



(51) International Patent Classification:
C12M 3/00 (2006.01)

(21) International Application Number:
PCT/SE2012/050187

(22) International Filing Date:
21 February 2012 (21.02.2012)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
1150154-1 23 February 2011 (23.02.2011) SE

(71) Applicant (for all designated States except US): **GE HEALTHCARE BIO-SCIENCES AB** [SE/SE]; Patent Department, Björkgatan 30, S-751 84 Uppsala (SE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ANDERSSON, Andreas** [SE/SE]; GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE). **CARLSSON, L. Johan** [SE/SE]; Schottisvågen 1, S-196 37 Kungsängen (SE). **ELNEGÅRD, Christian** [SE/SE]; Murkelvägen 7, S-132 44 Saltjö-Boo

(SE). **ERIKSSON, Henrik, K.** [SE/SE]; GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE). **FALKMAN, Thomas** [SE/SE]; GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE). **FRICKING, Patric** [SE/SE]; GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE). **PAULER, Linnéa** [SE/SE]; GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE). **PETERSON, Claes** [SE/SE]; GE Healthcare, Björkgatan 30, S-751 84 Uppsala (SE).

(74) Agents: **GE HEALTHCARE BIO-SCIENCES AB** et al.; Patent Department, Björkgatan 30, S-751 84 Uppsala (SE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

[Continued on next page]

(54) Title: BIOREACTOR INCLUDING A ROCKING DEVICE

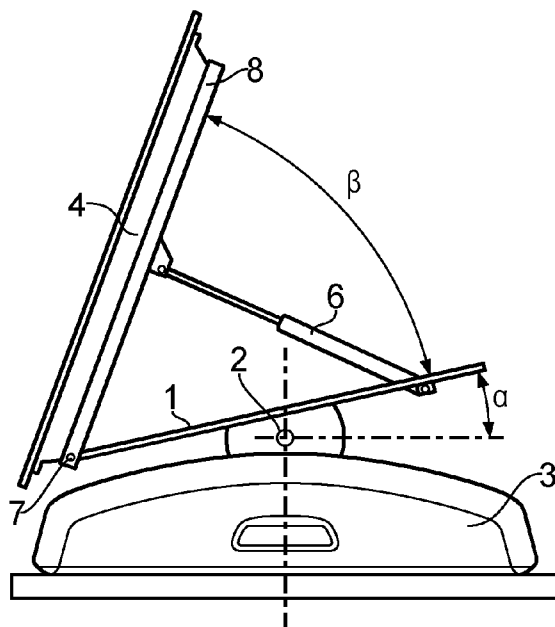


FIG. 1

(57) Abstract: The present invention relates to a bioreactor including at least one reactor vessel in form of a plastic bag, a tray (4) for holding said at least one bag, a rocking device for limited rocking motions of the tray (4) around a rocking axis (2). According to the invention the bioreactor comprises a device (6,7,8,9) for enabling swinging of the tray (4) around a second axis (7) parallel to and distanced from the rocking axis (2).



(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS,

SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

BIOREACTOR INCLUDING A ROCKING DEVICE

TECHNICAL FIELD

- 5 The present invention relates to a bioreactor including at least one reactor vessel in form of a plastic bag, a tray for holding said at least one bag, a rocking device for limited rocking motions of the tray around a rocking axis.

BACKGROUND TO THE INVENTION

10

Bioreactors of the above mentioned type are for example manufactured by GE Healthcare, Uppsala, Sweden under the trade name WAVE Bioreactor TM in several variants for different sizes of reactor bags. Other bioreactors of this type are also known. In reactors of this type, bags containing cell culture medium is placed on a tray which in turn is attached to a rocking device. The rocking motion of this device induces waves in the cell culture medium. These waves provide mixing and oxygen transfer, resulting in a perfect environment for cell growth.

20 The bags are clamped at two ends to the tray which for this purpose contains clamping devices. Bioreactors of moderate sizes are often placed on benches in laboratories and the like. If the bench is not accessible from two sides, the person who is to take off a used bag or placing a new bag on the tray must then lean over the bioreactor to reach the clamp on one side of the tray. Such leaning is not suitable from an ergonomic point of view and for shorter persons it can even be hard to reach the clamp in question.

