

PATIENT INFORMATION:

The **INVO**cell™ Intravaginal Culture System

The INVOcell Culture System: The INVOcell Culture System is designed to hold your eggs and sperm in culture media while incubating them in the upper vaginal cavity during fertilization and early embryo development. If you have had Intracytoplasmic Sperm Injection (ICSI), where a spermatozoon is injected into the egg for fertilization, the INVOcell Culture Device will hold your ICSI embryos in the same way.

Indications for Use:

The INVOcell Intravaginal Culture System consists of the following components:

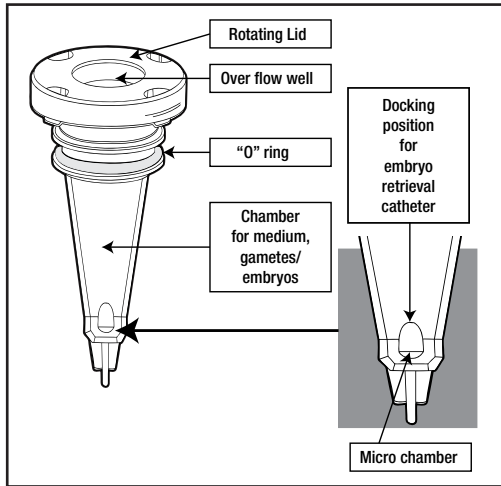
The INVOcell Culture Device is indicated for use in preparing, holding, and transferring human gametes or embryos during In Vitro Fertilization/Intravaginal Culture (IVF/IVC) and Intra-Cytoplasmic Sperm Injection Fertilization/Intravaginal Culture (ICSI/IVC) procedures. The INVOcell Culture Device is indicated for use with the INVOcell Retention Device. The INVOcell Culture Device is not indicated for incubation periods exceeding 72h.

The INVOcell Retention Device is indicated for use with the INVOcell Culture Device to aid in retention of the INVOcell Culture Device in the vaginal cavity during the incubation period. The INVOcell Retention Device is not indicated for use exceeding 72 hours.

As a patient, you will need to use the INVOcell Culture Device and the INVOcell retention device to incubate your eggs, sperm, and/or embryos.

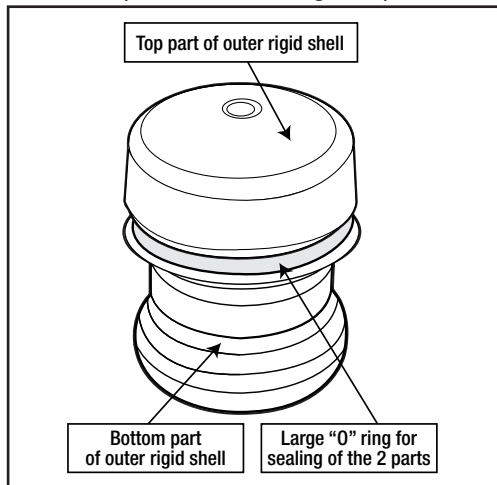
Description of the INVOcell Culture Device: The INVOcell Culture Device is made up of two components: the inner vessel, and the outer shell. The inner vessel (**Figure 1**) holds the eggs and sperm, or ICSI-fertilized embryos in cell culture media.

FIGURE 1: Inner Vessel



The outer shell (**Figure 2**) is a two-part container that surrounds the inner vessel and protects it during vaginal incubation.

**FIGURE 2: Outer Rigid Shell for Cell Culture Container
(Contents of Package Two)**

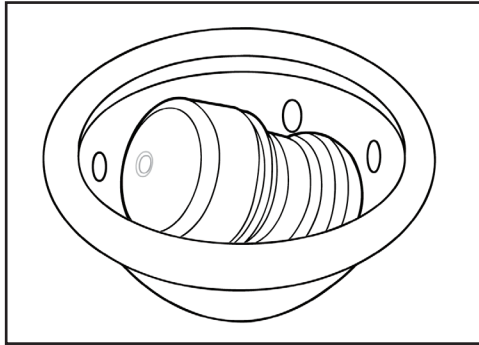


Once assembled, the complete INVOcell Culture Device is placed in the vaginal cavity for 72 hours to allow fertilization and/or embryo development to occur.

Description of the INVOcell Retention Device: The INVOcell Retention Device (**Figure 3**) is made of medical grade silicone that has holes placed in it to allow for any vaginal fluids to flow out naturally during the 72 hour incubation period. The INVOcell Retention Device comes in a single size.

It is placed into the vaginal cavity with the INVOcell Culture Device to assure that the INVOcell Culture Device stays in the vaginal cavity for the full 72 hour incubation period.

FIGURE 3: INVOcell RETENTION DEVICE Cradling the INVOcell Culture Device



You should not use the INVOcell Culture Device and INVOcell Retention Device if:

- You cannot tolerate the placement or wearing of the INVOcell culture device and retention device in your vagina

IMPORTANT: You should discuss with your doctor whether the INVOcell procedure is appropriate for you.

IMPORTANT: In order to maximize the chances of fertilization and embryo development you must wear both the INVOcell Culture Device and INVOcell Retention Device within your vagina for 3 days (72 hours). You should discuss your suitability for the Intravaginal Culture procedure with your doctor before you decide to attempt this method of fertilization.

