May 11, 2018

Vitrolife A/S
Belinda Dueholm
Regulatory Affairs Specialist
Jens Juuls Vej 20
DK-8260 Viby J
Denmark

Re: K173264
Trade/Device Name: EmbryoScope+
Regulation Number: 21 CFR§ 884.6120
Regulation Name: Assisted Reproduction Accessories
Regulatory Class: II
Product Code: MQG, MQK, MTX
Dated: April 6, 2018
Received: April 12, 2018

Dear Belinda Dueholm:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies.

You must comply with all the 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 Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Charles Viviano -S

For Benjamin R. Fisher, Ph.D.
Director
Division of Reproductive, Gastro-Renal,
and Urological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K173264

Device Name
EmbryoScope+

Indications for Use *(Describe)*

EmbryoScope+ consists of the following devices with the following indications for use:

The EmbryoScope+ incubator provides an environment with controlled temperature and gas concentrations (CO2 and O2) for the development of embryos at or near body temperature. Use of the EmbryoScope+ incubator is limited to five days (120 hr) covering the time from post insemination to day five of development.

The EmbryoSlide+ culture dish is intended for preparing, storing, and transferring human embryos. The EmbryoSlide+ culture dish must be used together with the EmbryoScope+ incubator.

The EmbryoViewer software is intended for displaying, comparing, storing, and transferring images generated by the EmbryoScope+ incubator. This software includes a user annotation function for capturing information on embryo development parameters as well as a user-defined modeling function, which allows the user to combine annotated information on embryo development parameters to aid in embryo selection. The EmbryoViewer software does not control any hardware components in the EmbryoScope+ incubator.

The ES Server software is intended to store, archive and transfer data. In addition, this software includes functions for managing models and performing calculations based on image data and embryo development parameters.

The EmbryoScope+ incubator, EmbryoViewer software, and ES Server software must be used together to export embryo images from the EmbryoScope+ incubator. The EmbryoViewer software and ES Server software must be used together to analyze the embryo images.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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# 510(k) Summary
# (K173264)

## 1. Submitter Information

| | |
|---|---|
| Submitter | Vitrolife A/S<br>Jens Juuls Vej 20<br>DK-8260 Viby J<br>Denmark |
| Contact Person: | Ms. Belinda Dueholm |
| Telephone: | +45 7221 7900 (main)<br>+45 2076 3707 (direct) |

**2. Date Prepared:** May 11, 2018

## 3. Device Information

| | |
|---|---|
| Proprietary Name: | EmbryoScope+ |
| Common Name: | Embryo Incubator |
| Regulation Number: | 21 CFR 884.6120 |
| Regulation Name: | Assisted Reproduction Accessories |
| Product Code: | MQG (Accessory, Assisted Reproduction), MQK (Labware, Assisted Reproduction), MTX (Microscope and Microscope Accessories, Reproduction, Assisted) |
| Regulatory Class | II |

## 4. Predicate devices

EmbryoScope time-lapse incubator (K133712) manufactured by Unisense FertiliTech A/S and EmbryoSlide culture dish (K150961) manufactured by Vitrolife A/S. These predicate devices have not been subject to any design related recalls.

## 5. Device Description

EmbryoScope+ consists of the following devices: EmbryoScope+ incubator, EmbryoSlide+ culture dish, EmbryoViewer software, and ES Server software.

The EmbryoScope+ incubator is a bench top embryo incubator with a time-lapse imaging function. It provides temperature control, gas control, and time-lapse microscopy at multiple focal planes. This device can hold up to 15 culture dishes (EmbryoSlide+ culture dish) in the incubation chamber. The culture dishes are placed on the dish holder in the EmbryoScope+ incubator. The holder provides direct heat transfer to the EmbryoSlide+ culture dish. The built-in microscope consists of an LED illumination unit and an inverted microscope/camera unit. During image acquisition, each culture dish located on the culture dish holder is rotated to the microscopy system and individual image stacks are acquired from all individual embryos in each culture dish.