25

Depending on the size of the bag or bags to be placed on a tray, different sizes of trays are used in the same bioreactor. For a bench placed bioreactor the means for fixing the tray to the rocking device are on one side hidden from view by the tray itself which makes the changing of trays troublesome and time consuming. Furthermore, the lifting off a tray from the rocking device and the placing of a new tray onto the rocking device can not be performed in suitable way from an ergonomic point of view.

30

WO 00/66706 discloses a bioreactor of the above mentioned type, in which the tray can be swung up to a vertical position around a centre axis in order to obtain stratification of the mixture in the reactor vessel.

- 5 The objective of the present invention is to improve bioreactors of the above mentioned type so that application and changes of plastic bags and the removal and application of trays can be performed in a better way from an ergonomic point of view.

SUMMARY OF THE INVENTION

10

This objective is accomplished by a bioreactor including at least one reactor vessel in form of a plastic bag, a tray for holding said at least one bag, a rocking device for limited rocking motions of the tray around a rocking axis, characterized by a device for enabling swinging of the tray to an upright position around a second axis parallel to and distanced
15 from the first axis. Thereby, the bioreactor can be placed on a bench so that the tray is pivoted against the front side of the bench, i.e. towards a person who intend to change reactor vessel or tray, whereby such a change can be performed in an acceptable way from an ergonomic point of view. Also a change of tray can be performed in an ergonomic manner. Another advantage by an upright position of the tray is that emptying
20 of fluid in the reactor vessel is assisted by gravity.

In a preferred embodiment, the device for enabling swinging of the tray around a second axis comprises at least one gas spring damper.

- 25 The bioreactor comprises in a second embodiment means for releasably locking the tray in set positions.

In the preferred embodiment, the tray is detachably attached to an intermediate plate which is attached to the rocking device by a hinge connection located at a distance from
30 the rocking axis and to which one end of the at least one gas spring damper is pivotally attached. The rocking device comprises preferably a rocking platform to which the intermediate plate is attached by a hinge connection and to which the at least one gas spring damper is pivotally attached.

A yoke can be provided, which in one end is pivotally attached to the intermediate plate, the opposite end of the yoke being insertable into locking means provided on the rocking platform for locking the intermediate plate against downward swinging.

- 5 In the preferred embodiments the tray can be pivotable around an axis being perpendicular to the plane of the tray.

BRIEF DESCRIPTION OF THE DRAWING

10

The invention will now be described with reference to the enclosed figures, of which;

fig. 1 shows a schematic side view of a bioreactor without reactor vessel according to a first preferred embodiment of the present invention,

15

fig. 2 schematically shows a perspective view from behind of the bioreactor in figure 1 with the tray separated from the intermediate plate,

20

fig. 3 schematically shows a side view of a bioreactor according to a second preferred embodiment, and

fig. 4 schematically shows a perspective view from the front side of a bioreactor according to a third preferred embodiment.

25 DESCRIPTION OF EMBODIMENTS

The different embodiments in figures in figures 1-4 are all based on a bioreactor manufactured by GE Healthcare, Uppsala, Sweden under the trade name WAVE Bioreactor TM. Such a bioreactor comprises a rocking platform 1 and a mechanism for pivoting platform 1 back and forth around a rocking axis 2. This mechanism and means

30

for controlling the rocking mechanism are located in a housing 3. During rocking movements of the platform 1, the platform forms an angle α to the horizontal in the end of the upward movement thereof. Thus, the rear end of the platform moves back and forth from an angle of $-\alpha$ to $+\alpha$. The construction of such a bioreactor is well known to persons skilled in the art and need not be further described in order to enable an understanding of the present invention.

In the known version of said bioreactors, a tray 4 is releasably attached to the platform 1. The reactor vessels in forms of plastic bags (not shown in the figures) are clamped to the tray 4 with the aid of clamping devices 5 (see figures 2 and 4). The angle α is only about 12° , which means that a person who is to take off a used bag or placing a new bag on the tray 4, when this is in alignment with the rocking platform 1, must lean over the bioreactor to reach the clamp on the rear side of the tray (to the right in the figures) if the reactor is placed on a bench. Such leaning is not suitable from an ergonomic point of view and for shorter persons it can even be hard to reach the clamping device in question.

