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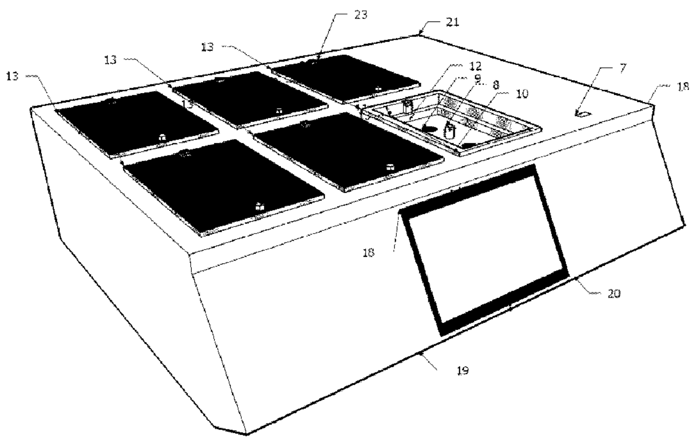

Fig. 1

(57) Abstract: The present invention describes an incubator for cell culturing, said incubator having more than one independent cell culture chamber, a premixed, a CO_2 and a N_2 gas inflow and/or a premixed CO_2/N_2 gas inflow, at least one cell culture chamber specific heating element, one or more cell culture chamber specific sensors, and a computer controller unit linked to said one or more cell culture chamber specific sensors, wherein the incubator also has a gas mixing chamber where CO_2 and N_2 gas is mixed, and wherein the incubator has at least one O_2 concentration sensor and at least one CO_2 concentration sensor being in connection with the computer controller unit and functioning as value providers for a user to be able to set and/or change a desired value (SP) of the O_2 concentration and CO_2 concentration in the gas mixing chamber. The incubator concept according to the present invention is also direct to providing a system where the computer controller unit has a WEB link and as such allows for cell culture chamber independent WEB monitoring with respect to said one or more cell culture chamber specific sensors and also allows for control by interaction with the incubator via a user WEB interface.

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BENCHTOP DRY INCUBATOR

Field of the invention

The present invention relates to an incubator for cell culturing.

Technical Background

Cell culturing incubators are devices used to grow microbiological cultures or cell cultures, e.g. embryos. The control of the environment in the so called incubator chamber where the actual growing occurs is very important. Parameters to measure and/or control are temperature, humidity, content of carbon dioxide (CO_2 in the following) and oxygen (O_2 in the following) and the pH level. Advanced incubators, such as those intended for cultivation of mammalian cells often have some kind of ability to control the temperature, humidity or the CO_2 level. Moreover, most incubators include some kind of timer and some can also be programmed with respect to temperature, humidity levels, etc. for the culturing cycles.

There are major concerns today in relation to the actual cell environment when culturing human cells, e.g. embryos. To provide a sterile environment for the cells and keep this environment at steady state with respect to temperature, humidity, and gas content are three key issues.

The present invention is directed to providing an improved incubator for cell culturing. The incubator concept according to the present invention is directed to providing inter alia an increased ability to control essential parameters, an increased security in terms of usage and traceability and an increased user-friendliness, when compared to existing incubators on the market today.

A first aspect of the invention

The stated purpose above is achieved by an incubator for cell culturing, said incubator having more than one independent cell culture chamber, a CO_2 and a N_2 gas inflow and/or a premixed CO_2/N_2 gas inflow, at least one cell culture chamber specific heating element, one or more cell culture chamber specific sensors, and a computer controller unit linked to said one or more cell culture chamber specific sensors, wherein the incubator also has a gas mixing chamber where CO_2 gas and N_2 gas is mixed, and wherein the incubator has at least one O_2 concentration sensor and at least one CO_2 concentration sensor being in connection with the computer controller unit and functioning as value providers for a user to be able to set and/or change a desired value (SP) of the O_2 concentration and CO_2 concentration in the gas mixing chamber.

The expression “more than one independent cell culture chamber” implies that the incubator according to the present invention comprises at least two chambers which are totally separate from each other. This also implies that each chamber should be seen as a closed environment. Moreover, just as an example, this also implies that the actual physical condition may differ in one chamber from another, such as e.g. where the temperature may differ more than 2°C, e.g. even more than 5°C, such as even more than 10°C between different chambers. This possibility of holding different temperatures in different chambers, independently of one another, may be of interest e.g. when different cell culturing are performed in one and the same incubator according to the present invention.

Moreover, an individual cell culture chamber is the actual physical chamber where one or more cell culture dishes are placed on a dish holder for long term culturing.

Furthermore, the incubator has a CO_2 and a N_2 gas inflow and/or a premixed CO_2/N_2 gas inflow, or may optionally also have a separate O_2 gas inflow or contain O_2 gas in the premixed gas inflow. The actual gas is mixed to achieve an intended and preset gas level concentration, such as with a variation of e.g. only ± 1% from the desired value or set point (SP). As an example, 100% CO_2 and 100% N_2 may be supplied to the system and it is being mixed in a mixing chamber according to the SP. Moreover, in a premixed model, the mixing function will be disabled. However, the O_2 and CO_2 concentration will still be monitored and alarm the end user if concentration drops below the expected set point.

One specific embodiment and design of the incubator according to the present invention is further presented in the drawing. This is also further explained below. Other specific embodiments and possible added technical features of the present invention are discussed below.

