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**Datasheet for the decision
of 3 September 2020**

Case Number: T 1449/18 - 3.4.02

Application Number: 12156921.4

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B01D21/26, B01L3/00

Language of the proceedings: EN

Title of invention:

Systems and methods for particle focusing in microchannels

Applicant:

The General Hospital Corporation d/b/a
Massachusetts General Hospital

Headword:

Relevant legal provisions:

EPC Art. 84

Keyword:

Claims - clarity (no) - essential features

Decisions cited:

T 0032/82

Catchword:



Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 1449/18 - 3.4.02

D E C I S I O N
of Technical Board of Appeal 3.4.02
of 3 September 2020

Appellant: The General Hospital Corporation d/b/a
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 2 February 2018
refusing European patent application No.
12156921.4 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman R. Bekkering
Members: A. Hornung
G. Decker

Summary of Facts and Submissions

- I. The applicant appealed against the decision of the examining division refusing European patent application No. 12156921.4 on the basis of Article 97(2) EPC because the requirements of Articles 84, 83 and 123(2) EPC were not fulfilled.
- II. The applicant requested that the decision under appeal be set aside and a patent be granted on the basis of the claims according to a main request or one of the first to seventh auxiliary requests, all requests filed with the statement setting out the grounds of appeal, wherein the present fourth to seventh auxiliary request correspond to the main request and first to third auxiliary request underlying the appealed decision, respectively.
- III. Oral proceedings before the board were held on 3 September 2020. At the end of the oral proceedings, the applicant confirmed that it upheld its initially filed requests.
- IV. Claims of the requests

Main request

Independent claim 1 according to the main request reads as follows:

"A method for focusing cells in a moving fluid, comprising:

providing cells suspended in a moving fluid into a channel, wherein the channel is curved and has a rectangular cross-section, a height, a width, and a

hydraulic diameter equal to $2 * \text{height} * \text{width} / (\text{width} + \text{height})$;

flowing the fluid through the channel under conditions such that inertial forces acting on the cells result in the localization of a flux of cells in the channel, wherein a lift/drag ratio for the cells is greater or equal to one over a limited region of the channel cross section and the magnitude of the forces is large enough to create focusing of the flux of cells to one or more streams that are localized to within an area having a smallest dimension of, at most, five times the width of the particles."

First auxiliary request

Independent claim 1 according to the first auxiliary request differs from claim 1 of the main request in that it comprises the following additional feature at the end of the claim:

"wherein the channel Reynolds Number of the fluid flow is between about 1 and 250".

Second auxiliary request

Independent claim 1 according to the second auxiliary request differs from claim 1 of the first auxiliary request in that the expression "having a smallest dimension of, at most, five times the width" reads "having a width of, at most, five times the width" and in that it comprises the following additional feature at the end of the claim:

"and wherein a first particle diameter divided by a hydraulic diameter of the channel is greater than or equal to about 0.07 and less than or equal to about 0.5".

Third auxiliary request

Independent claim 1 according to the third auxiliary request differs from claim 1 of the second auxiliary request in that the expression "having a width of, at most, five times the width" reads "having a smallest dimension of, at most, five times the width" and in that it comprises the following additional feature at the end of the claim:

"and wherein a Dean number of the moving fluid is less than or equal to about 20".

Fourth to seventh auxiliary requests

Independent claim 1 according to the fourth to seventh auxiliary request differs from claim 1 of the main request and of the first to third auxiliary request, respectively, only in that the following feature

"that are localized to within an area having a smallest dimension of, at most, five times the width of the particles"

is deleted from claim 1 of the main request, first auxiliary request and third auxiliary request and in that the following feature

"that are localized to within an area having a width of, at most, five times the width of the particles"

is deleted from claim 1 of the second auxiliary request.

Reasons for the Decision

1. Main request - Clarity

Claim 1 lacks clarity (Article 84 EPC).

1.1 According to the description as originally filed, the objective of the present invention corresponds to the "need for a continuous particle sorting, separation, enumerating" (page 2, lines 30 to 32). It provides devices and methods "that result in and use the self-ordering of particles suspended in a fluid traveling through a microfluidic channel" (page 3, lines 3 to 5). More specifically, the present invention provides a system "for focusing particles suspended within a moving fluid into one or more localized stream lines" (page 3, lines 5 to 7).

1.2 Consistent with the objective of the present invention, claim 1 defines a method for focusing cells in a moving fluid "such that inertial forces acting on the cells result in the localization of a flux of cells in the channel" and "to create focusing of the flux of cells to one or more streams", but without defining how the focusing of cells is effectively obtained. This amounts to defining the claimed method for focusing cells in terms of a mere result to be achieved, instead of defining it in terms of technical structural features responsible for achieving the claimed result.

1.3 Such a definition of the claimed subject-matter is contrary to the established case law of the boards of appeal, according to which a claim "must define clearly the object of the invention, that is to say indicate all the essential features thereof. As essential features have

to be regarded all features which are necessary to obtain the desired effect or, differently expressed, which are necessary to solve the technical problem with which the application is concerned" (see T 32/82, point 15 of the Reasons).