The EmbryoSlide+ culture dish is a radiation-sterilized polystyrene culture dish containing two separate reservoirs. Each reservoir has eight culture wells, and each well is used to culture one embryo. Therefore, a total of 16 embryos can be cultured on one dish. Each dish includes four special wells that are only used for rinsing and handling the embryos either before or after incubation. An adhesive barcode label printed from the EmbryoViewer software is used to mark each dish. The barcode label contains two different 2D data matrices that provide information on the patient (name, patient ID, treatment ID, and insemination time). The EmbryoSlide+ culture dish has a sterility assurance level of $10^{-6}$ and a shelf-life of four years. This device is subject to mouse embryo assay (MEA) and endotoxin testing before lot release.

The EmbryoViewer software is used for displaying, comparing, storing, and transferring images generated by the EmbryoScope+ incubator. The data that can be viewed using this software includes embryo images, incubation details, alarms, log files and other instrument parameters. This software also includes a user annotation function for capturing information on embryo development parameters as well as a user-defined modeling function, which allows the user to combine annotated information on embryo development parameters to aid in embryo selection. The EmbryoViewer software neither controls any hardware components in the EmbryoScope+ incubator nor performs any diagnostics.

The ES Server software allows users to update and view common data. The server acts as the central unit, which stores data and controls the data flow to and from the connected devices. The server can be connected to multiple EmbryoScope+ incubators and computers with the EmbryoViewer software installed.

**6. Indications for Use**

EmbryoScope+ consists of the following devices with the following indications for use:

The EmbryoScope+ incubator provides an environment with controlled temperature and gas concentrations (CO2 and O2) for the development of embryos at or near body temperature. Use of the EmbryoScope+ incubator is limited to five days (120 hr) covering the time from post insemination to day five of development.

The EmbryoSlide+ culture dish is intended for preparing, storing, and transferring human embryos. The EmbryoSlide+ culture dish must be used together with the EmbryoScope+ incubator.

The EmbryoViewer software is intended for displaying, comparing, storing, and transferring images generated by the EmbryoScope+ incubator. This software includes a user annotation function for capturing information on embryo development parameters as well as a user-defined modeling function, which allows the user to combine annotated information on embryo development parameters to aid in embryo selection. The EmbryoViewer software does not control any hardware components in the EmbryoScope+ incubator.

The ES Server software is intended to store, archive and transfer data. In addition, this software includes functions for managing models and performing calculations based on image data and embryo development parameters.

The EmbryoScope+ incubator, EmbryoViewer software, and ES Server software must be used together to export embryo images from the EmbryoScope+ incubator. The EmbryoViewer software and ES Server software must be used together to analyze the embryo images.

**7. Comparison of Intended Use and Technological Characteristics of the Subject and Predicate Devices**

<u>Intended Use</u>

| Devices | Subject device (K173264) | Predicate device (K133712) | Predicate device (K150961) |
|---|---|---|---|
| Indications for Use | EmbryoScope+ consists of the following devices with the following indications for use:<br><br>The EmbryoScope+ incubator provides an environment with controlled temperature and gas concentrations ($CO_2$ and $O_2$) for the development of embryos at or near body temperature. Use of the EmbryoScope+ incubator is limited to five days (120 hr) covering the time from post insemination to day five of development.<br><br>The EmbryoSlide+ culture dish is intended for preparing, storing, and transferring human | The EmbryoScope (Version D) provides an environment with controlled temperature, $CO_2$ (and other gases) for the development of embryos. This model has an integrated inverted microscope and imaging system for embryo viewing. Device use is limited to five days (120 hr) covering the time from post-fertilization to day 5 of development.<br><br>The EmbryoViewer software is an optional accessory software | The EmbryoSlide culture dish is intended for preparing, storing, and transferring human embryos. It is intended to be used only with the EmbryoScope device. |