Depending on the size of the bag or bags to be placed on a tray, different sizes of trays 4 are used in the same bioreactor. For a bioreactor placed on a bench the means for fixing the tray 4 to the rocking platform 1 are on one side hidden from view by the tray itself which makes the changing of trays troublesome and time consuming. Furthermore, the lifting off a tray from the rocking platform and the placing of a new tray onto the rocking platform can not be performed in suitable way from an ergonomic point of view.

In order to enable handling in an ergonomic manner of reactor vessels in the form of plastic bags clamped to the tray 4, a bioreactor according to the present invention includes means for placing the tray in an upright position. In the embodiments shown in the figures, the means for placing the tray 4 in an upright position are a pair of gas spring dampers 6, which in the figures are shown in a fully extended state and which pivot the tray 4 around a second axis 7. In figure 1, the angle β , i.e. the angle with which the tray swings up from the rocking platform 1, is about 60° . The tray 4 forms thus in figure 1 and 2 an angle $\alpha + \beta =$ about 72° to the horizontal. In such a position of the tray 4, the clamping devices 5 on both the front side and the rear side of the tray are easily accessible to a person who shall remove a used plastic bag and/or replace it with a new plastic bag. Furthermore, it is easier to empty a plastic bag on the tray in the upright position thereof than in a position when the tray is in alignment with the rocking platform 1 due to the greater influence of gravity in the upright position of the tray. Also

the working position for a person who shall change tray is acceptable from an ergonomic point of view when the tray is placed in its upright position. In the upright position the angle $\alpha + \beta$ lies preferably between 60-90°.

5 In the embodiments shown, the tray 4 is indirectly attached to the rocking platform 1 via an intermediate plate 8, which carries the pair gas spring dampers 6 and the front end of which is hinged to the front end of the rocking platform 1. As can be seen in figures 2 and 4, the rocking platform 1 has through-going elongate openings 9 for accommodating the gas spring dampers 6 in the downfolded position of the intermediate plate. In the
10 downfolded position of the intermediate plate, the hinged connection of the gas spring dampers to the rocking platform would be located nearer to the plane of the rocking platform than the hinged connection between the gas spring dampers and the intermediate plate. Thereby, the gas spring dampers will in the downfolded position of the intermediate plate act with a force directed away from the intermediate plate and the
15 rocking platform, a so called over-center mounting. In the downfolded position of the intermediate plate, the gas spring dampers thus act to hold together the intermediate plate and the rocking platform. It is first when the intermediate plate has been moved a small distance upwards that the gas spring dampers act to move the intermediate plate to its end position shown in the figures. The force of the gas spring dampers should be such
20 that the tray 4 with full reactor vessels clamped thereto automatically or with the aid of a very small manual force will be moved to the end position shown in figure 1.

In order to enable the tray 4 to be replaced by a different tray, the intermediate plate 8 is provided with quick couplings similar to the quick couplings provided on the rocking
25 platform of a WAVE Bioreactor™. It is of course possible to provide trays and intermediate plates with other types of co-operating elements to establish quick couplings.

In figure 3, a second preferred embodiment is schematically disclosed. This embodiment
30 differs from the embodiment according to figures 1 and 2 only in that means 10-12 for locking the intermediate plate in set positions are present. In all other aspects the bioreactor according to figure 3 is similar to the bioreactor described with reference to figures 1 and 2 and identical elements in the bioreactors according to the first and second embodiments are given the same reference numbers. The means for locking the
35 intermediate plate in set positions consist of two upstanding flanges 11 extending in a rearward direction on the rocking plate 1. Each upstanding flange has a row of upwardly open openings 12 extending along the flange. A U-shaped yoke 10 has legs hinged to the

intermediate plate and is dimensioned to fit in the openings 12 in the flanges 11. The openings 12 are configured to hold the yoke in the openings against the action of the gas spring dampers 6.

- 5 It is possible to dispense with the gas spring dampers in the embodiment according to figure 3 and only rely on the locking means 10-12 for holding the tray in an upright position.

