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Datasheet for the decision of 12 February 2025

Case Number: T 0455/23 - 3.3.08

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Language of the proceedings: EN

Title of invention:
A METHOD FOR CONTROLLING CULTURE PARAMETERS IN A BIOREACTOR

Patent Proprietor:
Cytiva Sweden AB

Opponent:
Sartorius Stedim Biotech GmbH

Headword:
METHOD FOR CONTROLLING CULTURE PARAMETERS/CYTIVA

Relevant legal provisions:
EPC Art. 56

Keyword:
Auxiliary requests 1 to 8, 14 and 15 - inventive step (no)

Decisions cited:
T 1179/16, T 1701/22

Catchword:

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Case Number: T 0455/23 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 12 February 2025

Appellant: (Patent Proprietor)	Cytiva Sweden AB Björkgatan 30 751 84 Uppsala (SE)
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Appellant: (Opponent)	Sartorius Stedim Biotech GmbH August-Spindler-Strasse 11 37079 Göttingen (DE)
Representative:	Huber, Michael Knall, Robert Müller-Boré & Partner Patentanwälte PartG mbB Friedenheimer Brücke 21 80639 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 22 December 2022 concerning maintenance of the European Patent No. 2516682 in amended form**

Composition of the Board:

Chairwoman	T. Sommerfeld
Members:	D. Pilat
	A. Bacchin

Summary of Facts and Submissions

I. European patent No. 2 516 682 is based on European patent application No. 10 839 894.2, originally filed as international patent application published as WO 2011/078773. The patent was opposed on the grounds of Article 100(a) EPC, in conjunction with Articles 54 and 56 EPC, and of Article 100(b) and (c) EPC. In an interlocutory decision, the opposition division considered that Article 100(c) EPC prejudiced the maintenance of the patent as granted, that auxiliary request 1 did not comply with Article 56 EPC, but that the patent could be maintained in amended form on the basis of auxiliary request 2 filed during oral proceedings.

II. The patent proprietor and the opponent both filed an appeal against this decision.

III. In a communication under Article 15(1) RPBA, the parties were informed of the board's provisional opinion on the issues of the case.

IV. In appeal, the patent proprietor (appellant I) requested *inter alia* that the appealed decision be set aside and the patent be maintained as granted (main request) or alternatively on the basis of the claims of any of auxiliary requests 1 to 15, and that the inventive step attack based on document D8a be disregarded. During oral proceedings before the board, appellant I withdrew the main request and auxiliary requests 9 to 13, as well as its objection regarding the admittance of document D8a into the proceedings.

V. Claim 1 of **auxiliary request 1** reads as follows:

"1. A method for controlling at least one culture parameter in a bioreactor bag (1; 31a, 31b) provided in a bioreactor system, said method comprising the step of:
- providing bioreactor information to a control unit (5; 35) controlling the bioreactor system; the method being characterised in that it includes the further step of:
- controlling the at least one culture parameter in dependence of the bioreactor information;

wherein the bioreactor information is the size of the bioreactor bag, and/or the weight of the bioreactor bag; the method being further characterised by the step of:
- choosing, by the control unit (5; 35), one specific set among a number of different sets of control parameters in dependence of the bioreactor information."

Claim 1 of **auxiliary request 2** differs from claim 1 of the first auxiliary request in that it further specifies "wherein the culture parameter is temperature, and/or pH, and/or DO".

Claim 1 of **auxiliary request 3** differs from claim 1 of the auxiliary request 1 in that it further specifies "wherein the culture parameter is temperature and/or pH".

Claim 1 of **auxiliary request 4** differs from claim 1 of auxiliary request 3 in that it deletes the feature "and/or the weight of the bioreactor bag".

Claim 1 of **auxiliary request 5** differs from claim 1 of auxiliary request 4 in that it further specifies that "choosing, by the control unit (5; 35), one specific set among a number of different predefined sets of control parameters in dependence of the bioreactor information, wherein the predefined sets of control parameters comprise a dedicated set of control parameters for each possible bioreactor bag size, wherein..." (introduced amendments underlined).