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|---|---|---|---|
| | embryos. The EmbryoSlide+ culture dish must be used together with the EmbryoScope+ incubator.<br><br>The EmbryoViewer software is intended for displaying, comparing, storing, and transferring images generated by the EmbryoScope+ incubator. This software includes a user annotation function for capturing information on embryo development parameters as well as a user-defined modeling function, which allows the user to combine annotated information on embryo development parameters to aid in embryo selection. The EmbryoViewer software does not control any hardware components in the EmbryoScope+ incubator.<br><br>The ES Server software is intended to store, archive and transfer data. In addition, this software includes functions for managing models and performing calculations based on image data and embryo development parameters.<br><br>The EmbryoScope+ incubator, EmbryoViewer software, and ES Server software must be used together to export embryo images from the EmbryoScope+ incubator. The EmbryoViewer software and ES Server software must be used together to analyze the embryo images. | package for use in displaying, comparing, storing, and transferring images generated by the EmbryoScope time-lapse incubator (Version D). The software includes a user annotation function for capturing information on embryo development parameters as well as a user-defined modeling function, which allows the user to combine annotated information on embryo development parameters to aid in embryo selection. The EmbryoViewer software does not control any hardware components in the EmbryoScope time-lapse incubator (Version D). | |
| **Substantial equivalence discussion:**<br><br>Both subject and predicate devices are intended for culturing and monitoring embryos, handling embryo data, annotating embryos, and analyzing embryo parameters to aid in embryo selection using user-defined modeling function. Therefore, the subject and predicate devices have the same intended uses. | | | |

Technological Characteristics

| **EmbryoScope+ incubator, EmbryoViewer software, and ES Server software** | | |
|---|---|---|
| Devices | Subject device (K173264) | Predicate device (K133712) |
| **EmbryoScope+ incubator** | | |
| Culture dish capacity | 15 dishes | 6 dishes |
| Heating mechanism | Same as the predicate | Direct heat transfer |
| Temperature range | 36-39°C | 30-45°C |
| Temperature accuracy | +/- 0.2°C | +/- 0.1°C |
| $CO_2$ accuracy | +/- 0.3 % | +/- 0.2 % |
| $O_2$ accuracy | +/- 0.5 % | +/- 0.3 % |
| Recirculation rate | >100 L/h (full purification of gas volume every 6 min) | >60 L/h (full purification of gas volume every 20 min) |
| Recovery times when the load door is closed after a 30-second load door opening | $CO_2$ (5% ± 0.3 %) <5 min<br>$O_2$ (5% ± 0.5 %) <3 min | $CO_2$ (5% ± 0.3 %) <5 min<br>$O_2$ (5% ± 0.5 %) <15 min |
| Control of temperature and gas | Same as the predicate | Firmware |
| Computer | Same as the predicate | Integrated |
| Microscope | Same as the predicate | Inverted microscope |
| Type of camera | Monochrome CMOS | Monochrome CCD |
| Magnification | 16× | 20× |
| Focusing | Same as the predicate | Fully automated dish detection and embryo focusing |
| Numerical aperture | 0.5 | 0.4 |
| Number of pixels | 2048 × 1088 pixels | 1280 × 1024 pixels |
| Number of pixels in stored images | 800 × 800 pixels | 500 × 500 pixels |
| Resolution | Same as the predicate | 3 pixels per µm |

| | | |
|---|---|---|
| Maximum number of images | 7920 | 5040 |
| Light source (for imaging) | Low-power red LED 627 nm | Low-power red LED 635 nm |
| Illumination per image | <0.02 seconds | < 0.1 seconds |
| Total light exposure/embryo/day | <40 seconds | <50 seconds |
| Total light dose during a 5-day (120 hours) incubation ($J/m^2$) | 65.2 | 67.2 |
| Time-lapse system | Time-lapse imaging (Hoffman Modulation Contrast Objective). 10 Min cycle time for 11 focal planes for up to 5 days | Time-lapse imaging (Hoffman Modulation contrast objective). 10 min cycle time for a maximum of 7 focal planes. 2 min cycle time for a maximum of 1 focal plane for up to 5 days |
| **EmbryoViewer software/ES Server software** | | |
| Image display | Same as the predicate | High-resolution time-lapse images of single embryos |
| Data handling | Same as the predicate | Export, storage and transfer of embryo data |
| Embryo annotation and data analysis | Same as the predicate | • Embryo annotation tools which assist the user in selecting embryos<br>• Model designer<br>• Model management<br>• Data analysis using user-defined modeling function |
| Incubation condition monitoring | Same as the predicate | Inspection of incubation details, such as temperature and gas conditions |

**Substantial equivalence discussion:**

*EmbryoScope+ incubator*

The subject incubator is an updated version of the predicate device. The new device has the same fundamental design and comparable design specifications. The subject device has a narrower temperature range, and slightly decreased temperature, $CO_2$, and $O_2$ control accuracies. Regarding gas flow rate and recovery rate, the subject device has the same or improved performance specifications. The subject device has increased embryo culture capacity.

