



Food and Drug Administration
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November 2, 2015

INVO Bioscience
c/o Lori Kahler
President
The RC Insight Group
743 Passaic Avenue, Suite 147
Clifton, NJ 07012

Re: DEN150008
INVOcell™ Intravaginal Culture System
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 884.6165
Regulation Name: Intravaginal Culture System
Regulatory Classification: Class II
Product Code: OYO
Dated: July 1, 2015
Received: July 6, 2015

Dear Lori Kahler:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your *de novo* request for classification of the INVOcell Intravaginal Culture System, a prescription device under 21 CFR Part 801.109 that is indicated for the following:

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/Intra Vaginal 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 and the INVOcell Holding Block. 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.

The INVOcell Holding Block is indicated for use with the INVOcell Culture Device to aid in temperature maintenance of the INVOcell Culture Device during loading and collection procedures and to aid in positioning and observation of the INVOcell Culture Device during human gamete/embryo loading and collection procedures.

FDA concludes that this device should be classified into class II. This order, therefore, classifies the INVOcell, and substantially equivalent devices of this generic type, into class II under the generic name, Intravaginal Culture System.

FDA identifies this generic type of device as:

Intravaginal Culture System. An intravaginal culture system is a prescription device intended for preparing, holding, and transferring human gametes or embryos during intravaginal *in vitro* fertilization or intravaginal culture procedures.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This new law provides two options for *de novo* classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On February 23, 2015, FDA received your *de novo* requesting classification of the INVOcell Intravaginal Culture System into class II. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the INVOcell Intravaginal Culture System into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the *de novo* request, FDA has determined that the INVOcell Intravaginal Culture System, indicated for the following:

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/Intra Vaginal 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 and the INVOcell Holding Block. 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.

The INVOcell Holding Block is indicated for use with the INVOcell Culture Device to aid in temperature maintenance of the INVOcell Culture Device during loading and collection procedures and to aid in positioning and observation of the INVOcell Culture Device during human gamete/embryo loading and collection procedures.

can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in Table 1.

Table 1 – Identified Risks to Health and Mitigation Measures

Identified Risk	Mitigation Measure
Damage to gametes and/or embryos or disruption of the IVF process	Non-clinical performance testing Shelf life testing Clinical testing Sterilization validation Labeling
Patient injury (e.g. hypersensitivity, toxicity, abrasion, discomfort)	Non-clinical performance testing Shelf life testing Biocompatibility Clinical testing Sterilization validation Labeling
Infection	Sterilization validation Reprocessing validation Non-clinical performance testing Shelf life testing Clinical testing Labeling
Transfer of incorrect embryos to patient	Labeling

In combination with the general controls of the FD&C Act, the Intravaginal Culture System is subject to the following special controls:

1. Clinical performance testing must demonstrate the following:
 - a. Comfort and retention of the intravaginal culture device
 - b. Adverse vaginal tissue reactions associated with intravaginal culture
 - c. Maximum number of gametes and/or embryos that can be placed in a device
 - d. Rates of embryo development to the designated stage, implantation rates, clinical pregnancy rates, live birth rates, and any adverse events or outcomes.
2. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be demonstrated:
 - a. Mouse Embryo Assay (MEA) testing to assess embryotoxicity by evaluating the gamete and embryo-contacting device components' effect on the growth and development of mouse embryos to the blastocyst stage

- b. Endotoxin testing on gamete and embryo-contacting components of the device
 - c. Cleaning and disinfection validation of reusable device components
 - d. Sterility maintenance of the culture media within the device throughout the vaginal incubation period and subsequent embryo extraction
 - e. Ability of the device to permit oxygen and carbon dioxide exchange between the media contained within the device and the external environment throughout the vaginal incubation period.
3. The patient-contacting components of the device must be demonstrated to be biocompatible.
4. Performance data must demonstrate the sterility of the device components intended to be provided sterile.
5. Shelf-life testing must demonstrate that the device maintains its performance characteristics and the packaging of device components labeled as sterile maintain integrity and sterility for the duration of the labeled shelf-life.
6. Labeling for the device must include:
 - a. A detailed summary of the clinical testing, including device effectiveness, device-related complications, and adverse events
 - b. Validated methods and instructions for reprocessing of reusable components
 - c. The maximum number of gametes or embryos that can be loaded into the device
 - d. A warning that informs users that the embryo development is first evaluated following intravaginal culture
 - e. A statement that instructs the user to use legally-marketed assisted reproductive media that contain elements to mitigate the contamination risk (e.g., antibiotics) and to support continued embryonic development over the intravaginal culture period.
7. Patient labeling must be provided and must include:
 - a. Relevant warnings, precautions, and adverse effects and complications
 - b. Information on how to use the device
 - c. The risks and benefits associated with the use of the device
 - d. A summary of the principal clinical device effectiveness results.

In addition, this is a prescription device and must comply with 21 CFR 801.109. Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the Intravaginal Culture System they intend to market prior to marketing the device and receive clearance to market from FDA.

Please be advised that FDA's decision to grant this *de novo* request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD & C Act's requirements, including, but not limited to: registration and listing (21 CFR Part

807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD & C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the **Federal Register**. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the *de novo* request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Dr. Jason Roberts, Ph.D., at 1-301-240-402-6400.

Sincerely,

Jonette R. Foy -S

Jonette Foy, Ph.D.
Deputy Director
for Engineering and Science Review
Office of Device Evaluation
Center for Devices and
Radiological Health