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**Datasheet for the decision
of 2 February 2012**

Case Number: T 0913/09 - 3.3.08

Application Number: 01966295.6

Publication Number: 1352083

IPC: C12Q 1/04

Language of the proceedings: EN

Title of invention:

Compositions and methods for detecting target microorganisms
in a sample

Patentee:

BioControl Systems, Inc.

Opponent:

BIOMERIEUX SA

Headword:

Campylobacter/BIOCONTROL SYSTEMS

Relevant legal provisions:

EPC Art. 84, 83, 56

Keyword:

"Admission of late filed request (yes)"
"Sufficiency of disclosure (yes)"
"Inventive step (yes)"

Decisions cited:

G 0001/03, T 0931/04, T 0879/05, T 0631/06, T 0012/07

Catchword:

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Case Number: T 0913/09 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 2 February 2012

Appellant:
(Patent Proprietor)

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Respondent:
(Opponent)

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Decision under appeal:

Decision of the Opposition Division of the
European Patent Office posted 9 February 2009
revoking European patent No. 1352083 pursuant
to Article 101(3)(b) EPC.

Composition of the Board:

Chairman: M. Wieser
Members: B. Stolz
D. S. Rogers

Summary of Facts and Submissions

- I. The patentee (appellant) filed an appeal against the decision of the opposition division to revoke European Patent EP No. 1352083.
- II. The opposition division decided that the main request before it, claims 1 to 22 as granted, was not novel, and that auxiliary request 1, filed on 19 November 2008, lacked an inventive step.
- III. With its grounds of appeal, the appellant requested that the decision under appeal be set aside, and the patent be maintained as granted. As an auxiliary measure it requested that the patent be maintained on the basis of the Auxiliary request on which the decision of the opposition division was based.
- IV. In a letter dated 22 December 2009, the opponent (respondent) submitted its response to the grounds of appeal, and referred to newly cited documents D16 to D20.
- V. The board summoned the parties to oral proceedings to be held on 15 November 2011. A communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) dated 21 July 2011, annexed to the summons, informed the parties of the preliminary non-binding opinion of the board on some of the issues of the appeal proceedings. The communication provided that any further submissions by the parties should be filed one month before the date of the oral proceedings, that is by 15 October 2011.

VI. Further observations of the respondent were received on 14 October 2011.

The appellant's reply to the board's communication as well as a new main request and auxiliary requests I and II, replacing the requests previously on file, were received on 20 October 2011, that is 5 days after the expiry of the time limit set by the board for filing further submissions.

VII. In response to a request by the respondent, the oral proceedings were postponed until 2 February 2012.

VIII. Both, the appellant and the respondent made further submissions in writing, subsequent to 15 November 2011 - the original date of the oral proceedings.

IX. Oral proceedings were held on 2 February 2012. In the course of the oral proceedings, the appellant withdrew its main request and its auxiliary request I, and renamed and resubmitted auxiliary request II, filed with letter dated 20 October 2011, as its new main request.

X. The final requests of the parties were:

The appellant requested that the decision under appeal be set aside and the patent be maintained upon the basis of claims 1 to 10 of its main request submitted at the oral proceedings on 2 February 2012.

The respondent requested that the appeal be dismissed and that the main request not be admitted into the proceedings.

XI. Claims 1, 12 and 14 as granted read:

"1. A composition for detecting a target microorganism in a sample, comprising a conditionally detectable marker, wherein said marker is capable of providing a detectable signal when in contact with a viable microorganism, and a substrate for an aminopeptidase that is substantially absent from the target microorganism, wherein said substrate comprises a signal moiety linked to the substrate, the signal moiety capable of providing a detectable signal when cleaved by substantially all non-target microorganisms.

12. The composition of claim 1, further comprising a growth-supporting medium for the target microorganism.

14. The composition of claim 12, wherein said growth supporting medium contains antibiotics to suppress the growth of non-target microorganisms."

