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Datasheet for the decision of 24 March 2022

Case Number: T 1588/19 - 3.3.01

Application Number: 05854636.7

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Language of the proceedings: EN

Title of invention:
RAPID MICROBIAL DETECTION AND ANTIMICROBIAL SUSCEPTIBILITY TESTING

Patent Proprietor:
Accelerate Diagnostics, Inc.

Opponent:
bioMérieux Inc.

Relevant legal provisions:
EPC Art. 54, 123(2)
RPBA Art. 12(4)

Keyword:
Novelty - (no)
Late-filed auxiliary requests - requests withdrawn before the opposition division
Amendments - allowable (no)

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Case Number: T 1588/19 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 24 March 2022

Appellant: (Patent Proprietor)	Accelerate Diagnostics, Inc. 3950 S. Country Club Road, Suite 470 Tucson, AZ 85714 (US)
Representative:	Arends, William Gerrit Marks & Clerk LLP 15 Fetter Lane London EC4A 1BW (GB)
Respondent: (Opponent)	bioMérieux Inc. 100 Rodolphe Street Durham, NC 27712 (US)
Representative:	Murgitroyd & Company Murgitroyd House 165-169 Scotland Street Glasgow G5 8PL (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 20 March 2019 revoking European patent No. 1831692 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	A. Lindner
Members:	R. Hauss
	L. Bühler

Summary of Facts and Submissions

I. European patent No. 1 831 692 (patent in suit) was granted with a set of 11 claims.

II. The patent in suit was opposed under Article 100(a), (b) and (c) EPC on the grounds that the claimed subject-matter lacked novelty and inventive step, was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, and extended beyond the content of the application as filed.

III. The documents cited in the opposition proceedings included the following:

D1: Applied and Environmental Microbiology 70(2), 675-678 (February 2004)

IV. The patent proprietor requested that the opposition be rejected (main request) and, in the course of the opposition proceedings, submitted a number of amended sets of claims as auxiliary requests.

V. During the oral proceedings held before the opposition division, the patent proprietor withdrew auxiliary requests 3 to 14 filed on 30 November 2018 and filed two further sets of claims as its new auxiliary requests 3 and 4 (see the minutes of the oral proceedings of 31 January 2019: page 1, "Opening and requests" and page 3, first and penultimate paragraphs and the decision under appeal: page 2, point 8).

VI. The decision under appeal is the opposition division's decision revoking the patent in suit, announced on 31 January 2019 and posted on 20 March 2019. It is

based on the claims as granted (main request), the claims of auxiliary requests 1 and 2 (both filed with the submission dated 30 November 2018) and the claims of auxiliary requests 3 and 4 (both filed during the oral proceedings before the opposition division).

VII. In the decision under appeal, the opposition division ruled as follows:

(a) The claims of the main request and auxiliary request 1 were not allowable because they contained added subject-matter (Articles 100(c) and 123(2) EPC).

(b) While the claims of auxiliary request 2 met the requirements of Article 123(2) EPC, the subject-matter of claim 1 lacked novelty over the disclosure of document D1 (Articles 100(a), 52(1) and 54(2) EPC).

(c) Auxiliary requests 3 and 4 were admitted. However, the subject-matter of claim 1 of both these requests lacked novelty over the disclosure of D1.

VIII. The patent proprietor (appellant) filed an appeal against this decision. With the statement setting out the grounds of appeal, the appellant submitted an amended main request and auxiliary requests I to V.

IX. The **main request** is identical to former auxiliary request 2 considered in the decision under appeal. Claim 1 (the sole independent claim) reads as follows:

"1. A method for detecting growth of individual microorganism cells in a sample comprising:

(a) contacting the sample with a biosensor comprising at least one detection surface, a detection module and a concentration module;

(b) concentrating the individual microorganism cells onto the at least one detection surface such that each individual cell is at a discrete site that is spatially separated;

(c) subjecting the individual microorganism cells to growth conditions for a first period of time in the presence or absence of one or more antimicrobial agents; and

(d) detecting growth of the individual microorganism cell or cells on the at least one detection surface as an indication of their viability."