According to one specific embodiment of the present invention, each independent cell culture chamber has an O_2 concentration sensor and a CO_2 concentration sensor which are in connection with the computer controller unit. As mentioned above, both the O_2 concentration and the CO_2 concentration are very important parameters for mammalian and human cell culturing, and should as such be monitored with very high accuracy. This is provided by the present invention. The gas concentration in the mixing chamber is being closely monitored by the O_2 sensor and the CO_2 sensor according to the present invention. In addition, the pressure in the mixing chamber may also be monitored to prevent variations in the gas concentration as well as damage to the O_2 and CO_2 sensors.

Another possible added feature according to the present invention, with respect to this aspect, is a possible implementation of a gas sample routine in the circuit of the incubator according to the present invention. This is further explained below.

Another interesting aspect of the gas feeding is the actual regulation thereof. According to one specific embodiment of the present invention, wherein regulation of feeding from the gas mixing chamber to each independent cell culture chamber is performed by using a closed loop PID technology. This implies that the integrated gas mixer feeds the individual chambers with a supply of pure mixed gas using a closed loop PLC technology. Moreover, each gas supply to the incubator can also be independently closed when not in use.

Furthermore, according to one specific embodiment, the incubator also comprises a gas/airflow recirculation loop. Such a re-circulated gas/airflow may be sterilized continually. Up to approximately 70% of the gas may be reused within the circuit according to the present invention.

As hinted above, ensuring a sterile environment is often very important. According to one specific embodiment of the present invention, the incubator also comprises a UV light, VOC, HEPA and/or PLASMA filter for sterilization of the gas which is the internal culture gas. In relation to this technical feature it may be mentioned that some of the components above are used today in incubators. For instance, in US6878177, there is disclosed an incubator having an interior chamber adapted to be heated and humidified. An easily accessed blower is located within the gaseous environment of the incubator chamber and includes a HEPA filter and VOC filter which is said to be readily replaceable by the user from within the chamber. It should be noted that in US6878177 a single chamber system is disclosed. Furthermore, the gas inflow system and internal gas circuit of the present invention are very different from the gas system of US6878177. This also implies that the arrangement of the VOC and/or HEPA filter has different requirements when comparing the present invention with US6878177.

Moreover, possible added features according to the present invention, and in this respect, are inter alia monitoring counters linked to the software in order to warn the end user as when it is time to change the above mentioned components, and once again also providing future reference for every change made via logging capability. Moreover, in order to keep the environment sterile, all the parts that come in contact with the cells must be able to be sterilized in an autoclave or through other accepted processes. This applies to both the gas mixture as such but also multi-well dishes used.

Furthermore, and as understood from above, holding temperature and preventing contamination are key issues when performing culturing. Due to this fact, the individual cell culture chamber should be opened for as little time as possible. As for the creation and monitoring of the environment, the design team faces the challenges of ensuring specified parameters remain within their tolerance. For example, temperature will have to be maintained within +/- 0.3°Celsius. This will require accurate sensors, and a sophisticated control program to interpret information given by sensors, and take appropriate action when necessary. For this action alone, PT1000 sensors along with a temperature PID control are one suitable example according to the present invention to monitor every single chamber.

Furthermore, also other aspects of the incubator and incubator parts of the present invention may be regarded as other possible technical add-ons. For instance, the chamber may be made completely of aluminium, which is an excellent choice of material when the intentions are to hold a temperature at the SP value as stable as possible, but also in relation to keeping a sterile environment. Moreover, the mentioned heating element may in fact constitute a heating foil. Moreover, the incubator design according to the present invention may be what you may call “horizontal”, i.e. of benchtop type. Furthermore, for instance the possible sterilization filters mentioned above may be arranged within an openable service compartment which is easy to access for a user in need of changing one of these parts. As such service is easy to perform for the user without the need of disassembling large part of or the entire incubator. Such easy replacement of the filters may also be valid for the UV lamp and different sensors, e.g. the O_2 sensor, according to the present invention. Other specific embodiments are disclosed below.

It should further be said that there are different benchtop dry incubators known today. For instance, in the product sheet “incuART™, Quadro benchtop incubators”, Tech2ART APS, published in 2011, one such is disclosed. Another type is disclosed in the product sheet “MIRI®, Multiroom CO_2 incubator for IVT”, ESCO Medical, from 2012.

Both of the documents above show incubators with gas mixers, however none of them disclose incubator systems which may be controlled via sensors being in connection with a computer controller unit enabling a user to better control the CO_2 and O_2 concentrations during operations, such as according to the present invention. This improvement according to the present invention, in addition to other important aspects and embodiments of the present invention discussed below and also not shown in any of the product sheets above, are very important for providing optimal conditions for a cell culture. This is further discussed below.

<u>Other aspects and specific embodiments of the present invention</u>

According to one aspect of the present invention there is disclosed an incubator for cell culturing, said incubator having more than one independent cell culture chamber, a CO_2 and a N_2 gas inflow and/or a premixed CO_2/N_2 gas inflow, at least one cell culture chamber specific heating element, one or more cell culture chamber specific sensors, and a computer controller unit linked to said one or more cell culture chamber specific sensors, wherein the computer controller unit has a WEB link and as such allows for cell culture chamber independent WEB monitoring with respect to said one or more cell culture chamber specific sensors and also allows for control by interaction with the incubator via a user WEB interface.