XII. Independent claims 1 and 10 of the main request read:

"1. A medium for detecting *Campylobacter* in a sample comprising:

a. a substrate for an L-alanine aminopeptidase;

b. a conditionally detectable marker, wherein said marker is capable of providing a detectable signal when in contact with a viable microorganism;

c. a signal moiety linked to the substrate, said moiety providing a detectable signal when cleaved by said aminopeptidase from a microorganism; and

d. a growth supporting medium for Campylobacter wherein said growth supporting medium contains antibiotics to suppress the growth of non-target microorganisms.

10. A method for detecting Campylobacter in a sample, the method comprising:

a. providing a medium according to claim 1;

b. inoculating the medium with the sample to be tested for the presence of Campylobacter;

c. incubating the inoculated medium under conditions suitable for the growth of Campylobacter; and

d. comparing the difference between the signal generated by conditionally detectable marker and the L-alanine aminopeptidase substrate, whereby the comparative absence or decrease in the signal generated by the L-alanine aminopeptidase substrate indicates the presence of Campylobacter in the sample, wherein said medium further comprises an anti-microbial agent."

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

D5: Corry et al., 1995, Int. J. Food Microbiology 26, 43-76

D6: Hernandez Molina J.M., 1991, Originales Breves, 637-639

D13: Park et al., 1984, Campylobacter - Compendium of Methods for the Microbiological Examination of Foods, Am. Pub. Health Assoc., Washington DC, pp 386-404

D15: Declaration of Drew Lienau, M.S.

D16: Abstracts and Final program of the 10th International Workshop on Campylobacter, Helicobacter and related Organisms, Baltimore, Maryland, September 12-16, 1999

D17 and D17bis: Manuel Milieux de Culture de bioMérieux 02-1994 / 002-03601, section Microbiologie: Hektoen - gélose,

D18: Carlone et al., 1983, J. Clinical Microbiology, 16(6), 1157-1159,

XIV. Appellant's arguments, insofar as they are relevant for the present decision, may be summarized as follows:

The main request was late filed but it represented a genuine attempt to overcome objections under Article 83 EPC which were not part of the decision under appeal but were raised by the board in its communication of 21 July 2011. The late filing did not affect procedural economy because the proceedings were delayed at the respondent's request leaving it enough time to prepare for oral proceedings. There were no facts on file that the claimed medium and method were insufficient for the detection of campylobacter. The claimed subject matter

could not be derived from the cited prior art in an obvious way.

XV. Respondent's arguments can be summarized as follows:

The main request was filed after the date for final submissions and should not be admitted into the proceedings because the issue of insufficiency of disclosure had already been raised in opposition proceedings. In the context of new claim 1, the term "antibiotics to suppress the growth of non-target microorganisms" was open to interpretation, leading to objections under Article 83 and 84 EPC. The claimed subject matter was obvious in view of documents D16 and D6 or D18.

Reasons for the decision

Admissibility of the main request

1. Even though Article 100(b) EPC was invoked as a ground of opposition and substantiated in respondent's opposition brief, neither the minutes of the oral proceedings before the first instance nor the decision under appeal made any mention of this issue.

2. The board, in its communication accompanying the summons to oral proceedings, expressed its view that claims 1 and 9, filed with the main request of the grounds of appeal (cf. section 9 above), were product claims in which the suitability of the claimed products for the detection of *Campylobacter* was part of the definition of the claimed subject matter.

However, claims 1 and 9 lacked a technical feature, i.e. the presence of antibiotics to suppress the growth of non-target microorganisms, which was essential for the detection of *Campylobacter*.

3. Only on 20 October 2011, i.e. five days after the date of 15 October 2011 set for final submissions, the appellant filed the main request which is the subject of the present decision. It did not present any arguments to justify this delay.

4. Admissibility of late filed requests is at the discretion of the board (Article 13(1) RPBA). In general, the boards of appeal admit amended claims into the proceedings if the amendments are properly justified, e.g. have been filed as a response to objections or comments which were not part of the decision under appeal but have been raised in writing during the appeal proceedings (cf. Case Law of the Boards of Appeal, 6th edition, 2010, VII.E.16.4.2).