Warnings and Precautions:

WARNING: Please consult your doctor before using INVOcell if:

- You have had recent pelvic surgery
- You have a history of toxic shock syndrome
- You currently have a severe case of vaginitis

WARNING: In traditional in vitro fertilization, embryos are typically monitored by a doctor or lab technician using a microscope during the first 72 hours of development. When using INVOcell, embryos are not able to be monitored in this way. Therefore, problems with the embryos that occur during this 72 hour incubation period may not be detected. This may increase the risk of abnormal embryos being transferred to the uterus later in the IVF treatment.

CAUTION: Do not remove the INVOcell Culture Device or INVOcell Retention Device from the vaginal cavity and avoid manipulation of the INVOcell Culture Device. The vaginal cavity provides the proper environment (temperature and gas) for fertilization and embryo development with the INVOcell Culture Device.

CAUTION: While wearing the INVOcell Culture Device and Retention Device:

- Do not bathe in a tub, showers are permissible.
- Do not swim
- Do not use a sauna
- Do not douche
- Do not have intercourse
- Do not perform strenuous activity
- Do not insert other objects or liquids into the vagina

Steps of the IVC Procedure:

Loading the INVOcell Culture Device with Sperm and Eggs or ICSI-Fertilized Embryos:

This part of the process is performed on the same day as sperm collection and egg retrieval and is different from standard IVF. For in vitro fertilization / intravaginal culture (IVF/IVC), up to seven eggs are mixed with the sperm in growth medium and placed in the INVOcell Culture Device. Insemination and fertilization takes place within the INVOcell Culture Device in your vagina. For ICSI / IVC, eggs are injected with sperm in the lab, to produce embryos. Up to seven of these embryos in growth media are placed in the INVOcell Culture Device for incubation and development. In traditional IVF methods, fertilization and embryo development are achieved in a culture dish and incubated at 37°C in a CO₂ incubator.

Intravaginal Culture: The INVOcell Culture Device will be placed in your vagina for 72 hours. You should not feel discomfort with wearing the device during the period of incubation. If you feel discomfort, call your physician. **DO NOT REMOVE THE INVOcell DEVICES DURING INCUBATION.** Do not perform any acts that may affect the temperature of the vagina and/or the temperature of embryo incubation such as bathing, vaginal douching or sauna.

Embryo Transfer: Embryo transfer is done at the end of the 72 hour vaginal incubation period. Your physician will remove the INVOcell Retention Device and the INVOcell Culture Device. An embryologist will then determine the quantity and quality of the embryos developed. The selection of the embryo(s), the transfer of the embryo(s), and the period of relaxation after transfer will be done according to the standard procedures for IVF. You will be consulted on the number of embryos to be transferred to your uterus.

Repositioning of the Device:

If the INVOcell Culture device moves down towards the opening of the vagina or falls out, follow the instructions below and call your doctor.

Scenario 1: In the event the INVOcell Culture Device and the INVOcell Retention Device move down the vaginal channel and you feel it near the opening of the vagina, immediately clean your hands with soap and water and move them back deeper into the vagina (**see Figures 6 and 7**).

Scenario 2: In the event the INVOcell Culture Device and the INVOcell Retention Device “fall out” of the vagina, clean your hands with soap and rinse with warm water, rinse the device quickly with warm water and then replace the device immediately in the vaginal cavity (**see Figures 4 - 7**). After placement of the Culture Device, rinse the retention system with warm water, and replace it in the vaginal cavity (**see Figure 8**).

WARNING: Hot water should not be used to rinse the device. This could potentially stop the embryo development.

If either of the above scenarios occurs, call your physician. You will need to go to the physician's office, so your doctor can confirm the INVOcell Culture Device and the INVOcell Retention Device have been placed correctly. The doctor may also recommend replacing the INVOcell Retention Device.

FIGURE 4

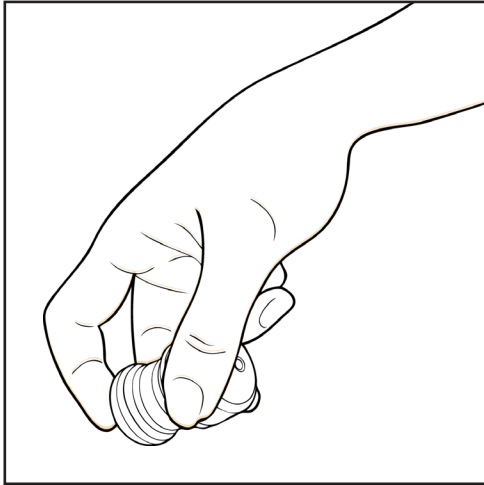


Figure 4: With one hand, firmly hold the device by placing your thumb and middle finger on the central portion. Orient one of the rounded ends of the rigid outer container toward your body.

FIGURE 5



Figure 5: With your other hand, gently spread the skin surrounding your vaginal opening. Insert the rounded end of the device into the vagina.