The WEB link provides the possibility for a WEB client to both monitor and control. The WEB interface according to above may also provide or be linked to other possible added features according to the present invention. As an example, full data logging capabilities may be provided on every input and output in the system. Examples of applications and software therefore are discussed below.

Moreover, according to yet another aspect of the present invention there is provided an incubator for cell culturing, said incubator having more than one independent cell culture chamber, a CO_2 and a N_2 gas inflow and/or a premixed CO_2/N_2 gas inflow, at least one cell culture chamber specific heating element, one or more cell culture chamber specific sensors, and a computer controller unit linked to said one or more cell culture chamber specific sensors, wherein the incubator is provided with an O_2 and/or CO_2 auto calibration capability when being connected to an O_2 and/or CO_2 gas external monitoring system, respectively.

The O_2 and/or CO_2 auto calibration is implemented in the software according to the present invention.

In relation to the aspects of the present invention disclosed above, it should be noted that also these embodiments are valid as possible specific embodiments. As such, the incubator may also in this case have at least one O_2 concentration sensor and at least one CO_2 concentration sensor being in connection with the computer controller unit and which functions as value providers for a user to be able to set and/or change a desired value (SP) of the O_2 concentration and CO_2 concentration in the gas mixing chamber. Moreover, each independent cell culture chamber may have an O_2 concentration sensor and a CO_2 concentration sensor which are in connection with the computer controller unit. Moreover, the regulation of feeding from the gas mixing chamber to each independent cell culture chamber may be performed by using a closed loop PID technology.

Furthermore, as mentioned above, the incubator may also have an O_2 gas inflow. This is a valid embodiment possibility for all aspects of the present invention. Therefore, according to one specific embodiment of the present invention, the incubator has a CO_2, an O_2 and a N_2 gas inflow and/or a premixed $CO_2/N_2/O_2$ gas inflow.

Specific embodiments of different aspects of the invention

Below, specific embodiments according to the present invention are discussed in more detail. According to one embodiment, the incubator has at least three independent cell culture chambers, such as at least four independent cell culture chambers, e.g. six independent cell culture chambers. The number of independent and individual cell culture chambers most suitable depends on the intended use thereof. For embryo culturing, six independent cell culture chambers is a suitable choice according to the present invention.

Furthermore, according to one specific embodiment of the present invention, one or more of the independent cell culture chambers are provided with a cross directional gas nozzle in order to control and maintain a fast recovery of the gas concentration within the chamber.

Moreover, according to yet another specific embodiment, each independent cell culture chamber is provided with an independent temperature PID control. According to yet another embodiment, the incubator also has a gas flow closed loop PID regulation on CO_2 gas consumption, N_2, O_2 gas consumption and/or premixed gas consumption. As an example, these may be regulated on proportioning valves which are valves relying on fluid pressure laws.

Furthermore, the number of type of sensors may also vary according to the present invention. According to one specific embodiment, one or more of the independent cell culture chambers are provided with a pH sensor connected to the computer controller unit so that the incubator has a pH monitoring/control system. The pH level is one of the very important parameters to control for embryo culturing, and the suggested approach above may facilitate such work. According to yet another embodiment, at least one of the independent cell culture chambers has a temperature sensor, a humidity sensor and a pH sensor as said one or more cell culture chamber specific sensors. These sensors may be provided as individual separate sensors or may be implemented together. For instance, there are pH sensors on the market today which may incorporate also other sensor capabilities. For the application of embryo culturing it is preferred that each individual chamber of the incubator according to the present invention has a temperature sensor, a humidity sensor and a pH sensor.

According to yet another embodiment, the incubator is also provided with a gas sampling system connected to the computer controller unit so that sampling frequency may be set and the gas sampling may be monitored and logged. According to this embodiment, a “gas sample” routine may be implemented in the circuit. Through the software, the number of gas samples taken from the mixing chamber may be controlled. This may be essential during culture as high deviations in the mixing ratio will affect the embryo development. As an example, to only allow a 180 seconds sample time frame every five minutes is a suitable security choice. This gas sampling routine may be logged as well for future reference.

According to yet another embodiment, the computer controller unit has an independent WEB logging system. Such WEB logging system may as an example be JAVA based. When such logging system is implemented according to the present invention, it is easier to do a follow-up on what has been performed and by whom.

Moreover, there should be a possibility to copy the log files and to interact with the incubator, also from a distance. The WEB interface and logging system according to the present invention assures these possibilities as well as to independently gather software predefined log data and transfer them to another format of choice.

According to yet another specific embodiment of the present invention, each independent cell culture chamber has a (culture dish) ID chamber check in/out system also linked to the computer controller unit. This ID chamber check in/out system may be provided as a built in 2D barcode reader or based on RFID technology. The ID chamber check in/out system according to the present invention provides the patient traceability demanded today through the whole IVF/cell culture process. It is essential that the end user will be able to ID every patient and to be able to track these patients in every chamber.

An example of the 2D barcode reader system according to the present invention may function according to the following. Every time the lid is opened, a photocell detects de opening of the lid. The end user will be asked either to scan the pre-labelled dish or to type in the patients ID number. Every action through this process may be logged. The patient ID will be visible on the specific chamber. If the lid is being opened again within the same chamber, the end user will be asked again if there will be a check in/check out event. Based on the chosen action the system will act and log accordingly.

It should be mentioned that a 2D barcode reader are disclosed in US7326565, as a possible means for reading identification information provided on a container. US7326565 is related to an incubator wherein a microplate transport device is disposed inside a chamber. In US7326565 there is mentioned that when a new container is to be installed inside the storage apparatus, the identification information of the container, such as the identification number and type information, may be read by the information reading means, and the read information is stored in a storage means. Also in this case the incubator disclosed in US7326565 differs completely from the incubator according to the present invention, inter alia in terms of the gas applying and circuit system, sensors, regulation and chamber configuration. Moreover, the incubator according to US7326565 is not a multiple independent chamber incubator as the present invention.

According to yet another specific embodiment of the present invention, more than one of the essential service components being at least filter(s), UV lamps, O_2 sensors are mounted in an end user accessible room in the incubator. As mentioned above, such arranging provides high serviceability for an end user.

Furthermore, according to yet another specific embodiment, one or more of the independent cell culture chambers are provided with a lid opening detector sensor connected to the computer controller unit so that the lid movement is being monitored and logged.

Moreover, the computer controller unit may have an independent control and monitoring wireless system, e.g. ANDROID based. Additionally, the computer unit may have a controlling and monitoring system which is independent WEB SCADA based.

According to yet another embodiment, one or more of the independent cell culture chambers are provided with a time lapse image analysis system connected to the computer controller unit so that the cell culture process is being monitored and logged for controlling purposes.

Furthermore, according to another specific embodiment, one or more of the independent cell culture chambers are provided with a bio computer control cell closely monitored by an image analysis system for logging and cell culture environment control purposes. The bio computer control cell will in this case be able to detect the molecules carrying the required information within the culture, perform digital computations with NOT, AND, NAND and N-IMPLY expression logic in single mammalian cells, then sample the data such as metabolic activites and amount of protons (H+) in order to trigger the necessary action to maintain a stable cell culture.

Description of the drawings

Below, the figures will be explained shortly. It should be noted that the figures only present different specific embodiments of the present invention.

In fig. 1 there is disclosed one incubator according to one embodiment of the present invention.

Fig. 2 shows one chamber embodiment according to the present invention, where the independency of the chambers is clearly demonstrated.

Fig. 3 shows a service access view.

In fig. 4 there is disclosed a mixing chamber unit according to the present invention.

Fig. 5 shows an independent chamber heating assembly accoridng to one embodiment of the presnt invention.

Fig. 6 shows a panel having a gas and data acess view according to one embodiment of the present invention.

In the figures, the following units or parts are presented with reference numbers:

1. CO_2 sensor holder
2. Gas output access
3. Gas input access
4. External sample port access
5. Sample port access
6. Heating foil
7. 2D barcode viewer
8. X nozzle
9. Time-lapse imaging system access
10. pH sensor locator
11. Photo sensor viewer
12. Gas output port access
13. Independent chamber
14. Mixing chamber
15. VOC/HEPA filter access
16. O_2 sensor access
17. UV lamp access
18. WEB touch interface access
19. USB port access
20. Sample port access
21. incuART
22. Handle lid
23. Hinge lid

Once again, all of the figures only represent possible specific embodiments of different aspects the present invention, and they should only be viewed as examples.

<u>Conclusions</u>

The incubator system according to the present invention provides several advantages in comparison to existing apparatuses today. First of all, the key parameters temperature, humidity and pH value may be adjusted individually for each chamber. Even if the target condition is the same for all chambers an incubator need to be able to adjust each chamber conditions individually to reach the set target. The reason is that one chamber may be placed near the transformer or a fan which mean a lot for e.g. temperature. The described incubator system can do this unlike other incubators.

Secondly, the incubator according to the present invention is designed to provide optimal conditions for a cell culture via closely monitoring such key environment parameters that gives a high quality and consistent environment. Moreover, the consistent environments is secured by the possibility of online built in sensors with feedback loops resulting in rapid temperature and gas recovery after opening the lid of a chamber and real time display of key parameters, e.g. over a WEB interface for monitoring and direct control of the parameters.

Moreover, by some specific alternatives according to the present invention, optimization towards different applications may be achieved. As an example, by the secured isolated chambers and addition of UV lamps and VOC/HEPA filtration, the risk of cell contamination may be achieved. Furthermore, high flexibility may be obtained as the environment in each chamber can be individualized to predefined conditions, such as temperature and ID etc.

Another important perspective is usability. According to the present invention, a WEB interface may be implemented so that the operations may be real-time monitored and controlled, also from a distance. Also warning systems may be implemented for controlling key parameters. Furthermore, a logging system may be implemented for increasing the follow-up possibilities and security.

Another aspect is serviceability. The incubator according to the present invention allows for a quick access, either through internet or on site. Moreover, and as mentioned above, the end user may have a direct and easy access to an O_2 sensor, UV lamp and a VOC/HEPA filter. Moreover, a service engineer will also be able to guide the end user over the phone/web when replacement of a component is needed. Furthermore, a service log file can be accessed over internet.

Claims

1. An incubator for cell culturing, said incubator having more than one independent cell culture chamber, a CO_2 and a N_2 gas inflow and/or a premixed CO_2/N_2 gas inflow, at least one cell culture chamber specific heating element, one or more cell culture chamber specific sensors, and a computer controller unit linked to said one or more cell culture chamber specific sensors, wherein the incubator also has a gas mixing chamber where CO_2 and N_2 gas is mixed, and wherein the incubator has at least one O_2 concentration sensor and at least one CO_2 concentration sensor being in connection with the computer controller unit and functioning as value providers for a user to be able to set and/or change a desired value (SP) of the O_2 concentration and CO_2 concentration in the gas mixing chamber.

2. An incubator according to claim 1, wherein each independent cell culture chamber has an O_2 concentration sensor and a CO_2 concentration sensor which are in connection with the computer controller unit.

3. An incubator according to claim 1 or 2, wherein regulation of feeding from the gas mixing chamber to each independent cell culture chamber is performed by using a closed loop PID technology.

4. An incubator according to any of claims 1-3, wherein the incubator also comprises a gas/airflow recirculation loop.

5. The incubator according to any of claims 1-4, wherein the incubator also comprises a UV light, VOC, HEPA and/or PLASMA filter for sterilization of the gas which is the internal culture gas.

6. An incubator for cell culturing, said incubator having more than one independent cell culture chamber, a CO_2 and a N_2 gas inflow and/or a premixed CO_2/N_2 gas inflow, at least one cell culture chamber specific heating

element, one or more cell culture chamber specific sensors, and a computer controller unit linked to said one or more cell culture chamber specific sensors, wherein the incubator is provided with an O_2 and/or CO_2 auto calibration capability when being connected to an O_2 and/or CO_2 gas external monitoring system, respectively.

7. An incubator according to any of claims 1-6, said incubator having a computer controller unit linked to said one or more cell culture chamber specific sensors, wherein the computer controller unit has a WEB link and as such allows for cell culture chamber independent WEB monitoring with respect to said one or more cell culture chamber specific sensors and also allows for control by interaction with the incubator via a user WEB interface.

8. An incubator according to any of claims 1-7, wherein the incubator has a $CO_{2,}$ an O_2 and a N_2 gas inflow and/or a premixed $CO_2/N_2/O_2$ gas inflow.

9. An incubator according to any of claims 1-8, wherein the incubator has at least three independent cell culture chambers.

10. An incubator according to any of claims 1-9, wherein each independent cell culture chamber is provided with an independent temperature PID control.

11. An incubator according to any of claims 1-10, wherein one or more of the independent cell culture chambers are provided with a pH sensor connected to the computer controller unit so that the incubator has a pH monitoring/control system.

12. An incubator according to any of 1-11, also provided with a gas sampling system connected to the computer controller unit so that sampling frequency may be set and the gas sampling may be monitored and logged.

13. An incubator according to any of claims 1-12, wherein the incubator also has a gas flow closed loop PID regulation on CO_2, O_2 gas consumption, N_2 gas consumption and/or premixed gas consumption.

14. An incubator according to any of 1-13, wherein the computer controller unit has an independent WEB logging system.

15. An incubator according to any of claims 1-14, wherein at least one of the independent cell culture chambers has a temperature sensor, a humidity sensor and a pH sensor as said one or more cell culture chamber specific sensors.

16. An incubator according to any of claims 1-15, wherein each independent cell culture chamber has an ID chamber check in/out system also linked to the computer controller unit.

17. An incubator according to any of claims 1-16, wherein more than one of the essential service components being at least filter(s), UV lamps, O_2 sensors are mounted in an end user accessible room in the incubator.

18. An incubator according to any of claims 1-17, wherein one or more of the independent cell culture chambers are provided with a lid opening detector sensor connected to the computer controller unit so that the lid movement is being monitored and logged.

19. An incubator according to any of claims 1-18, wherein one or more of the independent cell culture chambers are provided with a time lapse image analysis system connected to the computer controller unit so that the cell culture process is being monitored and logged for controlling purposes.

20. An incubator according to any of claims 1-19, wherein one or more of the independent cell culture chambers are provided with a bio computer control

cell closely monitored by an image analysis system for logging and cell culture environment control purposes.

21. An incubator according to any of claims 1-20, wherein one or more of the independent cell culture chambers are provided with a cross directional gas nozzle in order to control and maintain a fast recovery of the gas concentration within the chamber.

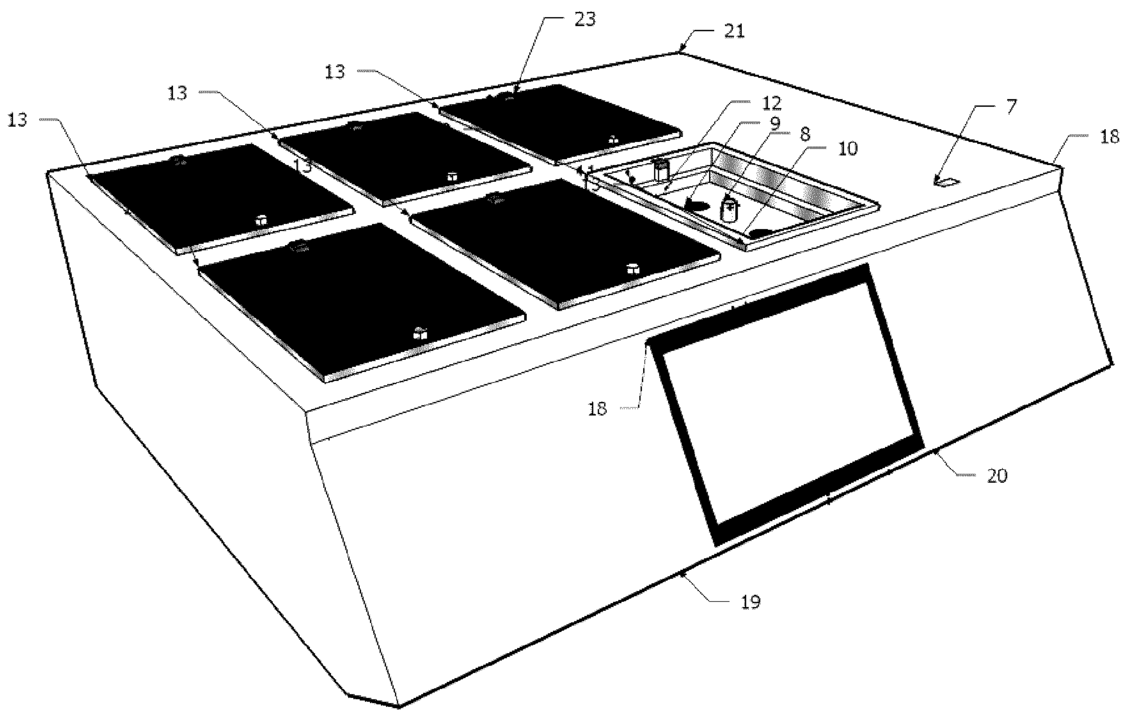

Fig. 1

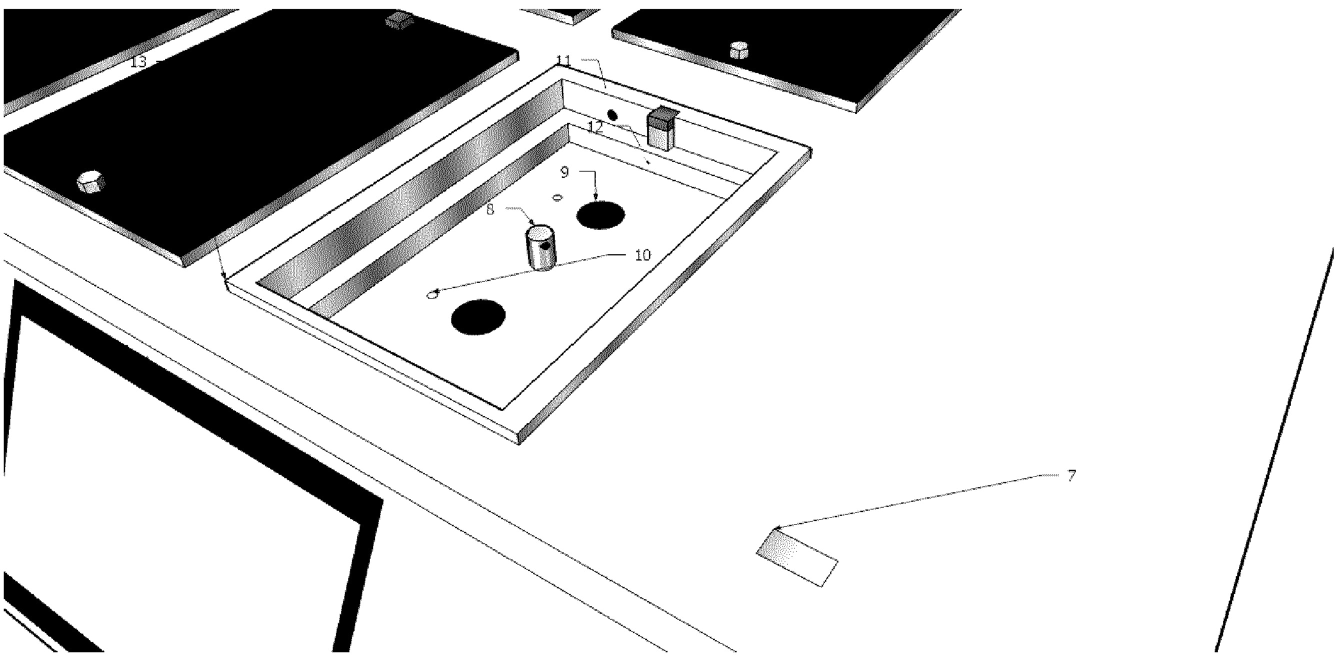

Fig. 2

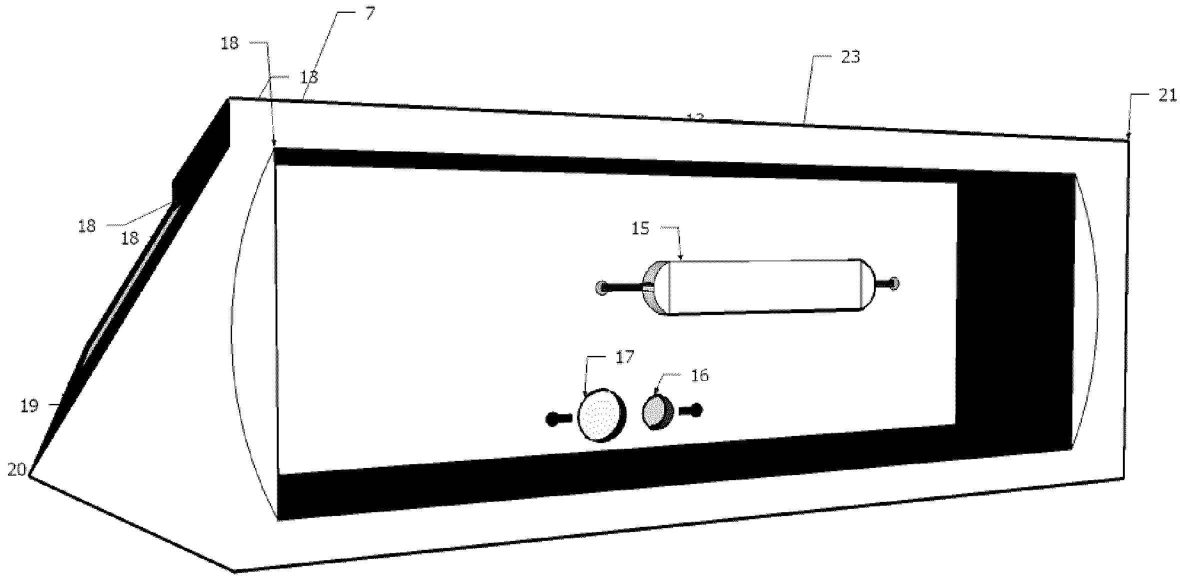

Fig. 3

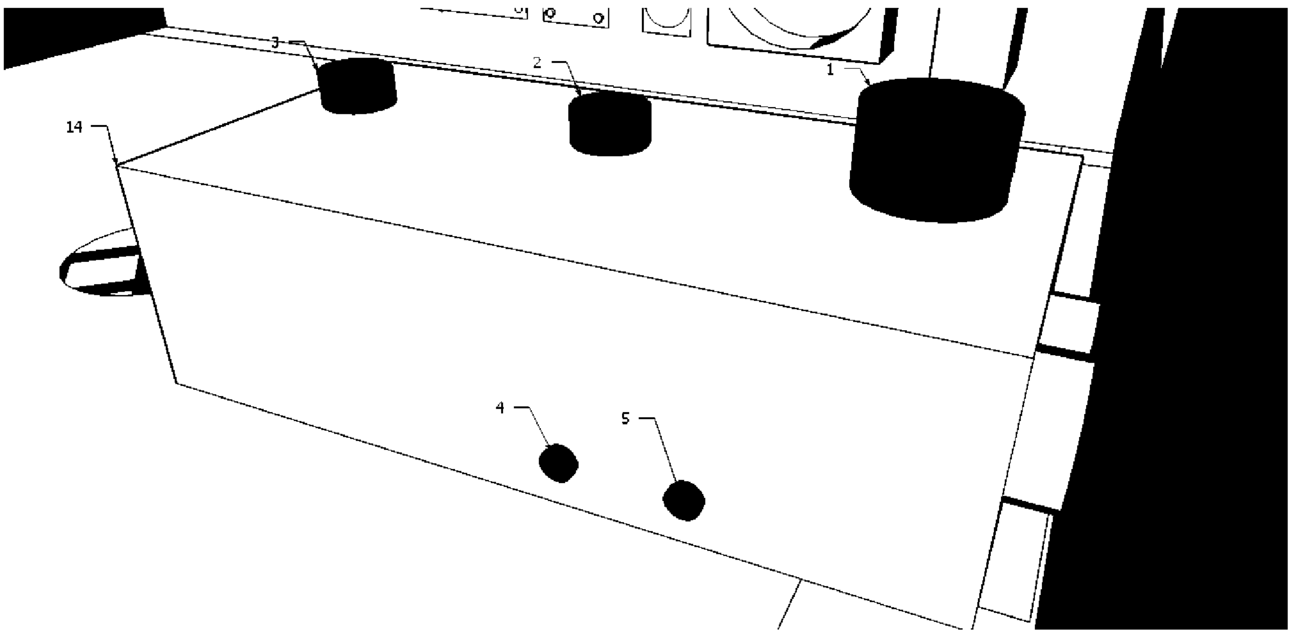

Fig. 4

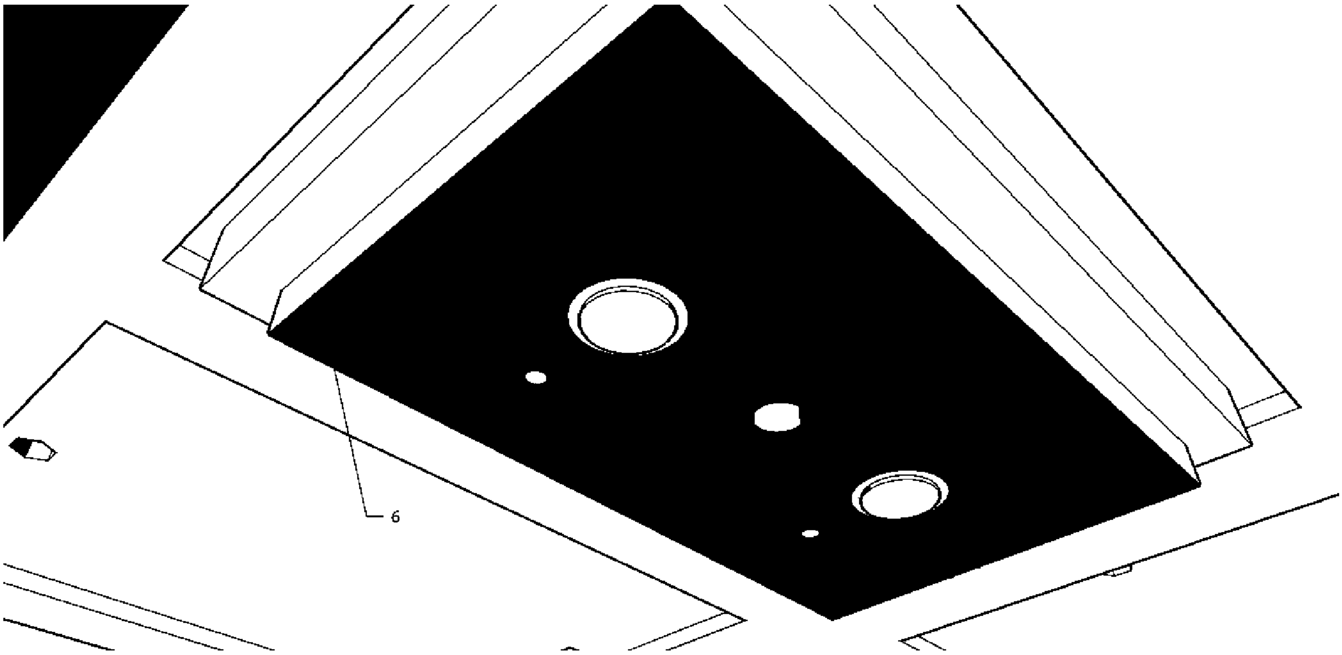

Fig. 5

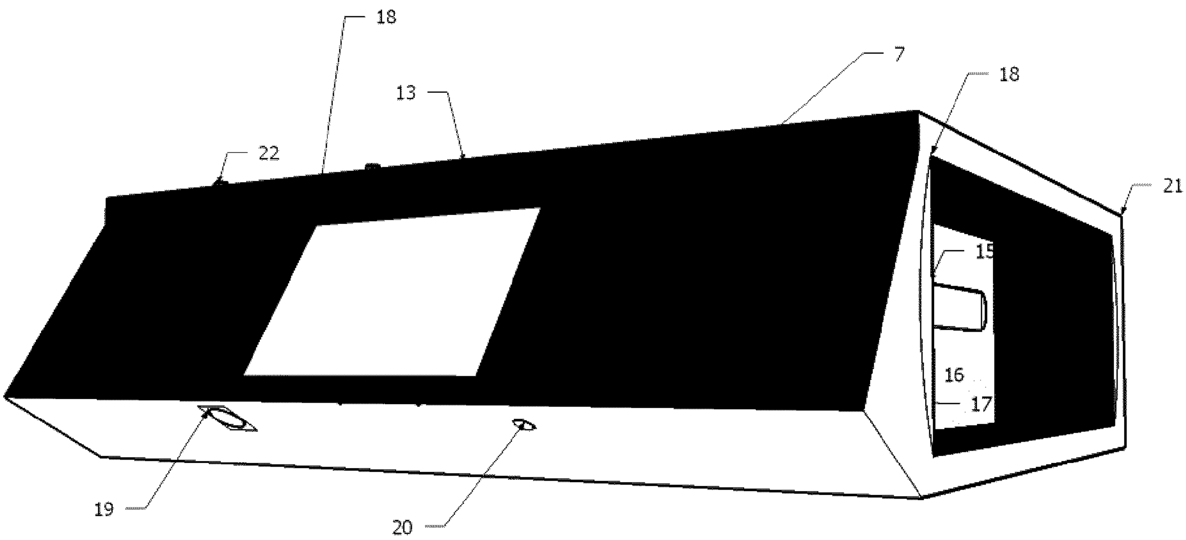

Fig. 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/075822

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12M1/00 C12M1/34
ADD.

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)
C12M B01L

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

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

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2003/092178 A1 (YERDEN RANDY [US]) 15 May 2003 (2003-05-15) paragraph [0037] - paragraph [0041] paragraph [0046] - paragraph [0049] paragraph [0051] figures 1,3-6 -----	1-3,6,8, 10,12 4,5,7,9, 11,13-21
Y	"Benchtop-Inkubation der 2. Generation", Journal of Reproductive Medicine and Endocrinology - J. Reproduktionsmed. Endokrinol, 2011, page 367, XP055100744, Retrieved from the Internet: URL:http://www.kup.at/kup/pdf/10210.pdf [retrieved on 2014-02-06] the whole document -----	4,5,7,9, 11,13-21

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"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	Date of mailing of the international search report
7 February 2014	28/02/2014

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Cubas Alcaraz, Jose

International application No
PCT/EP2013/075822

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2009/063190 A1 (RUSKINN LIFE SCIENCES LTD [GB]; SKINN ANDREW [GB]) 22 May 2009 (2009-05-22) page 1, line 3 - line 5 page 3, line 21 - line 27 page 6, line 25 - page 7, line 11 figure 1 -----	1-21

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2013/075822

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003092178 A1	15-05-2003	NONE	
WO 2009063190 A1	22-05-2009	EP 2209884 A1	28-07-2010
		US 2010313963 A1	16-12-2010
		WO 2009063190 A1	22-05-2009