1.4 As discussed during oral proceedings and as it is apparent from the description of the application as filed and from the appealed decision, the focusing of the cells depends on many parameters relating to the cells (size, shape, weight, speed, density, interaction between cells, ...), to the fluid (turbulent or laminar regime, velocity, interaction with the cells, viscosity, ...) and to the channel (aspect ratio and size of the rectangular cross-section, length, number of curved channel parts, radius of curvature of the curved channel parts, ...). Depending on these parameters, multiple kinds of forces (Dean drag, Stokes drag, inertial lift, pressure from Dean drag flow, additional forces in curved channels, centrifugal forces acting on individual particles, "wall effect" lift forces away from the wall and shear-gradient-induced lift forces directed toward the wall) having various magnitudes act on the cells.

1.5 The only feature in claim 1 which could be seen as being of any relevance to the question of how to achieve the claimed result corresponds to the lift/drag ratio being greater or equal to one over a limited region of the channel cross section. However, neither the exact meaning of the lift/drag ratio nor the way how to determine its exact numerical value and the way how to produce effectively the value is clear from the wording of the claim, especially in view of the large number of parameters influencing the behaviour of cells in a moving fluid and, hence, the meaning and determination of the lift/drag ratio. The additional general reference in

claim 1 to the relative magnitude of undefined forces is, due to its vagueness, also not suitable to guarantee the obtention of the claimed result.

One exemplary feature being essential for defining the invention is explicitly mentioned in the appealed decision, point 3. It relates to the fluid velocity. According to the description of the patent application, page 34, lines 16 to 23, focusing of the flux of cells occurs only for a certain range of fluid velocities, called "intermediate fluid velocities". Indeed, despite the lift/drag ratio R_f being larger than 1, as specified in claim 1, the desired technical effect of focusing cells in a moving fluid is not generally assured since at low fluid velocities "the magnitudes of F_z and F_D are too low to create focused streams within the length of channel". Claim 1 defines neither the required numerical value of the fluid velocity nor that of the forces involved for achieving focusing of the cells. In other words, depending on the exact fluid velocity and the exact forces involved, the method of claim 1 provides the result to be achieved or not.

Therefore, it can be deduced from the paragraph on page 34, lines 16 to 23, that defining an adequate fluid velocity is paramount for achieving the claimed result. Incidentally, it is to be noted that the expression "intermediate fluid velocities" as such has merely a relative meaning and that no clear method for determining the adequate "intermediate fluid velocity" appears to be disclosed in the patent application.

- 1.6 Since claim 1 does not define all essential features for focusing cells in a moving fluid, in particular, the fluid velocity is omitted in claim 1, claim 1 lacks clarity (Article 84 EPC).

1.7 Applicant's arguments

1.7.1 The applicant explained that numerous and complex interactions existed between the numerous parameters influencing the focusing of cells in a moving fluid. In particular, lift and drag forces were not independent parameters but interacted *inter alia* with the fluid velocity. As explained on page 34, lines 8 to 15, lift and drag forces inherently included the influence of the fluid velocity U_m . The applicant further referred to page 30, line 20 to page 31, line 9, showing that the inertial forces, i.e. lift and drag forces, the channel Reynolds number R_C and the particle Reynolds number R_P , representing further important parameters in the process of focusing cells, were all a function of the fluid velocity. By specifying in claim 1 a lower limit of 1 for the lift/drag ratio, together with the constraint that the magnitude of the forces is large enough to create focusing of the cells, the required fluid velocity was, albeit indirectly, defined in claim 1.

The applicant's reasoning that the missing essential feature is "indirectly defined" by defining it on the basis of the result to be achieved is not convincing since it goes round in circles. While the board acknowledges that the technical effect of the fluid velocity is somehow present in claim 1 through its influence on the claimed lift/drag ratio, it is not convinced by this argument. Indeed, in addition to be a function of the fluid velocity, the lift/drag ratio is also a function of numerous other parameters (see the formulas of the lift and drag forces F_Z and F_D in the application as filed, pages 31 to 33) which are also not specified in claim 1. Therefore, the mere dependency of the lift/drag ratio on velocity is not sufficient to deduce velocity values

accurately from the lift/drag ratio interval specified in claim 1. According to the description, page 34, lines 16 to 23, focusing of cells requires (i) a specific range of intermediate fluid velocities, (ii) a lift/drag ratio larger than 1 and (iii) forces sufficiently large. However, claim 1 does not specify the exact range of values of the fluid velocity and of the forces.