10 In figure 4, a third preferred embodiment is schematically disclosed. This embodiment differs from the embodiment described with reference to figures 1 and 2 only in that the tray 4 is attached to the intermediate plate pivotable around a third axis 13 perpendicular to the plane of the intermediate plate. Identical elements according to the first and third embodiments are given the same reference numerals. The pivotable connection forming the third axis 13 could be a pivot arm extending from the intermediate plate into a hole in
15 the tray 4. After releasing the quick coupling and moving the tray 4 out of the plane for the intermediate plate, the tray 4 can be pivoted around axis 13 for example in the direction indicated by an arrow in figure 4 to a position indicated by interrupted lines in figure 4. In such a position, liquid in a plastic bag attached to the tray 4 will gather in a corner. The possibility to swing the tray 4 around the third axis 13 thus enables a more
20 total emptying of a reactor vessel than in the embodiments according to figures 1-3.

The embodiments shown can be modified in several aspects without leaving the scope of invention. For example, it is not necessary to have to two gas spring dampers, one centrally placed gas spring damper can be enough. Other locking devices than the one
25 shown in figure 3 could be used. For example can lockable gas spring dampers be used which enables the user to lock the gas spring dampers in any set position. The gas spring dampers could be connected directly to the tray by easily releasable connections and the tray could then be attached to the front side of the rocking platform by easily releasable connections. Instead of an over-center mounting of gas spring dampers, the intermediate
30 plate can be releasably locked to the rocking platform by a snap connection which is releasable by a mechanism that can be actuated from the front side of the bioreactor. The rocking platform can be eliminated and the rear ends of the gas spring dampers then be attached to other parts of the rocking mechanism. The scope of the patent shall therefore not be limited by the embodiments described but only by the content of the enclosed
35 patent claims.

Claims

1. Bioreactor including at least one reactor vessel in form of a plastic bag, a tray (4) for holding said at least one bag, a rocking device for limited rocking motions of the tray (4) around a rocking axis (2), **characterized by** a device (6,7,8,9) for enabling swinging of the tray (4) around a second axis (7) parallel to and distanced from the rocking axis (2).
2. Bioreactor according to Claim 1, wherein the device (6,7,8,9) for enabling swinging of the tray (4) around a second axis comprises at least one gas spring damper (6).
3. Bioreactor according to Claim 2, wherein the bioreactor comprises means (10-12) for releasably locking the tray in set positions.
4. Bioreactor according to any one of Claims 1-3, wherein the tray (4) is detachably attached to an intermediate plate (8) which is attached to the rocking device by a hinge connection (7) located at a distance from the rocking axis (1) and to which one end of the at least one gas spring damper (6) is pivotally attached.
5. Bioreactor according to Claim 4, wherein the rocking device comprises a rocking platform (1) to which the intermediate plate (8) is attached by a hinge connection (7) and to which the at least one gas spring damper (6) is pivotally attached.
6. Bioreactor according to Claim 3 and Claim 5, wherein a yoke (10) in one end is pivotally attached to the intermediate plate (8), the opposite end of the yoke being insertable into locking means (11,12) provided on the rocking platform (1) for locking the intermediate plate in one or more set positions.
7. Bioreactor according to any one of claims 1-6, wherein the tray (4) is pivotable around an axis (13) being perpendicular to the plane of the tray (4).