Claim 1 of **auxiliary request 6** differs from claim 1 of the first auxiliary request in that it adds "the method further comprising weighing the bioreactor bag (1) with culture fluid automatically when it is placed into the bioreactor system and using the weight of the bioreactor bag with culture fluid as bioreactor information for controlling the at least one culture parameter."

Claim 1 of **auxiliary request 7** combines the amendments of auxiliary requests 2 and 6.

Claim 1 of **auxiliary request 8** differs from claim 1 of auxiliary request 7 in that it further specifies "wherein the at least one culture parameter is temperature and pH, temperature and DO, or temperature, pH and DO".

Claim 1 of **auxiliary request 14** reads:
"1. A bioreactor system comprising two bioreactor bags (31a, 31b) on one support (33) each comprising a respective culture fluid, the bioreactor system further comprising a control unit (5; 35) for controlling the bioreactor system, characterised in that said control unit (5; 35) comprises a receiving means (7; 37) adapted to receive bioreactor information and in that

said control unit (5; 35) is adapted to control at least one culture parameter in the bioreactor bags (1; 31a, 31b) independently in dependence of the bioreactor information of each said bioreactor bag, the system being characterised in that the bioreactor information is the size of the bioreactor bag, and/or the weight of the bioreactor bag; and in that the control unit chooses one specific set among a number of different sets of control parameters in dependence of the bioreactor information."

Claim 1 of **auxiliary request 15** differs from claim 1 of auxiliary request 14 in that it further specifies that "said bioreactor system further comprising at least one load cell (13) provided on the support (3) for the bioreactor bags and adapted to weigh the bioreactor bags with culture fluid, said receiving means (7) further being connected to said load cell (13) and the control unit (5) is adapted to control at least one culture parameter in the bioreactor bags (1) in dependence of the weight of the bioreactor bags."

VI. The documents cited in this decision include the following:

D5 US 2009/0042293 A1
D6 US 2008/0213874 A1
D8a WO 2007/134267 A2

VII. The parties' submissions, insofar as they are relevant to the present decision, are discussed in the Reasons for the Decision, below.

VIII. Appellant I's final requests are that the decision be set aside and the patent be maintained on the basis of

the claims of any of auxiliary requests 1 to 8, 14 and 15.

IX. Appellant II's final requests are, insofar as they are relevant to the present decision, that the decision under appeal be set aside and the patent be revoked in its entirety. Further it requested that new auxiliary requests 3 to 5, 12, 14 and 15 not be admitted into the proceedings.

Reasons for the Decision

Auxiliary request 1
Claim construction - claim 1

1. Claim 1 is directed to a method for controlling at least one culture parameter in a bioreactor bag provided in a bioreactor system. The method includes the step of providing bioreactor information (which is the size and/or weight of the bioreactor bag) to a control unit, followed by a step of controlling the at least one culture parameter, whereby one specific set of "control parameters" is chosen from among a number of different sets of control parameters, by the control unit, based on the bioreactor information (i.e. size and/or weight of the bioreactor bag).

2. It is established case law that the features in a claim must be given their broadest technically sensible meaning (see Case law of the Boards of Appeal of the European Patent Office 11th edition 2025, hereinafter "Case Law" Chapter I.C.4.1). In order to define what is encompassed by the claim, the following terms require interpretation: "culture parameters", "control parameters" and "bioreactor system".

3. In view of dependent claims 2 and 3, it is apparent that "culture parameters" include temperature, pH and dissolved oxygen (DO) (claim 3), while the control parameters are those that allow the output of the systems (e.g. heating) to be adjusted between the reference value (e.g. a temperature of 37 °C) and the measured values (e.g. the temperature measured by a sensor) in order to achieve the intended effect of the system. This interpretation is confirmed by claim 2, which refers to control parameters, such as PID. The control parameters are usually determined regularly and define how the controller reacts to the difference between a desired culture parameter reference and the actually measured value. Thus, "control parameters" include, independently or in any combinations, for example, the applied heating power, the duration of heating, including the start and end of application of power, or, with regard to the dissolved oxygen, the rocking amplitude, rocking speed, start and end time of application of power, alternatively the oxygen gas concentration delivered, the flow rate, including the start and end of application of the oxygen supply. Any combination of at least two such control parameters constitutes a set of control parameters according to claim 1.