1.7.2 While directing the board's attention to experimental results, the applicant highlighted the "extraordinary" and "unbelievable" technical effect achieved by the invention by referring to figure 24, showing the influence of the particle Reynolds number R_p on the focusing of the cells: if R_p is too small or too large, no focusing occurs; focusing occurs only for intermediate values of R_p . Since R_p varied proportionally with fluid velocity, the behaviour of R_p shown in figure 24 confirmed that focusing of the cells occurred for intermediate fluid velocities. Figure 24 also confirmed that the result achieved by the invention was easy to be detected and immediately apparent to the skilled person. The applicant further referred to figures 18A-C showing focusing of cells in a line and to figure 34B showing streamlining and ordering of cells depending on their size, all these effects of the invention being readily recognisable. Finally, the applicant referred to figure 33C showing that if the lift/drag ratio F_z/F_D was greater or equal to one, the cells were less displaced and, hence, were focused, consistent with the condition specified in claim 1.

The board does not contend that the experimental results of the invention submitted by the applicant "are somehow incorrect or worthy of doubt" (letter of reply of 3 August 2020, page 4, second paragraph). Nevertheless, the board cannot follow the argument of the applicant according to which the fact that the claimed result can

actually be achieved and is "extraordinary" and readily recognisable, is sufficient to fulfil the requirement of Article 84 EPC. In contrast, the board considers that Article 84 EPC requires the presence in claim 1 of all the features necessary to achieve the claimed result. The basic problem consists in that claim 1 does not specify all the features essential for achieving the result.

1.8 It follows that claim 1 of the main request lacks clarity.

2. First to third auxiliary requests - Clarity

Claim 1 of the first to third auxiliary requests lacks clarity (Article 84 EPC).

2.1 Claim 1 of the first auxiliary request has been amended with respect to claim 1 of the main request by adding a condition on the channel Reynolds number R_C .

Claim 1 of the second auxiliary request has been amended with respect to claim 1 of the first auxiliary request essentially by adding a condition on the particle diameter to hydraulic diameter ratio.

Claim 1 of the third auxiliary request has been amended with respect to claim 1 of the second auxiliary request essentially by adding a condition on the Dean number D_e .

Accordingly, claim 1 of the third auxiliary request is the claim which comprises the most technical features defining the circumstances under which focusing of cells may occur. Nevertheless, a large number of additional parameters influencing the focusing of cells in a moving fluid (see point 1.4 above) remains undefined in claim 1 of the third auxiliary request. The application as originally filed does not disclose that the three numerical conditions

defined in claim 1 of the third auxiliary request are sufficient to guarantee the obtention of the claimed result, i.e. the focusing of the flux of cells, under all the possible experimental set-ups covered by the wording of the claim. On the contrary, in view of for instance the lack of definition of the fluid velocity in claim 1 of the third auxiliary request, it can be deduced from the application as originally filed, describing that the fluid velocity is essential for focusing the flux of cells (see point 1.5 above), that claim 1 of the third auxiliary request does not define all features essential for achieving the claimed result.

Therefore, claim 1 of the third auxiliary request lacks clarity.

Since claim 1 of the first and the second auxiliary requests comprises even less technical features relevant to the obtention of the claimed result than claim 1 of the third auxiliary request, it lacks clarity for essentially the same reasons as claim 1 of the third auxiliary request.

2.2 The applicant submitted that the channel Reynolds number R_C is calculated by the formula $R_C = U_m * D_h / \nu$ (page 30 of the description of the patent application) and, therefore, R_C did include information concerning the fluid velocity U_m . Each of the three parameters specified in claim 1 of the first to third auxiliary requests, i.e. R_C , diameter ratio and D_e , had been carefully selected by scientists and described in the most succinct manner all the technical conditions required for focusing a flux of cells in a moving fluid. The applicant further referred to page 36, lines 4 to 11, disclosing that the features added to claim 1 of the main request provided the claimed result.

The board is not convinced by these arguments. R_C does not only depend on the fluid velocity U_m but also on the further parameters D and v whose numerical values are undefined in claim 1. The application as originally filed does not disclose that the fluid velocity may be deduced precisely and unambiguously from R_C . The passage referred to by the applicant on page 36, lines 4 to 11, of the patent application merely discloses that in certain embodiments the three added features in claim 1 of the third auxiliary request can be realised. However, from this disclosure it cannot be deduced that the three added features are essential and sufficient for achieving the claimed result under all the experimental circumstances falling under the scope of the claim.

2.3 It follows that claim 1 of the first to third requests lacks clarity.

3. Fourth to seventh auxiliary requests - Clarity

Claim 1 of the fourth to seventh auxiliary request differs from claim 1 of the main request and the first to third auxiliary request, respectively, essentially in that the feature clarifying the area of localization of the streams of flux of cells has been deleted. This amendment is not suitable to overcome the existing clarity objection since it enlarges the scope of protection instead of defining all the essential features, in particular, the fluid velocity.

Therefore, claim 1 of the fourth to seventh auxiliary requests lacks clarity (Article 84 EPC) for essentially the same reasons as claim 1 of the main request and the first to third auxiliary requests, respectively.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



M. Kiehl

R. Bekkering

Decision electronically authenticated