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(74) Agent: KUPECZ, Arpad; 20052, Weteringschans 96,  
1017 XS Amsterdam, Noord-Holland, NL-1000 HB  
Amsterdam (NL).

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(71) Applicant (for all designated States except US): VU  
MEDISCH CENTRUM [NL/NL]; De Boelelaan 1117,  
NL-1081 HV Amsterdam (NL).

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(72) Inventor; and

(75) Inventor/Applicant (for US only): HOMPES, Petrus  
Gerardus Alphonsus [NL/NL]; Wolfert van Borssele-  
weg 109, NL-1181 PJ Amstelveen (NL).

[Continued on next page]

(54) Title: SUITABLE APPARATUS FOR PRECISELY AND REPRODUCIBLY TRANSFERRING A FERTILIZED EGG-CELL (EMBRYO) TO THE UTERUS

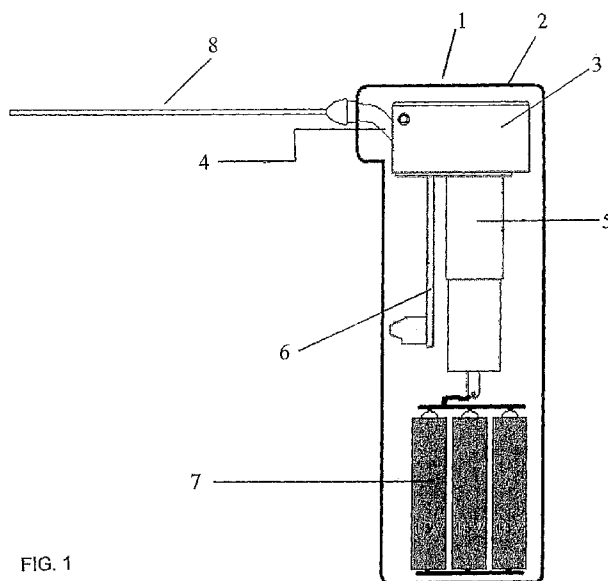


FIG. 1

(57) Abstract: The subject of the present invention is in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI), and relates to an apparatus with which embryo transfer can be standardised and which, in comparison with the currently used technique, may possibly result in higher pregnancy rates. This is realised by using an apparatus with which it is possible to precisely and reproducibly aspirate one or two embryos from a Petri dish and to transfer them to the uterus, to a particular distance from the fundus. It has been shown that the chance of pregnancy is best if the distance between the embryo and the fundus is 1-2 cm.

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**Published:**

— *with international search report*

— *with amended claims*

Suitable apparatus for precisely and reproducibly transferring a fertilized egg-cell (embryo) to the uterus

The present invention relates to a suitable apparatus for precisely and reproducibly transferring an outside the uterus fertilized egg-cell (embryo) to the uterus.

It is known that a considerable number of women are  
5 unable to become pregnant. The cause for this may rest with the man as well as with the woman.

Many of these women have a strong desire to have children and take recourse to artificial fertilization techniques such as in vitro fertilization (IVF) and intracytoplasmic sperm  
10 injection (ICSI).

The IVF/ICSI treatment involves several phases. The first phase concerns stimulation, wherein the patient receives hormones in order to bring a number of egg-cells to maturation. This is monitored by ultrasound.

15 The second phase involves puncturing, whereby the various follicles are pierced with the aid of a vaginal ultrasound probe, after which their contents are aspirated. The aspirated fluid is then passed on to the embryologist, who first establishes whether the fluid contains any egg-cells. If egg-  
20 cells are present, semen will be added in vitro to effect fertilization. After 2-3 days, the egg-cells are examined for cell division, whereby several fertilized egg-cells, also referred to as embryos, may be present.

In the third phase, the obtained fertilized egg-cells,  
25 embryos, are transferred to the uterus.