1/2

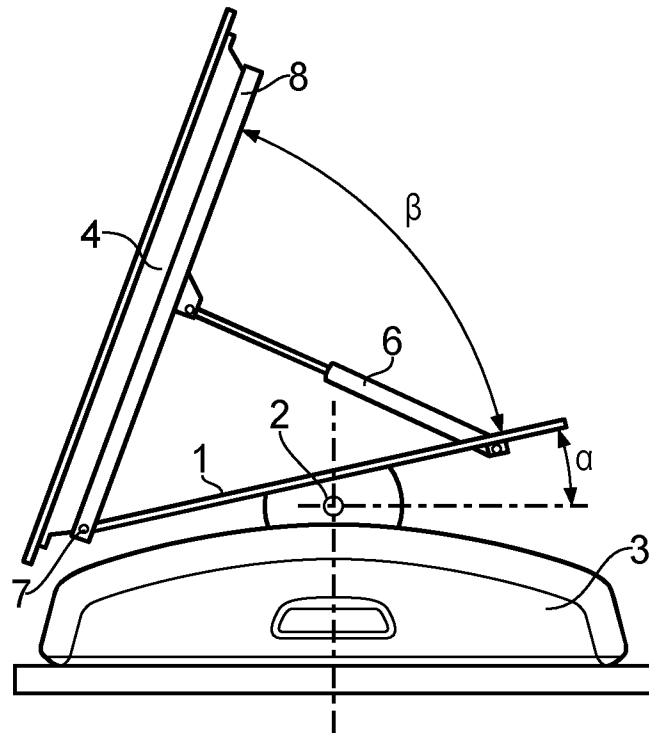


FIG. 1

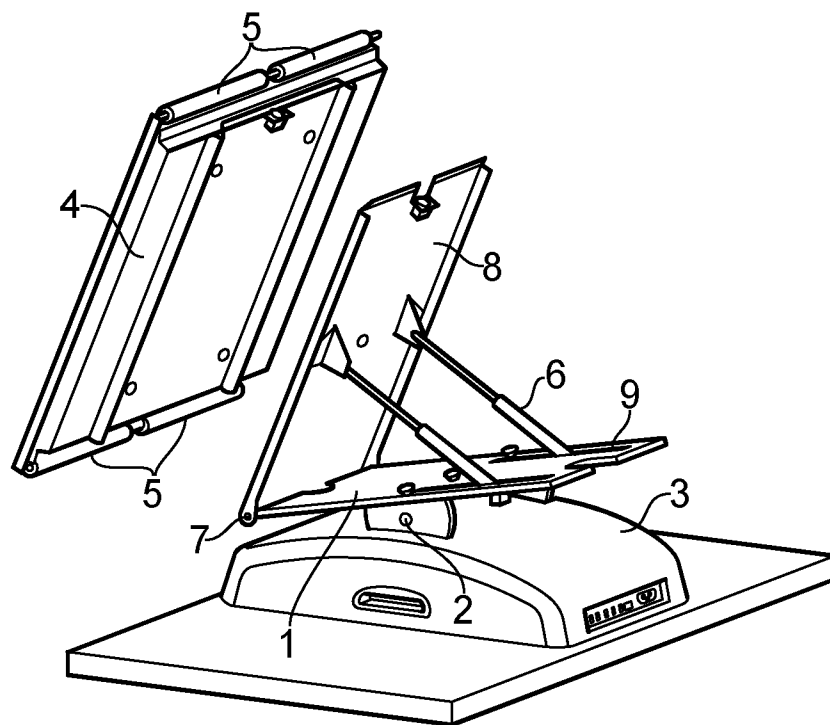


FIG. 2

2/2

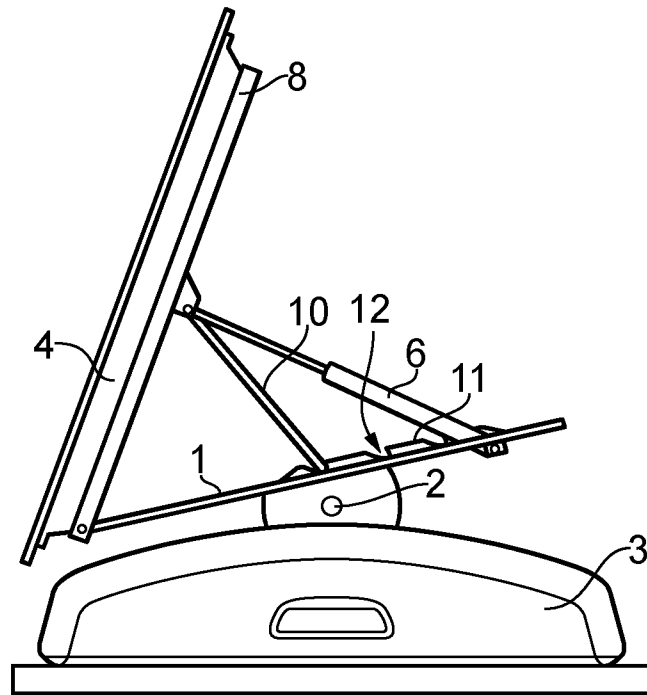


FIG. 3

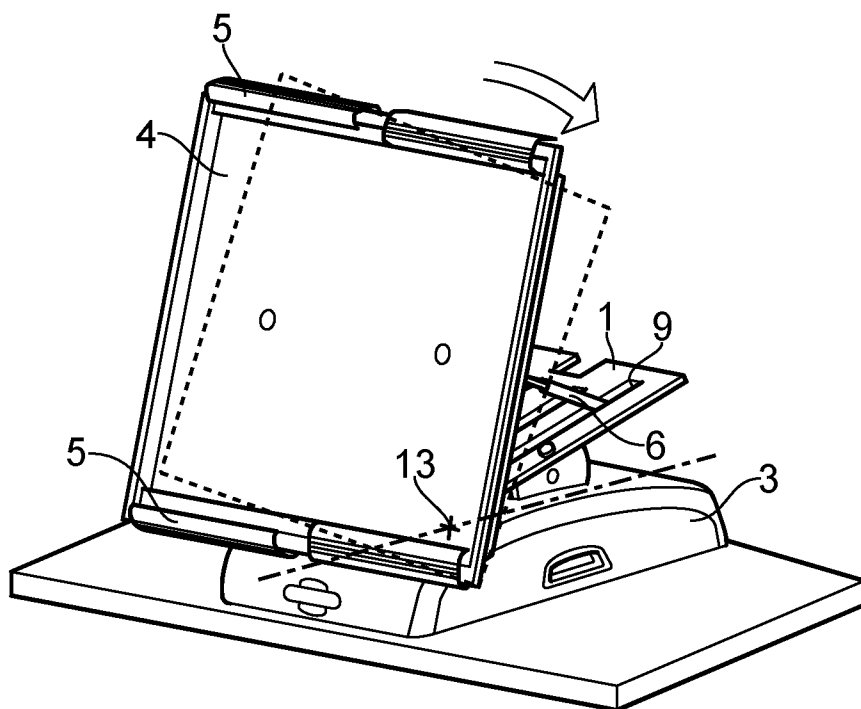


FIG. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2012/050187

A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: C12M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE, DK, FI, NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, PAJ, WPI data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP62289175 A, Shibata Masaru, 1986-06-09: (abstract) Retrieved from: EPODOC database; abstract --	1-7
A	GB 2411178 A (CESCO BIOENGINEERING CO LTD), 24 August 2005 (2005-08-24); abstract; claims -- -----	1-7



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

“A” document defining the general state of the art which is not considered to be of particular relevance

“E” earlier application or patent but published on or after the international filing date

“L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

“O” document referring to an oral disclosure, use, exhibition or other means

“P” document published prior to the international filing date but later than the priority date claimed

“T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“&” document member of the same patent family

Date of the actual completion of the international search

13-04-2012

Date of mailing of the international search report

16-04-2012

Name and mailing address of the ISA/SE

Patent- och registreringsverket
Box 5055
S-102 42 STOCKHOLM
Facsimile No. + 46 8 666 02 86

Authorized officer

Carolina Gomez Lagerlöf

Telephone No. + 46 8 782 25 00

Continuation of: second sheet

International Patent Classification (IPC)

C12M 3/00 (2006.01)

Download your patent documents at www.prv.se

The cited patent documents can be downloaded:

- From "Cited documents" found under our online services at www.prv.se
(English version)
- From "Anförda dokument" found under "e-tjänster" at www.prv.se
(Swedish version)

Use the application number as username. The password is **KFJOSZAEBU**.

Paper copies can be ordered at a cost of 50 SEK per copy from PRV InterPat (telephone number 08-782 28 85).

Cited literature, if any, will be enclosed in paper form.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SE2012/050187

GB	2411178 A	24/08/2005	BE	1016538 A3	09/01/2007
			DE	102005007512 A1	08/09/2005
			FR	2866655 B1	11/05/2007
			US	20050186669 A1	25/08/2005