X. **Auxiliary request I** is identical to former auxiliary request 3 considered in the decision under appeal.

Claim 1 of auxiliary request I is identical to claim 1 of the current main request, except for the following addition in step (d) after *"viability"*:

", wherein said detecting comprises detecting the presence of daughter cells at substantially the same location on the at least one detection surface as the individual microorganism cells from which they are derived".

XI. Claim 1 of **auxiliary request II** ("clean" version) reads as follows (differences in comparison with claim 1 of auxiliary request I underlined by the board):

"1. A method for detecting growth of individual microorganism cells in a sample <u>such that a clonal relationship can be established</u> comprising:

(a) contacting the sample with a biosensor comprising at least one detection surface, a detection module and a concentration module;

(b) concentrating the individual microorganism cells onto the at least one detection surface such

that each individual cell is at a discrete site that is spatially separated;

(c) subjecting the individual microorganism cells to growth conditions for a first period of time in the presence or absence of one or more antimicrobial agents; and

(d) detecting growth of the individual microorganism cell or cells on the at least one detection surface as an indication of their viability, wherein said detecting comprises detecting the presence of daughter cells at substantially the same location on the at least one detection surface as the individual microorganism cells from which they are derived and obtaining a series of microscopy images over time of the daughter cells and the individual microorganism cells from which they are derived at said location such that a clonal relationship therebetween can be established."

XII. **Auxiliary request III** is identical to auxiliary request II, except that in feature (d) of claim 1, *"the individual microorganism cells from which they are derived"* becomes *"the individual microorganism cell from which they are derived"*. (difference underlined by the board, two occurrences)

XIII. **Auxiliary request IV** is identical to former auxiliary request 4 considered in the decision under appeal.

Claim 1 of this request reads as follows (differences in comparison with claim 1 of auxiliary request I underlined by the board):

"1. A method for detecting growth of individual microorganism cells in a sample such that a clonal relationship can be established comprising:

(a) contacting the sample with a biosensor comprising at least one detection surface, a detection module and a concentration module;

(b) concentrating the individual microorganism cells onto the at least one detection surface such that each individual cell is at a discrete site that is spatially separated,

wherein concentration of the individual microorganism cells onto the at least one detection surface is achieved by a method selected from the group consisting of electrophoresis, dielectrophoresis, centrifugation, affinity capture, phase partitioning, magnetic field capture, recirculation, diffusion or a combination of these methods;

(c) subjecting the individual microorganism cells to growth conditions for a first period of time in the presence or absence of one or more antimicrobial agents; and

(d) detecting growth of the individual microorganism cell or cells on the at least one detection surface as an indication of their viability, wherein said detecting comprises detecting the presence of daughter cells at substantially the same location on the at least one detection surface as the individual microorganism cells from which they are derived and obtaining a series of microscopy images over time of the daughter cells and the individual microorganism cells from which they are derived at said location such that a clonal relationship therebetween can be established."

XIV. **Auxiliary request V** differs from auxiliary request IV only by the deletion of the term *"diffusion"* from the list of concentration methods in step (b) of claim 1.

XV. In its reply to the grounds of appeal, the opponent (respondent) objected to, *inter alia*, the admission of auxiliary requests II and III and argued that claim 1 of auxiliary requests IV and V contained added subject-matter.

XVI. In preparation for oral proceedings, the board issued a communication under Article 15(1) RPBA advising the parties of its preliminary opinion. The communication mentioned, *inter alia*, the following points:

- As far as the main request and auxiliary request I were concerned, novelty appeared to be the principal issue addressed by the parties (see point 1.1 and sections 3 and 4 of the board's communication dated 12 March 2021).
- Admittance of auxiliary requests II and III might have to be discussed (points 1.2 and 6.1 to 6.4).
- The "clean" and "marked-up" versions of auxiliary request II provided by the appellant differed from each other (point 6.5). The appellant was requested to indicate which version was correct.
- Allowability under Article 123(2) EPC of the amendments in auxiliary requests IV and V might also require consideration (points 1.2, 8.2 and 10.1).