According to the prior art, this transfer takes place with the aid of a syringe attached to a catheter. By means of the syringe the embryos are aspirated with the fluid and with the aid of ultrasound guiding they are transferred to the  
30 uterus. The woman may decide whether one or two embryos are transferred to the uterus, with the chance of one or two children. For this purpose a standard commercially available 1 ml syringe is used. The catheter is comprised of a thin, flexible plastic tube, in which the embryos are enclosed between two air  
35 bubbles.

In an endeavour to improve the known method so as to increase the chance of a pregnancy much more attention is given to improving stimulation protocols than to improving the embryo transfer technique.

5           However, various studies have shown that the chance of pregnancy resulting from IVF/ICSI is influenced very particularly by the location to which the embryo is transferred in relation to the fundus of the uterus. It has been shown that the best chance of pregnancy is afforded by a distance of 1-2 cm  
10 between the transferred embryo and the fundus (see for example M. Lambers et al. 'The position of the transfer air bubbles after embryo transfer is related to pregnancy rates', accepted for publication in Fertility and Sterility 2006).

          However, the prior art technique is imprecise and not  
15 reproducible, making it difficult to determine the transfer position of the embryo. The imprecision and non-reproducibility are caused by a number of factors such as the syringe itself, the resistance of the plunger, the pressure exerted on the plunger by the physician, and possible intra-uterine resistance  
20 partly attributable to uterine contractions. Especially the varying pressures applied when ejecting the embryo from the catheter plays a considerable role in the above mentioned imprecision and non-reproducibility.

          Moreover, excessive ejection pressure may damage the  
25 embryos themselves.

          It is thus an object of the invention to provide an apparatus, which effectively eliminates the above mentioned drawbacks, and is able to significantly increase the chance of pregnancy resulting from an IVF treatment.

30           To this end, the present invention provides a suitable apparatus for precisely and reproducibly transferring to the uterus an egg-cell (an embryo) fertilized outside the uterus, which apparatus is characterised in that the same is provided with a pump, a flexible tube, a motor, control electronics, a  
35 power supply and a catheter.

          Surprisingly, it was shown that by using the apparatus according to the invention, the drawbacks of the prior art are effectively removed. A special feature of the electrical pump used for embryo transfer is that it is able to aspirate a very  
40 small amount of fluid (approximately 30 microlitres) within an

exact time limit, as well as to inject this small amount in a reproducible manner.

The person in question, usually a physician who has to transfer the embryo to the uterus, is able to do this with the aid of the present apparatus precisely and reproducibly, such that the embryo is placed in the uterus at a proven optimal distance, preferably at 1-2 cm from the fundus.

In accordance with the present apparatus, first an amount of IVF culture medium is aspirated into the catheter, then an air bubble, and then again an amount of IVF culture medium containing one or several embryo(s), then again an air bubble, and finally another amount of culture medium. The embryos are then, as it were, enclosed in the catheter between the two air bubbles.

With the aid of ultrasound guiding the treating physician then inserts the catheter into the uterus and ensures that the end of the catheter is positioned at the desired location, preferably at 1-2 cm from the fundus of the uterus. Then the pump is switched on and the embryos are ejected slowly and evenly from the catheter.

When the embryos have being placed into the uterus at the desired distance from the fundus, the catheter is withdrawn from the uterus.

The control electronics provided in the apparatus enable the suction and pushing force of the apparatus according to the invention to be adjusted with precision. In comparison with the prior art syringe, it is possible that the chance of pregnancy may be significantly increased with the aid of the apparatus according to the invention.

An important advantage of the present apparatus is further that diverse physicians are able to use it with the same precision and reproducibility because when ejecting the embryos from the catheter using the pump, the pressure can be kept constant, which is not possible with the syringe. The difference to using a syringe is that the ejection pressure may vary depending on the person operating the syringe.

The invention will now be further explained with reference to the accompanying Figures 1-3. The invention is not limited to the embodiments illustrated in the Figures 1 and 2.

Figure 1 shows the apparatus according to the invention.

Figure 2 shows the catheter according to the invention, and

5 Figure 3 shows the apparatus according to the prior art.

Figure 1 shows the apparatus (1) according to the invention, provided with a pump (3), a flexible tube (4), a motor (5), control electronics (6), a power supply (7) and  
10 catheter (8). It is usually that a battery serves as power supply, but the mains power system is also possible, in which case the apparatus is provided with a cord and plug.

