August 29, 2018

Shenzhen Vitavitro Bio-tech Co., Ltd
% Field Fu
Consultant
Shenzhen Joyantech Consulting Co., Ltd
NO. 55 Shizhou middle road, Nanshan District
Shenzhen, Guangdong 518000
CHINA

Re: K180073
Trade/Device Name: VitaVitro Vitrification Kit, VitaVitro Warming Kit, and VitaVitro Straw Set
Regulation Number: 21 CFR§ 884.6180
Regulation Name: Reproductive Media and Supplements
Regulatory Class: II
Product Code: MQL, MQK
Dated: July 26, 2018
Received: August 2, 2018

Dear Field Fu:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; 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 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,

Sharon M. Andrews -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)*
K180073

Device Name
VitaVitro Vitrification Kit,VitaVitro Warming Kit, and VitaVitro Straw Set

Indications for Use *(Describe)*
VitaVitro Vitrification Kit is intended for the vitrification of human blastocysts for assisted reproduction technologies (ART). This kit is designed for use with VitaVitro Warming Kit.

VitaVitro Warming Kit is intended for the warming of human blastocysts that have undergone vitrification using VitaVitro Vitrification Kit for ART procedures.

VitaVitro Straw Set is a cryopreservation storage device that is intended for use in vitrification procedures to contain and maintain human blastocyst stage embryos.

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.

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510(k) Summary
K180073

1. Contact Details

1.1 Applicant information

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Date Prepared	August 25, 2018

1.2 Submission Correspondent

Correspondent Name	Shenzhen Joyantech Consulting Co., Ltd
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Contact person	Field Fu; Christy Young; Jessie You;
Contact e-mail	christy@cefda.com; jessie@cefda.com;field@cefda.com

2. Device information

Trade name	VitaVitro Vitrification Kit, VitaVitro Warming Kit, and VitaVitro Straw Set
Common name	Vitrification Cryopreservation Media and storage devices
Regulation Name	Reproductive media and supplements
Regulation Number	884.6180
Product Codes	MQL (Media, Reproductive) and MQK (Labware, Assisted Reproduction)
Device Class	II

3. Legally Marketed Predicate Device

Trade Name	Cryotop® Vitrification Kit and Cryotop® Thawing Kit
510(k) Number	K160864
Manufacturer	KITAZATO BioPharma Co., Ltd.

The predicate device has not been subject to a design-related recall.

4. Device Description

VitaVitro Vitrification and Warming Kits, and the VitaVitro Straw Set are used for vitrification, storage, and warming of blastocysts as part of human assisted reproduction technology (ART) procedures.

The VitaVitro Vitrification Kit includes three media components, Human Holding Medium (HHM), Human Vitrification Solution 1 (HV1) and Human Vitrification Solution 2 (HV2). All three media have the same base formulation, but HV1 and HV2 contain the cryoprotectants ethylene glycol and dimethyl sulfoxide in increasing concentrations. HV2 also includes sucrose as a non-permeating cryoprotectant. During the vitrification process, blastocysts are first equilibrated in HHM, and then exposed sequentially to HV1 and HV2. Using this methodology, the permeating cryoprotectants replace water in the blastocyst prior to vitrification and storage in liquid nitrogen. The VitaVitro Vitrification Kit includes single 1.0 ml vials of HHM, HV1, and HV2.

The VitaVitro Warming Kit includes three media used stepwise for warming and removing cryoprotectants from vitrified blastocysts. The VitaVitro Warming Kit includes Human Warming Solution 1 (HW1), Human Warming Solution 2 (HW2) and HHM. These media products are the same with the exception that HW1 and HW2 also include sucrose in decreasing concentrations to aid in the rehydration of the blastocysts. The VitaVitro Warming Kit includes two 1.5 ml vials of HW1, one 1.0 ml vial of HW2, and one 1.8 ml vial of HHM.

The VitaVitro Straw Set consists of two components, a straw that holds the blastocysts, and a container that is used to protect the straw. Both components are made from copolyester. The closed end of the container also includes a weight to aid in maintaining the orientation of the device in liquid nitrogen and prevent floating. During use, the container is pre-cooled by placing the closed end in liquid nitrogen with the open end extending above the level of the liquid nitrogen. Straw loading is done by placing the narrow tip of the straw in a 1 µl drop of vitrification media, which draws the media and blastocysts into the storage device. The straw component is then inserted into the pre-cooled container component to effect vitrification. The container component is then sealed to prevent contact between the samples and liquid nitrogen.