4. According to the claim, the culture parameters are controlled by control parameters based on the size of the bioreactor bag and/or the weight of the bioreactor bag, which makes technical sense because if the control parameters were controlled independently of the bioreactor bag and/or the weight of the bioreactor bag, the culture parameters such as temperature, pH value and/or dissolved oxygen in the culture could not swiftly reach the desired reference values in the vast

majority of the bioreactor bags. An adequate heat supply for a 100-litre bag would be excessive for a 100-ml bag, while in the reverse case the appropriate heat supply for a 100-ml bag would be insufficient to bring about a rapid adjustment for a 100-litre bag (patent, paragraph [0013]). Claim 1 also covers control parameters that are continuously and independently determined on the basis of sensors signals during culture operation depending on the size or weight of the bioreactor bag. The control parameters must implicitly be based on the weight or the size of the bioreactor culture bag, because if this were not the case, the control command signal sent to the heating device and the material supply would, in the vast majority of the case, not be proportional to the technical effect (output) desired to correct the observed imbalance.

5. The term "bioreactor system" must be interpreted in its broadest technically meaningful way as any system comprising at least one bioreactor which comprises at least one bioreactor bag. Hence, the board disagrees with appellant I that the bioreactor system is only limited to a bioreactor containing more than one bioreactor bag.

6. The board moreover disagrees with appellant I that the method of claim 1 requires a selection from a predefined set of parameters. Although in one embodiment of the invention, predefined sets of parameters, possibly PID parameters, are described (e.g. patent, paragraph [0011]), such a reading is neither explicitly nor implicitly required by the wording of claim 1.

Inventive step (Article 56 EPC)

Closest prior art

7. Document D8a is a suitable starting point for the discussion of inventive step. In this respect, the board notes that appellant I, while arguing that document D8a should not be considered the closest prior art, has not in fact provided any alternative document as closest prior art. Moreover, an inventive step can only be acknowledged if the claimed subject-matter is not obvious having regard to any prior art; on the other hand, if an inventive step is to be denied, it is sufficient to show that the claimed subject-matter is obvious starting from at least one piece of prior art and the choice of starting point needs no specific justification (see T 1701/22, Reasons 4 and in general Case Law, I.D.3.1).

Distinguishing feature

8. The distinguishing feature between claim 1 and the method in document D8a is the step of "choosing, by the control unit (5; 35), one specific set among a number of different sets of control parameters in dependence of the bioreactor information, wherein the bioreactor information is the size of the bioreactor bag, and/or the weight of the bioreactor bag."

9. Contrary to appellant I, the board considers that document D8a does disclose the choosing by a control unit and control parameters; these may not be predefined or preprogrammed set of control parameters but, as discussed above under claim construction (point 6), claim 1 does not require a selection from a predefined or preprogrammed set of control parameters either. As regards choosing by the control unit, document D8a discloses in paragraph [0121] how a

control in the sense of the claims is carried out as illustrated in Figure 20, where a gas source 1766 and a thermal source or sink subsystem 1756 are involved and a controller 1750, which is microprocessor-based, receiving various sensory inputs and providing command output signals to the various components of the system 1700. Secondly, paragraphs [0120] and [0121] disclose also that a controller may be provided to receive various sensory inputs, and that said controller provides command signals to any of the various components of the system, wherein the provision of command signals to any of said components and any combination of said components represents the different sets of control parameters in the sense of the claims (e.g. last two sentences of [00121], Figure 20).

The technical effect and objective technical problem

10. In the board's view, in agreement with the opposition division and appellant II, a technical effect cannot be recognized over the whole breadth of claim 1. The patent provides information only as far as (i) the bioreactor information is the size of the bioreactor bag, and (ii) the heating of the bioreactor bag is concerned, which corresponds to the culture parameter of temperature (patent, column 4, paragraphs [0013] and [0014]). The data in the patent does not make it possible to attribute a technical effect to the distinguishing feature identified above with regard to document D8a when culture parameters other than temperature, such as pH and DO, are controlled based on the weight of the bag. Nor has this difference been demonstrated to be associated with a technical effect by any other evidence on file.