XVII. In a letter dated 14 February 2022, the appellant indicated that it would not be attending the oral proceedings scheduled for 24 March 2022 and that it relied on its written submissions. The appellant did

not reply in substance to the respondent's letter and the board's communication.

XVIII. Oral proceedings before the board were held on 24 March 2022 in the absence of the appellant, in accordance with Article 15(3) RPBA and Rule 115(2) EPC. At the respondent's request, the oral proceedings took place in the form of a videoconference.

XIX. The appellant's written arguments, as far as relevant to the outcome of this decision, may be summarised as follows.

Novelty - main request

Document D1 (e.g. Figure 3 and page 676, column 2, lines 13 to 17) did not unambiguously disclose that each individual cell on the detection surface was at a discrete spatially separated site (as required in step (b) of claim 1). Furthermore, D1 did not disclose a concentration step as defined in step (b) of claim 1.

Novelty - auxiliary request I

In addition to the differences in step (b), claim 1 of auxiliary request I further differed from the disclosure of document D1 in step (d), which required the detection of daughter cells.

By definition, a daughter cell was a separate independent cell. Frames 4 and 8 of Figure 3 in document D1 did not show daughter cells but only a single cell which changed in size over time. There was no direct and unambiguous disclosure in D1 of daughter cells being detected after their separation from the parent cell. Figure 4 of D1 added nothing over the disclosure of Figure 3 in this regard. The whole concept of D1 required that daughter cells be removed from the detection surface immediately after being

formed, i.e. the method was purposively designed not to detect daughter cells. Thus, D1 taught away from the claimed subject-matter.

Admittance - auxiliary requests II and III

Auxiliary request II was a new request which further modified step (d) of auxiliary request I on the basis of paragraph [0193] of the application as filed. The filing of this request was justified because the opposition division's conclusion that D1 described detecting the presence of a daughter cell had been unexpected.

Auxiliary request III was also a new request. It was based on auxiliary request II, but part (d) of claim 1 had been further amended on the basis of paragraph [0031] of the application as filed. This request was submitted in response to the opposition division taking the unexpected position that claim 1 could be interpreted to mean the detection of a series of images of any daughter cell and a parent cell.

Amendments - auxiliary requests IV and V

The concentrating methods recited in claim 1 of auxiliary requests IV and V were based on paragraph [0058] of the application as filed.

XX. The respondent's arguments, as far as relevant to the outcome of this decision, may be summarised as follows.

Novelty - main request

The subject-matter of claim 1 lacked novelty over the disclosure of document D1. The respondent agreed in this regard with the opposition division's reasoning set out in point 3.4.3 of the decision under appeal and referred to the title, abstract and Figures 1 and 3 of D1.

It was clear from D1 that the growth of individual cells could be tracked. This implied that each such cell was at a site discrete enough to allow such tracking to occur.

Contrary to the appellant's arguments,

- claim 1 did not require that the claimed method be set up to determine the absolute number of cells in a sample;
- there was no requirement that all cells from a sample should end up on the detection surface;
- the feature *"concentrating the individual microorganism cells onto the at least one detection surface"* simply meant that the number of cells on the detection surface was increased from zero to a value above zero.

Novelty - auxiliary request I

With the method of D1, daughter cells would inevitably be formed and detected before they were removed by the flow of the medium. The skilled person would clearly understand the growth profile shown in D1 as relating to the growth of a cell and its dividing in two and repeated growth. To generate an accurate data set of the generation times of the bacteria, the setup of D1 must detect when daughter cells are produced (D1: page 676, column 1, first full paragraph and page 678, column 1, lines 5 to 6).

Admittance - auxiliary requests II and III

The appellant's attempt to introduce the claim set of auxiliary request II was an abuse of process. In the first-instance proceedings, the appellant had withdrawn former auxiliary request 6, which had contained an almost identical claim 1. Auxiliary request II as well as auxiliary request III, which was a minor variant of

auxiliary request II, should therefore be held inadmissible.