All of the products are provided sterile with a six-month shelf-life. The media in the vitrification and warming kits undergo aseptic filtration, while the storage devices are ethylene oxide sterilized.

5. Indications for Use

VitaVitro Vitrification Kit is intended for the vitrification of human blastocysts for assisted reproduction technologies (ART). This kit is designed for use with VitaVitro Warming Kit.

VitaVitro Warming Kit is intended for the warming of human blastocysts that have undergone vitrification using VitaVitro Vitrification Kit for ART procedures.

VitaVitro Straw Set is a cryopreservation storage device that is intended for use in vitrification procedures to contain and maintain human blastocyst stage embryos.

6. Substantial Equivalence Comparison

The following table compares the VitaVitro Vitrification Kit, VitaVitro Warming Kit, and VitaVitro Straw Set to the predicate device:

Table 1 – Comparison of Characteristics

	Subject Device K180073 – VitaVitro Vitrification Kit, VitaVitro Warming Kit, and VitaVitro Straw Set	**Predicate Device K160864 – Kitazato Cryotop Vitrification Kit and Cryotop Thawing Kit**	**Comparison**
Indications for Use	VitaVitro Vitrification Kit is intended for the vitrification of human blastocysts for assisted reproduction technologies (ART). This kit is designed for use with VitaVitro Warming Kit. VitaVitro Warming Kit is intended for the warming of human blastocysts that have undergone vitrification using VitaVitro Vitrification Kit for ART procedures. VitaVitro Straw Set is a cryopreservation storage device that is intended for use in vitrification procedures to contain and maintain human blastocyst stage embryos.	The Cryotop® Vitrification Kit – Vitrification is indicated for use in the preparation, vitrification and storage of pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos. The Cryotop® Thawing Kit – Thawing is indicated for use in the preparation and thawing of vitrified pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.	Different: The subject and predicate devices indications are not identical. All components of the subject device are only for vitrification, storage and warming of blastocyst stage embryos, while the predicate can be used with pronuclear to blastocyst stage embryos. The subject device also includes a standalone indication for the VitaVitro Straw Set, which is sold separately from the media kits, which is different than the predicate where storage devices are included within the vitrification kit. These differences do not impact the overall intended uses of these devices, which are the same (vitrification, storage, and thawing of embryos).
Components	Vitrification Media Thawing Media	Vitrification Media Thawing Media	Different: Predicate device includes plates as a

	Cryopreservation storage device	Cryotop Repro Plate 35 mm dish	convenience to users that would typically be obtained separately. The storage device for the subject device is provided separately as compared to the predicate. These differences do not raise different questions of safety and effectiveness (S&E).
Media Components			
Vitrification Formulation	Medium 199, Ethylene Glycol (7.5 – 16%), DMSO (7.5 – 16%), Sucrose (0.68 M), HSA	Medium 199, Ethylene Glycol, DMSO, Trehalose, Hydroxypropyl Cellulose (specific concentrations in predicate media not known)	Different: The predicate and subject device formulas include many similar components. However, the predicate uses trehalose instead of sucrose and hydroxypropyl cellulose instead of serum. However, the use of a different sugar/serum replacer do not raise different questions of S&E. In addition, the concentrations of specific components in the predicate media are not known; however, differences would not raise different questions of S&E.
Thawing Formulation	Medium 199, Sucrose (0.5 – 1 M), HSA	Medium 199, Trehalose, Hydroxypropyl Cellulose	Different: The predicate and subject device formulas include many similar components. However, the predicate utilizes trehalose instead of sucrose and hydroxypropyl cellulose instead of serum (see rationale above). In addition, the concentrations of specific components in the predicate media are not known; however, differences would not raise different questions of S&E.
Endotoxin	< 0.25 EU/mL	Same	Same
MEA	2-Cell MEA: ≥ 80%	1-Cell MEA: ≥ 80%	Different: Testing using a 1-cell