In the present case, the amendments were clearly occasioned by objections which were not dealt with in the appealed decision and were intended to overcome an objection raised in the board's communication. The oral proceedings, originally scheduled for 15 November 2011, were postponed to 2 February 2012 upon request of the respondent. Thus, the respondent still had about three months time for preparing for the oral proceedings. Moreover, the amendments clearly addressed an issue originally raised by the respondent in opposition proceedings and could therefore not take it by surprise.

Under these circumstances the board decided to admit the main request.

Article 123(2),(3) EPC

5. The respondent had no objections, and also the board considers the requirements of Articles 123(2) and 123(3) EPC to be met.

Article 84 EPC

6. In opposition appeal proceedings, objections under Article 84 EPC can only be allowed if they arise out of amendments made in the course of the opposition or appeal proceedings (cf. Case Law of the Boards of Appeal, 6th edition, 2010, VII.D.4).
7. Claim 1 of the main request is directed to a medium comprising four characterising features labelled (a) to (d) (cf. section XII above).
8. Claim 1 as granted (cf. section XI above) referred to a composition for detecting a target microorganism in a sample, comprising a conditionally detectable marker with the technical features of part (b) of the main request, and a substrate for an aminopeptidase that is absent from the target microorganism comprising a signal moiety with the features of part (c) of the main request.

Dependent claims 12 and 14 as granted (cf. section XI above) further specified the composition to comprise a

growth supporting medium containing antibiotics to suppress the growth of non-target organisms.

9. The features of these dependent claims have been incorporated into part (d) of the main request. The consequence of these amendments is that the medium of claim 1 comprises the same features (b) to (d) as the composition of claim 14 as granted. The fact that the subject matter of claim 1 has changed from a composition to a medium does not affect the meaning of part (d). Thus, respondent's argument that the combination of parts (b), (c) and (d) gave rise to new ambiguities concerning the technical meaning of part (d) must fail.

Article 83 EPC

10. The medium of claim 1, is used for the selective enrichment of *Campylobacter* from a sample and is characterised by three essential elements. The first element is a growth medium comprising antibiotics. The antibiotics are needed to suppress as much as possible the growth of microorganisms other than *Campylobacter*. The second element is a "conditionally detectable marker", providing a detectable signal when in contact with any viable microorganism. Thus, any microorganism surviving in the medium will produce a first detectable signal. The third element is a substrate for an L-alanine aminopeptidase linked to a signal moiety. Any microorganism comprising an L-alanine aminopeptidase will cleave the signal moiety from the substrate and produce a second detectable signal. *Campylobacter* lacks an L-alanine aminopeptidase and will, if present, not provide this second signal.

11. Claim 1 is a product claim defined by its components and its suitability for the detection of Campylobacter. In a case where the technical effect is expressed in the claim, the issue whether this effect is achieved across the whole scope of the claim is a question of sufficiency of disclosure (Decision of the Enlarged Board of Appeal, G 0001/03, OJ 2004, 413, Reasons 2.5.2).

It thus has to be established if the patent application puts the skilled reader, taking into account its general knowledge, in a position to prepare the medium of claim 1, and to practice the method of claim 10 readily and without undue burden across essentially the whole breadth of the claims.

12. The board disagrees with respondent's argument that the skilled person was not in a position to select appropriate antibiotics and was left with a medium in which gram positive microorganisms could survive and create false results.

The patent teaches that Campylobacter lacks L-alanine aminopeptidase and uses this absence for the further characterization of any colonies surviving in a selective growth medium (cf. [0047] of the patent specification). It was furthermore known that L-alanine aminopeptidase is absent from gram-positive bacteria (documents D6 and D18; also [0047], second sentence). Antibiotics selectively suppressing the growth of gram-positive microorganisms were well known in the art (cf. point 13 below) and also mentioned in [0048] of the patent specification.

13. Referring to paragraphs [0002] and [0052] of the patent specification, the respondent argued furthermore that selecting appropriate antibiotics was difficult because some were used to suppress the growth of certain gram-negative microorganisms. Such antibiotics could affect the sensitivity and selectivity of the method for detecting *Campylobacter*.