Amendments – auxiliary requests IV and V

Claim 1 of auxiliary request IV contained added subject-matter since the application as filed did not disclose some of the concentrating methods recited in step (b) of claim 1 in the same context.

For instance, affinity capture was disclosed in the application as filed only for the purpose of pre-concentration prior to step (a); not for attaching the cells to the detection surface (after contacting the sample with the biosensor) in step (b). The same objection applied to claim 1 of auxiliary request V.

XXI. The appellant requested that the decision under appeal be set aside and that the case be remitted to the opposition division for consideration of inventive step on the basis of the claims of the amended main request or one of auxiliary requests I to V, all submitted with the statement setting out the grounds of appeal.

XXII. The respondent requested that the appeal be dismissed.

The respondent also requested that auxiliary requests II and III be held inadmissible.

Reasons for the Decision

1. Novelty - main request

1.1 Document D1 describes a method for observing the growth of a large number of individual bacterial cells. The cells attach to a transparent solid surface in a flow chamber that is mounted on a microscope equipped with a digital camera. The shear force of the flow removes daughter cells, making it possible to monitor the consecutive divisions of a single cell. In this manner, the effects of different growth environments on cell growth can be studied (see D1: abstract; Figure 1 and page 676, column 2, lines 13 to 20).

1.2 The appellant argued that step (b) of claim 1 distinguished the claimed subject-matter from the disclosure of D1 owing to the concentrating step and the requirement of spatial separation.

1.3 The board considers that within the context of claim 1, "concentrating the cells onto the detection surface" means that conditions are created in which cells are captured to occupy sites on the detection surface. This also happens in D1.

1.4 Furthermore, according to D1, the growth of individual cells is tracked. These cells must necessarily be at discrete sites on the transparent surface. Claim 1 does not define the term "spatially separated" by any quantitative or relative criterion which might distinguish the claimed method from the disclosure of D1.

1.5 Taking these considerations into account, the disclosure of D1 anticipates the combination of

technical features disclosed in claim 1 of the main request.

1.6 For these reasons, the subject-matter of claim 1 of the main request lacks novelty (Articles 100(a), 52(1) and 54(2) EPC).

2. Novelty - auxiliary request I

2.1 Claim 1 of auxiliary request I differs from claim 1 of the main request by the additional requirement, in step (d), that a daughter cell is detected at substantially the same location as the original cell.

2.2 It was a matter of dispute whether this feature was suitable for distinguishing the claimed method from that described in D1.

2.3 The experimental set-up of D1 provides for cell growth and makes it possible to monitor cell divisions, and it provides for the removal of daughter cells (see D1: abstract and point 1.1 above). Hence, it is clearly understood in the context of D1 that daughter cells are formed.

Since the growth of the cells is observed, the formation of daughter cells is visible to the observer. According to D1, the characteristics studied included the size of the cells before and after division, the spatial and temporal distribution of the cell size, the generation times of single cells, and the variation in successive generation times of the same cell (see D1: page 676, left column, first full paragraph and page 678, left column, lines 5 to 6). The skilled person would understand the growth profile reported in D1 (e.g. in Figure 3) as relating to the growth of a cell and its subsequent splitting in two and repeated growth.

2.4 Claim 1 only requires that daughter cells are detected; there is no requirement that the daughter cells not be removed after their formation, or that they be observed for a longer period of time.

2.5 In view of these considerations, the feature according to point 2.1 above does not distinguish the claimed subject-matter from the disclosure of D1.

2.6 For these reasons, the subject-matter of claim 1 of auxiliary request I also lacks novelty (Articles 100(a), 52(1) and 54(2) EPC).

3. Admittance - auxiliary requests II and III

3.1 The clean and marked-up versions of auxiliary request II differ from each other. The appellant did not reply to the board's invitation to indicate which of the two was the intended version.