FIGURE 6

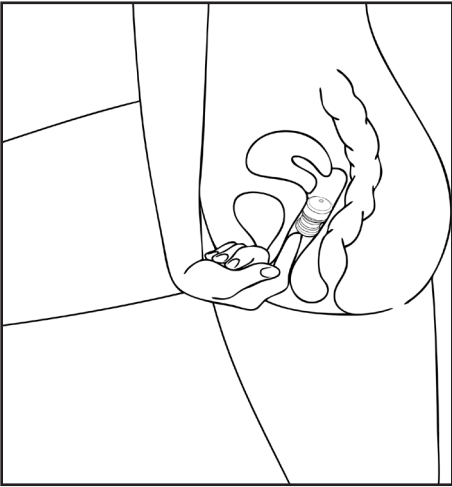


Figure 6: Stand with one leg up, relax your muscles and use the full length of your index finger to gently ease the device along the vaginal channel, towards your lower back.

FIGURE 7

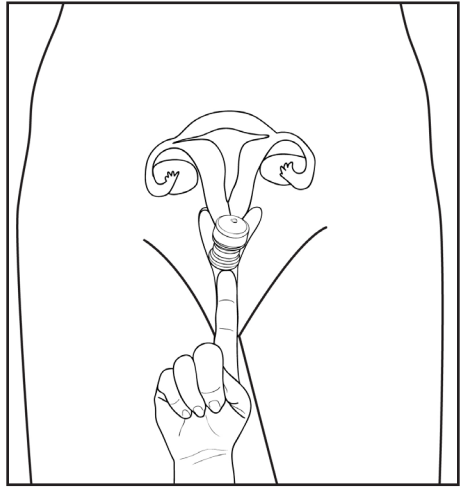


Figure 7: Position the device deep into the vagina, as far as you can. Then push the device into a sideways position horizontally behind the cervix.

FIGURE 8

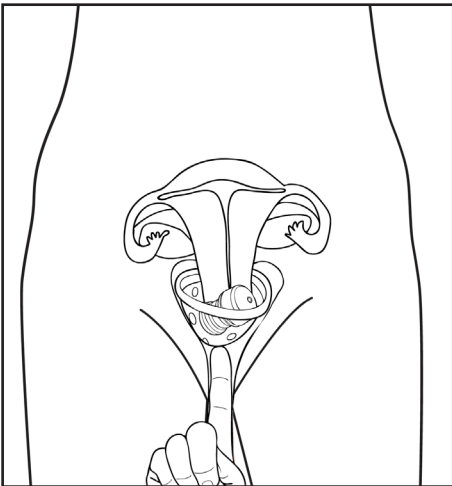


Figure 8: If you replace the retention system, bend the ring of the retention system and replace it deeply into the vagina. Go to your physician's office so he /she can confirm the INVOcell and its retention system have been correctly replaced.

INVOCell in Clinical Use

The INVOCell Intravaginal Culture System was evaluated in fertility clinics in Columbia, Bolivia, Brazil, and Peru. A total of 450 Intravaginal Culture cycles were performed. 330 of the cycles were Intravaginal Culture / In-vitro Fertilization (IVC/IVF), and 120 cycles were Intravaginal Culture / ICSI (IVC/ICSI). The following table summarizes outcomes for patients who used INVOCell during conventional IVF and patients who used INVOCell following intracytoplasmic sperm injection (ICSI) of the patient's oocytes:

Table 1: INVOCell IVC/IVF compared to IVC/ICSI in Four Fertility Clinics in South America

	INVOCell IVC/IVF	INVOCell IVC/ICSI
Cycles	330	120
Embryo transfers	308 (93% of cycles)	113 (94% of cycles)
Live births total*	78 (25% of transfers)	29 (26% of transfers)
Live births (survivors)**	76 (25% of transfers)	28 (25% of transfers)
Live born babies	98	34
Live born babies (surviving)	94	33

*Not included are 6 pregnancies with unknown outcomes, these pregnancies were 4 singles and 2 twins.

**Four IVC/IVF babies died after delivery, one after surgery for intestinal occlusion with no genetic abnormality detected, and 3 babies from a triplet delivery at 20 weeks.

One twin IVC/IVF baby from a 39 years old patient had down syndrome. One IVC/ICSI baby died due to major bone malformations and cardiopathy highly suggestive of genetic anomalies. Another IVC/ICSI premature baby born at 30 weeks had congenital scoliosis.

To report SUSPECTED ADVERSE EVENTS, contact Ferring Pharmaceuticals Inc. at 1-888-FERRING (1-888-337-7464) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For more information go to www.invocell.com, or call 1-888-FERRING (1-888-337-7464).

Distributed by:



FERRING PHARMACEUTICALS INC.
PARSIPPANY, NJ 07054

6206-01
(Rev. 15/2018)

INVOcell Patient Information Booklet_R7

Date: 12/18/2018



Job Specs

Oracle No.: N/A

Brand: INVOcell

Component: PI

Strength: N/A

Artwork Provider: Ferring Studio, Parsippany, NJ

Template/Die-Line No.: None

No. of pages: ?

Inks: Process Black

Smallest font size used: 8 pt.

PI Booklet Dimensions: 5.5”w x 7.125”h