The pump (3), flexible tube (4), motor (5), control electronics (6) and power supply (7) are preferably accommodated  
15 in a housing (2) for easy handling of the apparatus (1) and for the protection of the various components in the apparatus (1).

Via the catheter, the embryologist will with the aid of the apparatus first aspirate in vitro a small amount of culture medium, then an air bubble, then an amount of culture medium  
20 containing one or two embryos, depending on the wish of the patient, then air again and finally again an amount of culture medium. In total, the amount of inserted fluid is only 30 microlitres.

The treating physician, usually a gynaecologist, will  
25 subsequently take the apparatus to the treatment room where the transfer of the embryo takes place.

With the aid of ultrasound guiding the treating surgeon will insert the catheter into the uterus such that its end is located at a distance of 1-2 cm from the fundus. Using the present apparatus, the contents of the catheter are then gradually,  
30 at a constant pressure ejected from the catheter such that the air bubbles, and thus the embryos, are deposited at a distance of 1-2 cm from the fundus of the uterus. Any arbitrary physician is able to carry out this operation consistently and reproducibly,  
35 with the possible result of the thus treated woman having a significantly greater chance of pregnancy.

In the apparatus (1) according to the invention, the power supply (7) drives the motor (5) bringing about the pumping action of the pump (3). Instead of batteries, it is possible to  
40 use another power source, for example the electric power mains,

in which case batteries are superfluous. The suction and ejection pressure generated by the pump (3) is passed on via catheter (8), which by means of the flexible tube (4) is connected with the pump (3). It is preferred for the catheter to be remov-  
5 ably connected with the flexible tube (4).

Figure 2 shows a catheter (9), whose one end is provided with a connecting piece (10) for connecting to the end of the flexible tube (4).

In Figure 2, the amount of culture medium is indicated  
10 with reference numeral (11), the air bubbles carry reference numeral (12), and the embryo(s) reference numeral (13).

The apparatus according to the prior art is represented in Figure 3. In Figure 3, the catheter (15) is connected with a syringe (14) by means of a connection (16).

15 With regard to precision and reproducibility, this apparatus is inferior to the apparatus according to the invention, as a consequence of which the chance of pregnancy when using such an apparatus is significantly smaller than when using the present apparatus.

20 It should be noted that the present invention is not limited to the embodiments shown in the Figures 1 and 2 of the present invention.

CLAIMS

1. A suitable apparatus (1) for precisely and reproducibly transferring an outside the uterus fertilized egg-cell (embryo) to the uterus, which apparatus (1) is provided with a pump (3), a flexible tube (4), a motor (5), control electronics (6), a power supply (7) and a catheter (8), **characterised** in that the pump (3), the flexible tube (4), the motor (5), the control electronics (6), and the power supply (7) are accommodated in a housing (2).
2. An apparatus according to claim 1, wherein the power supply is a battery.
3. An apparatus (1) according to claim 1 or 2, **characterised** in that the catheter (8) is removably connected with the flexible tube (4).



**AMENDED CLAIMS**

received by the International Bureau on 06 August 2008 (06.08.2008).

1. Apparatus (1) suitable for precisely and reproducibly transferring an outside the uterus fertilized egg-cell (embryo) to the uterus, which apparatus (1) is provided with a pump (3), a flexible tube (4), a motor (5), control electronics (6), a power supply (7) and a catheter (8), **characterised** in that the pump (3), the flexible tube (4), the motor (5), the control electronics (6), and the power supply (7) are accommodated in a housing (2).

2. An apparatus (1) according to claim 1, wherein the power supply (7) is a battery.

3. An apparatus (1) according to claim 1 or 2, **characterised** in that the catheter (8) is removably connected with the flexible tube (4).

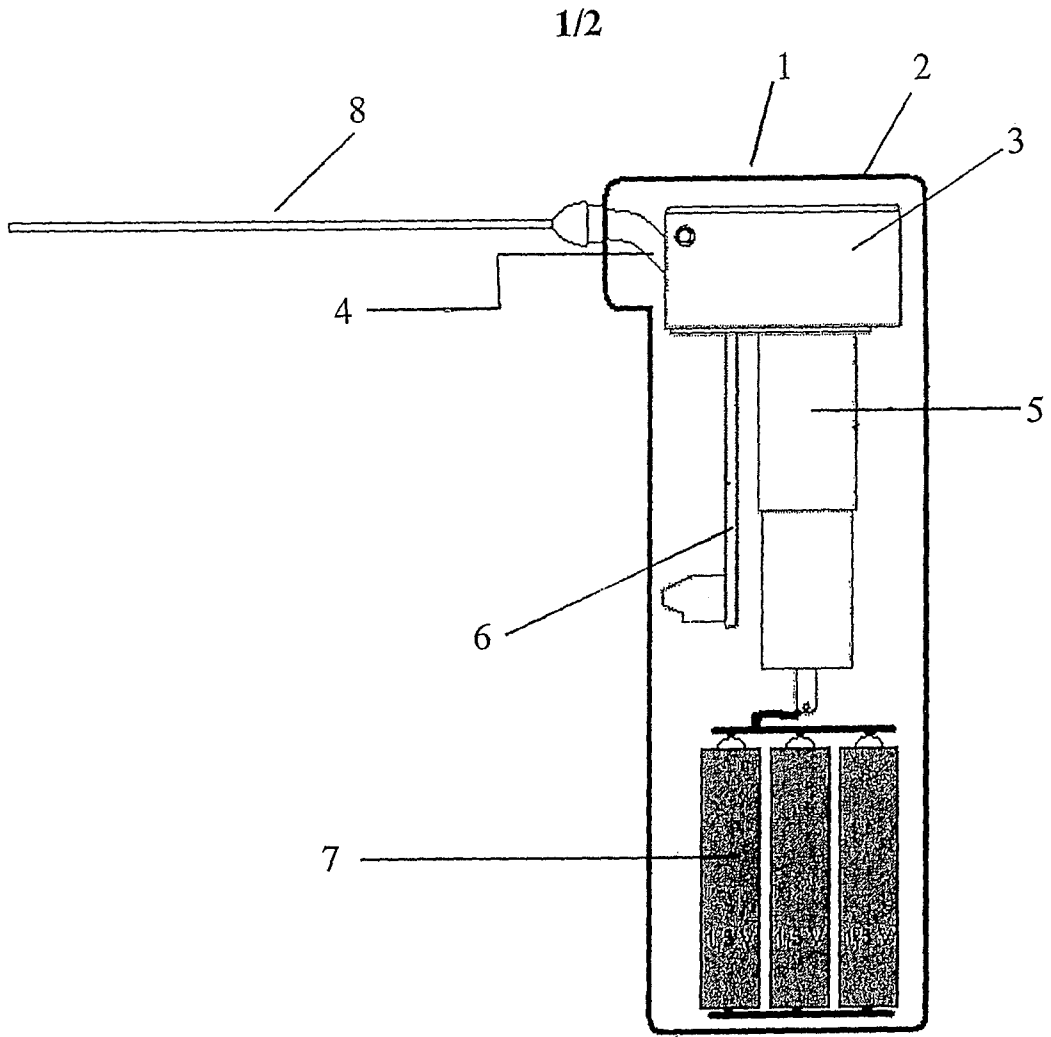


FIG. 1

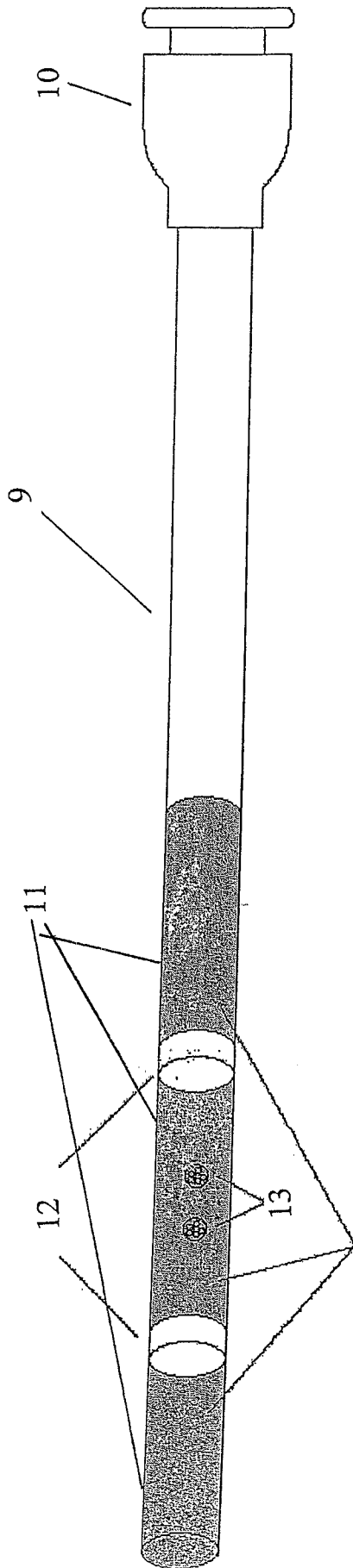


FIG. 2

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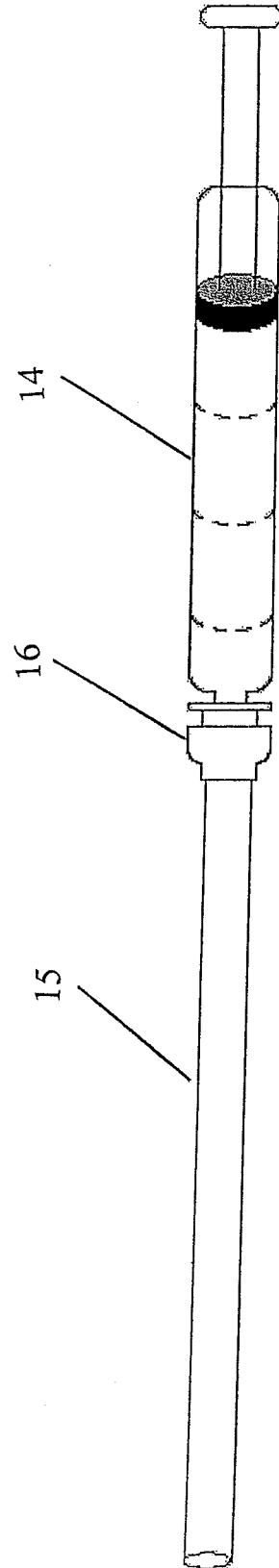


FIG. 3

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/NL2008/050116

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. A61B17/425 A61B17/43

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)

A61B A61D

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 practical, 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	US 2005/038315 A1 (ECKSTEIN NACHMAN [IL] ET AL) 17 February 2005 (2005-02-17) abstract; figures paragraphs [0007] - [0010], [0028] - [0044], [0052] - [0055]	1-3
Y	WO 99/18872 A (A R T MEDICAL INSTR LTD [IL]; BERGER ABRAHAM [IL]; HAIM BEN ZION [IL];) 22 April 1999 (1999-04-22) abstract; figures page 1, lines 10-13 page 1, line 25 - page 2, line 5 page 5, line 22 - page 8, line 29	1-3
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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
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- \*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.
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Date of the actual completion of the international search

4 June 2008

Date of mailing of the international search report

13/06/2008

Name and mailing address of the ISA/

European Patent Office, P.B. 5816 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Giménez Burgos, R

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/NL2008/050116

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4 988 481 A (JARVIMAKI KARI [FI] ET AL) 29 January 1991 (1991-01-29) abstract; claim 1; figures column 1, lines 40-44 column 2, lines 4-29 column 3, line 60 - column 4, line 6	1-3
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Information on patent family members

International application No PCT/NL2008/050116
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