3.2 Auxiliary request II: clean version

Claims 1 to 8 of auxiliary request II (clean version) are identical to claims 1 to 8 of former auxiliary request 6 of 30 November 2018, except that claim 1 of former auxiliary request 6 contained an additional word in the passage *"such that each cell is associated at a discrete site that is spatially separated"* (difference underlined by the board). The deletion of the word *"associated"* does not change the meaning of the claim. Former auxiliary request 6 also contained two more dependent claims (claims 9 and 10).

3.3 Auxiliary request II: marked-up version

In comparison with the clean version, the marked-up version has nine instead of eight claims and does not contain the phrase *"such that a clonal relationship can be established"* in lines 1 to 2 of claim 1.

As this same wording is, however, still present in part (d) at the end of the claim, the deletion of its redundant second occurrence does not result in a change in meaning, either. Additional dependent claim 9 is identical to dependent claim 10 of former auxiliary request 6.

3.4 Auxiliary request III is identical to the clean version of auxiliary request II, except that in feature (d) of claim 1, the phrase *"the individual microorganism cells from which they are derived"* becomes *"the individual microorganism cell from which they are derived"* (see point XII. above). Since both versions refer, in any case, to individual cells and to *"(d) detecting growth of the individual microorganism cell or cells"*, this does not result in a change in meaning.

3.5 Owing to the strong similarity of the independent claims, with minor amendments that do not result in a change in meaning, the submission of auxiliary requests II and III is considered an attempt to reinstate auxiliary request 6, which was previously withdrawn (see point V. above). This conclusion applies to either version of auxiliary request II.

3.6 If the appellant wanted a decision on the claims of auxiliary request 6, it should not have withdrawn this request in the first-instance proceedings. This withdrawal precluded the opposition division from deciding on it.

3.7 In view of these considerations, the board held auxiliary requests II and III inadmissible under Article 12(4) RPBA 2007.

4. Amendments - auxiliary requests IV and V

4.1 Claim 1 of auxiliary request IV contains the following feature in step (b):

> *"wherein concentration of the individual microorganism cells onto the at least one detection surface is achieved by a method selected from the group consisting of electrophoresis, dielectrophoresis, centrifugation, affinity capture, phase partitioning, magnetic field capture, recirculation, diffusion or a combination of these methods"*

4.2 Paragraph [0058] of the description is the presumed basis for this feature in the application as filed.

4.3 Paragraph [0058] is a general statement which relates to methods:

> *"to concentrate the microorganisms within the sample either prior to, during or after application to the biosensor and the detection surface(s)"*.

This is followed by a list of concentration methods which includes all the methods recited in claim 1 of auxiliary request IV.

4.4 Application to the biosensor corresponds to step (a) in claim 1, while application to the detection surface(s) corresponds to step (b).

4.5 "Affinity capture" is described only in paragraphs [0061] to [0063] of the application as filed. These paragraphs contain numerous references that this is supposed to be a preconcentration step to be conducted before application of the samples to the biosensor (see the headings *"Preconcentration"* and *"Pre-cartridge: Affinity capture"* and the first

sentence of paragraph [0061] on page 15 of the description).

4.6 The passage in paragraph [0061] explains that the samples containing the microorganisms are passed through a column with a material that binds the microorganisms. Once the sample has been run through the column, the microorganisms are eluted. Such a collector can be used, *inter alia*, to concentrate the microorganisms in a smaller volume of buffer.

4.7 Paragraph [0064], penultimate sentence, makes it clear that a pre-concentration surface (such as in a column used in affinity capture) is not the same as a detection surface (as recited in claim 1).

4.8 Thus, affinity capture is disclosed in the application as filed only in a pre-concentration step prior to step (a) but is recited in claim 1 of auxiliary request IV for use on the sample after contact with the biosensor, in step (b).

4.9 For this reason, claim 1 contains subject-matter going beyond the content of the application as filed, contrary to the requirements of Article 123(2) EPC.

4.10 The same reasoning and conclusion apply to claim 1 of auxiliary request V, which therefore also contravenes the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated