D8 does not contain any hint to use the hypervariable P3 region in a method for interspecies differentiation of chlamydia or mycobacteria.

24. In conclusion, a review of the content of prior art documents D5, D7 and D8 shows that they do not contain any teaching which would have prompted a skilled person to amend the disclosure in the closest prior art document D1 and to analyse the P3 hypervariable region of the RNase P RNA gene in order to perform an interspecies differentiation of mycobacteria or chlamydia.

25. Therefore, the subject-matter of claim 1 involves an inventive step. The same applies to the subject-matter of claim 4 and of dependent claims 2 to 3 and 5 to 7. The main request complies with the requirements of Article 56 EPC.

Adaptation of the description

26. The Board concludes that, by filing amended pages 2, 3 and 5 at the oral proceedings, the description has been satisfactorily amended in accordance with the EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to maintain the patent in the following version:

   - Claims 1 to 7 according to the main request filed during oral proceedings;

   - Description pages 2, 3 and 5 as filed during oral proceedings;

   - Description pages 4, 6 to 16 as in the patent as granted;

   - Sequence listing as in the patent as granted;

   - Drawings 1 to 8 as in the patent as granted

The Registrar: The Chairman:

A. Wolinski M. Wieser

Decision electronically authenticated