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D E C I S I O N
of 13 March 2003

Case Number: T 1047/99 - 3.3.5

Application Number: 94914494.3

Publication Number: 0699101

IPC: B01D 21/00

Language of the proceedings: EN

Title of invention:

Particle settler for use in cell culture

Applicant:

BIOSCOT LIMITED

Opponent:

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Headword:

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Relevant legal provisions:

EPC Art. 123(2), 52(1), 56, 111(1)

Keyword:

"Amendments - substantive"

"Inventive step (yes) - after amendments"

"Remittal for further prosecution with additional search"

Decisions cited:

-

Catchword:

-



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Boards of Appeal

Chambres de recours

Case Number: T 1047/99 - 3.3.5

D E C I S I O N
of the Technical Board of Appeal 3.3.5
of 13 March 2003

Appellant: BIOSCOT LIMITED
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Representative: Sheard, Andrew Gregory
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 2 July 1999
refusing European patent application
No. 94 914 494.3 pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: R. K. Spangenberg
Members: A. T. Liu
J. H. Van Moer

Summary of Facts and Submissions

- I. The appeal is from the decision of the examining division refusing the European patent application No. 94 914 494.3.
- II. The decision was based on two sets of claims filed by letter of 19 February 1999, citing *inter alia* the following prior art document:
- D3: Batt et al, Biotechnol. Prog. 6, pages 458 to 464 (1990)
- III. With the statement of the grounds of appeal, the appellant submitted new claims and arguments to the effect that the examining division's finding was incorrect. An amended page 15 of the description and an amended Figure 2 were also filed on the same occasion.
- IV. In the annex to the summons to attend oral proceedings, the Board expressed the preliminary view that it failed to recognise that the claimed devices involved an inventive step with respect to the closest prior art document D3.
- V. At the oral proceedings which took place on 13 March 2002, a new set of amended claims was submitted which consisted of independent claims 1, 13 and 16 directed to a device, a bioreactor apparatus and a process, respectively, with respective dependent claims 2 to 12, 14 to 15 and 17 to 24.

The independent claims read as follows:

"1. A device (1) for separating mammalian cells from a cell supernatant liquid under aseptic or sterile conditions comprising a box member, means defining a plurality of removable plates formed from mirror-polished stainless steel (3), the plates being inclined to the vertical, and means for causing liquid containing the cells to flow upwardly over the said plates at such a rate as to allow cells to be separated from the liquid to form sediment layers on the plates and slide down them, wherein the plates are contained within a housing (5) provided with an inlet (13) for liquid containing cells to be separated which is located at the bottom of the plates, an outlet for liquid from which cells have been separated (21) and a collection outlet for separated cells (11), each inlet and outlet being provided with a sanitary connector, the box member being provided to occupy space left by any plates that are removed, so as to preserve separation between the plates.

13. A bioreactor apparatus, the apparatus comprising a fermenter vessel (31) adapted to contain cells in liquid medium, and a device (1) as claimed in any one of claims 1 to 13 for operation under aseptic or sterile conditions, the device being so coupled to the fermenter vessel to allow cells, or a population of cells, in the liquid medium to be separated from liquid medium and returned to the fermenter vessel.

16. A process for separating mammalian cells from a cell supernatant liquid under aseptic or sterile conditions, the process comprising the use of a device as claimed in claim 1."

VI. The appellant's arguments may be summarised as follows:

- The technical problem to be solved with regard to the closest prior art (D3) was the scaling up.
- The skilled person was not given any incentive from the available prior art to provide the device of D3 with removable plates as settlement surfaces and a box member.

VII. The appellant's request was that the decision under appeal be set aside and that the case be remitted to the first instance for further prosecution on the basis of the set of claims submitted at the oral proceedings.

Reasons for the Decision

1. *Amendments*

1.1 The present claim 1 has been amended with regard to claim 1 as originally filed by the incorporation of the following features; the basis therefor in the application documents as originally filed is given in parenthesis:

- separating mammalian cells from a cell supernatant liquid (page 6, lines 24 to 29 and page 12, lines 27 to 28);
- aseptic or sterile conditions (page 2, lines 26 to 28);
- plurality of removable plates formed from mirror-polished stainless steel (page 7, lines 18 to 29);

- box member to occupy the space left by any plates that are removed, so as to preserve separation between the plates (page 10, lines 12 to 18);
- inlet located at the bottom of the plates (page 10, lines 22 to 24);
- outlet for liquid (page 10, lines 27 to 28);
- collection outlet for separated cells (page 11, line 3);
- each inlet and outlet provided with a sanitary connector (page 10, lines 22 and 29).

The above additional features are referred to in the original description in general terms as part of the device according to the invention. Their combination as in claim 1 is therefore in compliance with the requirements of Article 123(2) EPC.

1.2 Claim 16 has been essentially amended by the incorporation of a back reference to claim 1 in lieu of a recitation of the essential technical features thereof. The remaining claims 2 to 15 and 17 to 24 substantially correspond to original claims 2, 4 to 8, 10 to 17, 29, 22 to 25, 27 to 29. These claims are therefore also allowable under Article 123(2) EPC.

1.3 The description at page 15 now corresponds to the description as originally filed with the removal of the phrase "which contains a draft tube" which had been added at lines 21 to 22 during the international phase of the application. Figure 2 has been amended consequentially by the deletion of the reference numeral 10. These submissions are therefore in conformity with Article 123(2) EPC.

2. *Novelty*

The subject-matter of present claim 1 is novel in view of the available prior art documents. The reason for this will also be clear from the following discussion on inventive step.

3. *Inventive step*

3.1 Claim 1

Claim 1 is directed to a device for separating mammalian cells from a cell supernatant liquid under aseptic or sterile conditions, the device comprising inclined plates as settlement surfaces.

3.2 Closest prior art document

D3 is a paper describing a study of the feasibility of using inclined sedimentation to selectively separate nonviable hybridoma cells in the suspension bioreactor (page 459, left hand column, third full paragraph). In these experiments, the sediment is allowed to slide down the inclined wall of the settler and returned to a bioreactor while the supernatant liquid is removed as settler overflow stream (see summary page 458; paragraph bridging right hand column page 459 and left hand column page 460 with Figure 1).

The Board therefore can accept D3 as the starting point for the assessment of inventive step.

3.3 Technical problem with regard to D3

The experiments reported in D3 are clearly conducted on a laboratory scale, using glass plates as inclined sedimentation channels (page 459, right hand column, second paragraph). The Board therefore accepts the

appellant's submission that, with respect to D3, the problem to be solved can be seen in the provision of a device that enables the scaling up of cell culture without proportionally increasing cell residence time.

3.4 Solution proposed in claim 1.

In order to solve the above stated technical problem, claim 1 proposes that the separation device incorporate

- (i) removable inclined plates formed from mirror-polished stainless steel, and
- (ii) a box member to occupy space left by any plates that are removed, so as to preserve separation between the plates.

3.5 The incorporation of a plurality of removable plates (feature (i)) is to achieve greater flexibility for the scaled up device, enabling the number of plates to be adapted to the volume of the media containing cells.

Whenever one or more settlement plates are removed from the housing, the gap is filled by the insertion of a box member , thereby preserving the spacing between the settlement surfaces (feature (ii)). The insertion of a box member is under these circumstances essential to maintain the rate of flow of the media (see also description page 9, line 13 to page 10, line 18 and page 18, lines 8 to 15).

The Board thus does not have any doubt that the technical problem of scaling up is actually solved by the device as proposed in claim 1.

- 3.6 The combination of the essential features (i) and (ii) is not described in any of the prior art documents on file. The Board therefore must conclude that the device as claimed is not obvious in view of the available prior art.
4. Claim 13 is directed to a bioreactor comprising the device of claim 1 and claim 16 directed to a process making use of the device of claim 1. The dependent claims 2 to 12, 14 to 15 and 17 to 24 are directed to preferred embodiments of the device, bioreactor and process according to claims 1, 13 and 16, respectively. Their subject-matter is also new and involves an inventive step with regard to the documents on file.
5. The Board, however, notes that a claim presenting the essential features of removable plates combined with a box member has not been subjected to a search. Since the patentability of the present set of claims relies on these features, the Board exercises its power under Article 111(1) EPC to remit the application to the first instance with the task of carrying out an additional search.

Provided that the search does not reveal any relevant document that discloses a device presenting a combination of removable settlement plates and a box member, the application may proceed to grant on the basis of the claims now on file, with the description and the drawings to be adapted accordingly. In this respect, the Board wishes to remark that the amendments to page 15 and Figure 2 as submitted with the statement of the grounds of appeal are not related to the amendments to the claims and should be taken into consideration accordingly.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the first instance for further prosecution on the basis of the set of claims submitted at the oral proceedings.

The Registrar:

The Chairman:

U. Bultmann

R. Spangenberg