The subject and predicate devices have similar microscopy systems; however, the subject device has improved image quality specifications. Also, they use comparable light sources and the subject device allows for reduced light exposure. Therefore, the image quality and photobiological safety of the subject and predicate devices are technologically comparable.

The differences between the subject and predicate devices do not raise different questions of safety and effectiveness.

*EmbryoViewer software*

The subject EmbryoViewer software represents an updated version of the predicate device and maintains most functions of the predicate device. The subject device is different from the predicate device in that it cannot export data from the incubator and perform data calculations. However, these functions are possessed by ES Server software that must work together with the EmbryoViewer software. Thus, the difference does not raise different questions of safety and effectiveness.

*ES Server software*

Unlike the predicate device, the subject device replaces some functions of the EmbryoViewer software, such as data handling and calculations. However, all functions of the predicate EmbryoViewer software remain when the subject EmbryoViewer software and ES Server software work together. The ES Server software also has new functions, including model management, remote access and wireless connection. However, these new functions do not raise different questions of safety and effectiveness and are seen in medical device software.

| **EmbryoSlide+ culture dish** | | |
|---|---|---|
| Device | Subject device (K173264) | Predicate device (K150961) |
| General design | Same as the predicate | Optically clear culture dish with a lid |
| Culture wells on the dish | 16 wells for individual embryo incubation | 12 wells for individual embryo incubation |
| Rinsing wells in the dish | 4 wells | 2 wells |
| Material | Same as the predicate | Polystyrene PS K158 |
| **Substantial equivalence discussion:** | | |

| |
|---|
| Both subject and predicate devices are customized embryo culture dishes. They have the same fundamental design and are manufactured with the same material. There is a difference in the number of culture wells and rinsing wells; however, these differences do not raise different questions of safety and effectiveness. |

**8. Summary of Non-Clinical Performance Testing**

The following studies have been conducted on the EmbryoScope+ incubator, EmbryoViewer software, and ES Server software to support substantial equivalence to the predicate device:

- Electrical safety testing per IEC 60601-1:2005 (Third Edition) + C1:2006 + C2:2007 + A1:2012 (IEC 60601-1:2012 reprint)
- Electromagnetic compatibility testing per EN/IEC 60601-1-2:2007
- Software verification and validation testing that met the requirements of the FDA Guidance Document, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" issued on May 11, 2005
- Bench performance tests that met design specifications described in Section 7, as follows:
    * Gas maintenance testing to ensure that gas levels, flow rates, and gas recovery rates in chambers meet design specifications
    * Temperature control testing to ensure that culture chamber temperature conditions were within defined ranges and stable over time
    * Time-lapse testing to demonstrate that all design specifications of time-lapse function (image acquisition, quality, and resolution) are met
    * Light intensity testing to determine the maximum light dose embryos will be exposed to during device use, which was shown to be lower than the predicate device.

The following studies have been conducted on the EmbryoSlide+ culture dish to support substantial equivalence to the predicate device:

- Radiation sterilization validation testing per ISO 11137-2:2013
- Transportation simulation testing that met the requirements of ASTM D4169-16
- Package integrity testing after accelerated aging:
    * Bubble test per ASTM F2096-11
    * Peel strength testing ASTM F88/F88M-09
- Endotoxin testing per USP <85> and ANSI/AAMI ST72:2002. The testing demonstrated that the device met the specification of ≤20 EU/device.
- Mouse embryo assay (MEA) before and after accelerated aging:

  One-cell mouse embryos were exposed to subject devices and cultured at 37°C in an atmosphere containing 5% $CO_2$. The percent of embryos developed to the expanded blastocyst stage within 96 hours were assessed in comparison with the control group. The testing demonstrated that the device met acceptance criterion of "1-cell MEA ⩾80% embryos developed to blastocyst in 96 hours."

In addition, the cleaning and disinfection information provided in cleared K133712 was leveraged in the current submission to support substantial equivalence to the predicate device.

**9. Conclusion**

The subject and predicate devices have the same intended use and fundamental technological characteristics. The differences in technological characteristics between subject and predicate devices do not raise different questions of safety and effectiveness. The performance data demonstrate that the subject devices are substantially equivalent to the predicate devices.