The board notes that the addition of antibiotics to suppress the growth of gram positive and other microorganisms is not new in the field of detecting *Campylobacter*. It is a standard procedure in the art to selectively enrich *Campylobacter* in a medium comprising a variety of antimicrobial agents to suppress the growth of non-target microorganisms (D13, pp. 390-393; cf. also expert declaration D15, point 4, and references cited therein). Commercially available media for the detection of *Campylobacter* like "Campy line agar" and "Campy CEFEX agar" both comprise selective antibiotics to suppress the growth of non-target microorganisms (cf. D16 for Campy line agar, and D5 (page 51) for antibiotics present in Campy CEFEX agar).

14. The board further notes that no evidence or verifiable facts are on file to substantiate the respondent's objection under Article 83 EPC.
15. In the absence of any evidence to the contrary as well as in view of the teaching of the patent, and the fact that a range of antibiotics was routinely used in the prior art for the detection of *Campylobacter*, the board is convinced that the skilled reader, taking into account its general knowledge, was capable of readily

selecting appropriate antibiotics to inhibit the growth of non-target microorganisms, in particular gram-positive microorganisms.

Article 54 EPC

16. The respondent had no objections with regard to novelty and the board is satisfied that the requirements of article 54 EPC are met.

Article 56 EPC

17. The board agrees with the parties that document D16 is the closest prior art. It discloses Campy-Line agar, a selective differential agar for the isolation and enumeration of Campylobacter, comprising selective antibiotics and triphenyl-tetrazolium chloride as a conditionally detectable marker.

18. As a first step, the technical problem underlying the present invention has to be defined.

The appellant argued that the Campy-Line agar of document D16 alone was not sufficient to differentiate Campylobacter from other gram-negative bacteria. Further time consuming and expensive steps were needed to confirm or deny the identity of colonies growing on this agar. The medium of claim 1 allowed the detection of Campylobacter without such additional steps. Thus, the technical problem to be solved by the invention consisted of providing improved means and methods to detect Campylobacter.

The respondent argued that the claimed solution did not solve the problem across the entire breadth of the claim because contaminating gram-negative bacteria also lacking the L-alanine aminopeptidase could not be distinguished from Campylobacter based on the enzyme activity. As a consequence, as with Campy-line agar, further confirmation steps were needed. Therefore, the technical problem had to be defined as the provision of alternative means and methods for detecting Campylobacter.

The board has not seen convincing evidence that gram-negative bacteria lacking the L-alanine aminopeptidase indeed pose a problem. Furthermore, the presence of two detectable marker molecules in the medium allows the simultaneous assessment of two properties, in the board's view clearly an improvement.

Thus, the board agrees with appellant's definition of the technical problem as the provision of improved means and methods for the detection of Campylobacter.

19. The solutions to this problem offered by the patent are the medium of claim 1 and the method of claim 10.

Claim 1 defines a medium comprising a conditionally detectable marker, a medium to support the growth of Campylobacter comprising antibiotics to suppress the growth of non-target microorganisms, and a substrate for an L-alanine aminopeptidase linked to a cleavable signal moiety. Campylobacter present in a medium of the invention, will provide a signal with the conditionally detectable marker but, due to its lack of L-alanine

aminopeptidase, will not provide a second signal from the cleavable enzyme substrate.

Claim 10 provides a method for detecting Campylobacter comprising the use of a medium according to claim 1.

As shown by the results of Examples 1 and 2, the absence of a detectable signal in a medium in which Campylobacter has grown provides a suitable indicator for the presence of Campylobacter. The board considers it plausible that the same effect is also achieved when Campylobacter is grown in a medium comprising antibiotics to suppress the growth of non-target microorganisms. The board is therefore satisfied that the technical problem is solved by the medium of claim 1 and the method of claim 10.

20. It remains to be established if the claimed solution involved an inventive step.

21. Based on its definition of the technical problem as the provision of an alternative method for detecting Campylobacter (cf. above), and referring to the Case Law (T 631/06 of 19 November 2008, T 879/05 of 26 September 2007, T 931/04 of 7 September 2007, and T 012/07 of 15 June 2010) the respondent argued that the correct approach in the assessment of inventive step was not whether the skilled person would have arrived but merely whether it could have arrived at the claimed solution. It was thus sufficient to verify if the skilled person could have selected an additional compound, in this case a substrate for an L-alanine aminopeptidase linked to a cleavable signal moiety,

from the prior art and added it to the medium disclosed in document D16.