11. Since the technical effect associated with the distinguishing feature has not been convincingly demonstrated to exist over the whole breadth of claim 1, the technical problem cannot be formulated as proposed by appellant I as "how to provide an improved method which allows for more versatile control of the bioreactor system" but rather must be reformulated in less ambitious terms as the provision of an alternative method for controlling cultivation in a bioreactor bag.

12. Contrary to appellant I's arguments that the technical effect resulting from the distinguishing feature arises regardless of whether the bioreactor information concerns the size or the weight of the bag, because these values are correlated (patent paragraph [0012], lines 14 to 18, [0013] and [0014]), the board considers that, in the absence of any evidence supporting appellant I's assertion, there is no clear correlation between the size and the weight of a bag. In fact, the size of the bag containing culture fluid is unique and fixed, whereas the weight of a bag with a defined size containing culture fluid can vary considerably.

Obviousness

13. Starting from the teaching of document D8a, it would be obvious to the skilled person, faced with the objective technical problem defined in 11. above, to provide a method according to claim 1, wherein a set of control parameters - at least two - are chosen in dependence of the weight of the bag. Firstly, paragraph [0121] of document D8a clearly motivates mixing and/or adding materials, such as controlling pH and DO, to correct any imbalance in temperature, pH, and dissolved oxygen content based on bag weight. On the other hand, document D5 discloses that culture parameters are

controlled using control parameters by sensors that transmit instructions to control units, based on the weight of the bag, which are, for example, starting and ending the addition of compounds, heating or supplying energy and/or gas, in order to maintain the cultivation parameters at the desired level (D5, paragraphs [0141], [0142], [0243]). Thus, starting from document D8a, the skilled person would have considered controlling cultivation by having each and any possible combination of culture parameters of a bioreactor bag monitored by sensors, which continuously measure critical variables within this bag and transmit instructions to control units so that control parameters react proportionally, in dependence of the bag's weight, to correct any observed culture parameter imbalance.

14. Appellant I argued that neither document D8a nor document D5 suggested selecting one specific set of control parameters from multiple available candidate sets or looking for a new control scheme that provides different sets of control parameters. Nor was there any teaching that this selection was based on the size and/or weight of the bag, as required by claim 1.

15. These arguments are not persuasive since the technical problem identified above is to provide an alternative method that does not require any motivation to arrive at the method according to claim 1. The mere selection of a specific combination of control parameters from all those equal alternatives disclosed in documents D8a and D5 cannot constitute the basis for acknowledging an inventive step.

16. This view is in line with decision T 1179/16, which states that if the only contribution of the invention is to propose something different from the prior art

(i.e. the provision of an alternative), then it is usually appropriate to consider that the skilled reader would take into account any alternative known in the underlying technical field (unless the closest prior art teaches away from it). In such cases, justifying the selection of a particular solution is not required, because it is assumed that an invention based on incorporating known features for the sole purpose of establishing novelty must be rendered obvious by a corresponding step of selecting any alternative known in the art (decision T 1179/16 point 3.4.4 of the reasons).

17. As regards appellant I's arguments that the teachings in D8a and D5 were technically incompatible, the board does not find them persuasive. The fact that document D8a relates to flexible tanks in which the culture is agitated with a mixing paddle, whereas document D5 relates to culture cassettes, does not render them technically incompatible, in particular in the context of the invention, which is a method for controlling culture parameters in any bioreactor system. As to document D5, even if paragraphs [0148], [0184], [0196], [0243] and [0325] in document D5 may be independent of each other, they all address how a control parameter can be used to correct a deviation from the reference value of a culture parameter in a culture fluid of bioreactor bag.

18. Auxiliary request 1 is thus considered not allowable for lack of compliance with Article 56 EPC.

Auxiliary requests 2 to 8

Admittance of auxiliary requests 3 to 5

19. Appellant II objected to the admittance of auxiliary requests 3 to 5. In view of the conclusions reached by the board as regards the substance of these requests, the board does not need to provide a reasoning for their admittance into the proceedings.