The board disagrees with the respondent for two reasons. First, the technical problem consisted of providing an improved medium (cf. point 18 above), a situation to which the cited decisions do not apply. Second, in the cases underlying the cited decisions, the available prior art contained lists of compounds known or suggested to be suitable for the intended purpose. Selecting compounds from these lists was considered to lack an inventive step. In the case at issue here, the prior art documents cited by the respondent (D6, D9, and D18) refer to the use of several compounds for a purpose different from that of the claimed invention. This represents an entirely different situation.

22. Therefore, the question to be answered is whether the skilled person would have combined the prior art teachings to arrive at the claimed solution with a reasonable expectation of success but not whether it merely could have done so. Furthermore, it is established case law that when assessing inventive step, an interpretation of the prior art documents as influenced by the problem solved by the invention, where the problem was neither mentioned or even suggested in those documents, must be avoided, such an approach being merely the result of an a posteriori analysis (cf. Case Law of the Boards of Appeal, 6th edition, 2010, I.D.5).

23. The respondent argued that the claimed solutions were obvious in view of document D16 in combination with any of documents D6 or D18.

24. Document D6 as well as document D18 relate to the use of L-alanine aminopeptidase as a marker for distinguishing gram-positive from gram-negative bacteria.

Document D6 evaluates the usefulness of a commercially available test to detect L-alanine aminopeptidase activity for differentiating the structure of bacterial cell walls. In essence a good correlation between the presence or absence of L-alanine aminopeptidase and a gram-stain was found. With the exception of *Campylobacter* and a few gram-negative anaerobic bacilli, all gram negative bacteria showed L-alanine aminopeptidase activity (cf. Table 1 and the section "Results and discussion"). Document D6 concludes with the statement that detection of the L-alanine aminopeptidase "can be of use to confirm the Gram stain reaction".

Document D18 is concerned with methods for distinguishing gram-positive from gram-negative bacteria and compares the gram stain with a "KOH test" and a test for the presence of L-alanine aminopeptidase (LANA test). The authors found that of all gram-negative bacteria examined only the micro-aerophilic *Campylobacteria* and two bacteroides species were LANA negative (cf. Table 1 and page 1159, left column, last para.). The authors conclude that "both the KOH and the LANA test may be useful adjuncts for characterizing

clinical isolates and therefore merit further evaluation".

25. Referring to documents D17 and D17bis and the skilled person's general knowledge, the respondent argued that "negative markers", were routinely used in the detection of microorganisms. (In the context of the patent under dispute, the substrate for L-alanine aminopeptidase is regarded as a "negative marker" for *Campylobacter* because the absence of a signal is used to confirm the presence of *Campylobacter*.) Since the use of such markers was known in the art, no inventive skills were needed to add a substrate for L-alanine aminopeptidase linked to a cleavable signal moiety to the medium of document D16. In the respondent's opinion the skilled person would have been prompted to do so because documents D6 as well as D18 showed that *Campylobacter* gave a negative signal with a substrate for L-alanine aminopeptidase.

This argument is not convincing because documents D6 and D18 were not concerned with the use of the substrate of an L-alanine amino peptidase for any purpose other than the distinction of gram-positive and gram-negative bacteria, let alone with its use as a negative marker.

26. Document D16 is silent about the inclusion of further marker substances to improve the detection of *Campylobacter*, and nothing in documents D6 or D18 points to or even remotely suggests the usefulness of a test for the presence or absence of L-alanine aminopeptidase for the detection of *Campylobacter*.

In the absence of any hints or clues leading or directing the skilled person to combine the cited documents, the solutions to the technical problems as defined in claims 1 and 10 must be considered non-obvious.

27. The board is therefore convinced that the skilled person trying to solve the above-mentioned technical problem would not have arrived at the solutions of independent claims 1 and 10 in an obvious way.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to maintain the patent with claims 1 to 10 of the Main Request submitted at the oral proceedings before the Board and a description to be adapted.

The Registrar:

The Chairman:

A. Wolinski

M. Wieser