Inventive step

20. Claim 1 of auxiliary requests 2 to 8 includes the differences set out in point V. above, namely: further definition of the culture parameter (auxiliary requests 2 to 5, 7 and 8), restriction of the bioreactor information to the size of the bioreactor bag (auxiliary requests 4 and 5), further specifying that the sets of control parameters are predefined and comprise a dedicated set of control parameters for each possible bioreactor bag size (auxiliary request 5), further comprising weighing of the bioreactor bag (auxiliary requests 6 to 8).

21. The board considers that since the above technical features were not shown to impart a technical effect, the objective technical problem still has to be formulated as the provision of an alternative method for controlling cultivating in a bioreactor bag.

22. The board is not persuaded by appellant I's argument that the culture parameters of the cited prior art were only described as being controlled from respective sensors, i.e. wherein temperature is controlled by temperature sensor etc., and that there was no indication that these parameters were controlled based on the size or weight of the bag. Indeed, the person skilled in the art would easily recognize that the above parameters are highly relevant with respect to the weight of the bag, since a heavier bioreactor bag

containing a cell culture would require (i) more energy to maintain temperature in a favourable range, (ii) a higher amount of pH regulatory agents and/or buffering agents to maintain pH in a favourable range, and (iii) a higher amount of oxygen to maintain DO in a favourable range. Appellant I's argument that the bioreactor culture bag of D5 was only weighed after the culture had started was also deemed unconvincing, since document D5 discloses that the weighing occurs both at the outset and during the culture process in paragraphs [00148] and [00243].

23. Hence, starting from D8a and faced with the objective technical problem identified above, the skilled person would have selected, for the same reasons as set out above for claim 1 of auxiliary request 1, the specific control parameters claimed in claims 1 of auxiliary requests 2 to 8 from among all the equal alternative control parameters, and would have arrived at the subject-matter of claim 1 in an obvious manner.

24. Auxiliary requests 2 to 8 are thus not allowable for lack of compliance with article 56 EPC.

Auxiliary requests 14 and 15

Admittance

25. Appellant II objected to the admittance of auxiliary requests 14 and 15. In view of the conclusions reached by the board as regards the substance of these requests, the board does not need to provide a reasoning for their admittance into the proceedings.

Inventive step

26. Claim 1 of auxiliary requests 14 and 15 is directed to a bioreactor system with the features as defined in point V. above.

27. The board agrees with appellant II that the bioreactor system according to claim 1 of auxiliary requests 14 and 15, comprising two bioreactor bags on one support, each containing a culture fluid, includes also a bioreactor system with two bags, which are identical in size and/or weight, positioned on one support, such as a shock-absorbing mat. In addition, the at least one load cell according to the wording of claim 1 of auxiliary request 15 can only be capable of weighing bioreactor bags, i.e. at least two, when at least two separate load cells for two individual bioreactor bags in a relation of one to one are used, which is however not required from the wording "at least one" of claim 1.

28. The board disagrees with appellant I that the bioreactor system according to claim 1 of auxiliary request 14 requires, firstly, that the two bags are independently controlled on a single support, secondly, that the two bags must have different sizes or weights so that the claimed system can be controlled in a more bespoke way. Even if, *arguendo*, claim 1 required bioreactor bags of different sizes and/or weights - which is denied -, the skilled person, starting from document D8a, which refers to one bag, and in the absence of any technical effect attributed to this difference beyond what is standard in the prior art, would have turned to the teaching of document D6, which describes a differentiated and personalised control of a bioreactor system with different bag sizes (document D6, abstract and [0047]) and would arrive at the claimed subject-matter without inventive activity.

Thus, even in this case, the subject-matter of claim 1 of auxiliary request 14 would lack an inventive step over the content of document D8a in combination with D6.

29. As to auxiliary request 15, the feature "at least one load cell" - or weight meter - "provided on the support (3) for the bioreactor bags" consists of a mere routine modification which does not impart any technical effect. Among all the obvious alternatives possible, the skilled person could have carried out a step of weighing and/or of automating the operative control of control parameters by the control unit to select from a specific set of control parameters. It can therefore not confer any inventive activity either (see point 21. above; e.g. document D5 paragraphs [00148], [00243]).

30. Thus, claim 1 of auxiliary requests 14 and 15 both lack an inventive step.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

C. Rodríguez Rodríguez T. Sommerfeld

Decision electronically authenticated