	blastocysts 72h	blastocysts 96 h	or 2-cell method does not raise different S&E questions.
pH	7.2 – 7.6	Same	Same
Osmolarity	HHM: 295-315 HV1: N/A HV2: N/A HW1: 600-850 (diluted 1:1) HW2: 850-1000	ES: 2,300 – 2,800 VS: 4,900 – 6,000 TS: 1,600 – 2,000 DS: 830 - 1020 WS: 240 - 300	Different: The osmolality specifications are different between the subject and predicate devices. Differences in osmolality do not raise different questions of S&E.
Sterilization method	Aseptic filtration	Same	Same
Storage Devices			
Material composition	Copolyester	Cryotop US, Cryotop SC, or Cryotop CL provided in kits Cryotop devices composed of PET, ABS, and Polypropylene	Different: The materials in the subject and predicate device are different. These differences do not raise different questions of S&E.
Sealing mechanism	Heat sealed	Cryotop US - The shaft handle contains a taper and stop. When inserted into the straw, a hermetically sealed closed system is formed. Cryotop SC and CL– the sample holding stick is heat sealed within an outer straw.	Different: The subject device has a comparable design/closure system to that used in the Cryotop SC and CL devices, but is different than the Cryotop US. This difference does not raise different S&E questions.
Cooling Rate	5,127 °C/min	3000°C/min for all versions	Different: The subject device has a higher cooling rate than the predicate. A higher cooling rate does not raise different questions of S&E.
Warming	17,899 °C/min	44000°C/min for all	Different: The subject device

rate		versions	has a lower warming rate than the predicate. A lower warming rate does not raise different questions of S&E. Note: the warming rate for the subject device is in line with other cleared devices of this type.
Open/closed system	Closed	Closed	Same
Sterilization method	EO	Radiation	Different: The subject and predicate device use different sterilization methods that are both common for medical devices. This difference does not raise different questions of S&E.
MEA	2-Cell MEA: ≥ 80% blastocysts 72 h	1-Cell MEA: ≥ 80% blastocysts 96 h	Different: Testing using a 1-cell or 2-cell method does not raise different S&E questions.
Endotoxin	< 0.5 EU/device	Same	Same

As shown in the table above, the intended uses of the subject and predicate devices are the same. In addition, the table shows many similarities between the subject and predicate devices; however, there are also differences (e.g., formulation, specifications, etc.). The differences noted between the subject and predicate device do not raise different questions of safety and effectiveness for the reasons stated in the table.

7. Non-clinical Performance Testing

VitaVitro Vitrification Kit and VitaVitro Warming Kit

- pH: 7.2-7.6 for all solutions
- Osmolality: see Table 1 for acceptance specifications
- Endotoxin (USP<85>): <0.25 EU/mL
- Mouse Embryo Assay (MEA):
  Two-cell mouse embryos were exposed sequentially to subject devices in the Vitrification and Warming Kits followed by culture at 37°C in an atmosphere containing 5% CO2. The percent of embryos developed to the expanded blastocyst stage at 72 hours were assessed in comparison with the control group. The acceptance specification was ≥80% development to blastocyst at 72h.
- Aseptic processing and validation testing that met the requirements of ISO 13408-1:2008 and ISO 13408-2:2003.
- Sterility Testing (USP<71>)
- Shelf-life testing to ensure that product specifications for pH, osmolality, MEA, endotoxin,

and sterility, were met over the six-month shelf-life period.

VitaVitro Straw Set

- Cooling Rate Testing: Cooling rate of 5,127℃/min
- Warming Rate Testing: Warming rate of 17,899℃/min
- Endotoxin (USP<85>): <0.5 EU/device
- Mouse Embryo Assay (MEA):
  Two-cell mouse embryos were exposed to test article extracts (media incubated with the test article for 30 min at 37°C) followed by culture at 37°C in an atmosphere containing 5% CO2. The percent of embryos developed to the expanded blastocyst stage at 72 hours were assessed in comparison with the control group. The acceptance specification was ≥80% development to blastocyst at 72h.
- Sealed Device Durability: No burst/breakage after 30 second immersion in liquid nitrogen
- Simulated distribution testing per ASTM D4169-16
- Package integrity testing per ASTM F1929:2012 (dye penetration) and ASTM F88:2009 (seal strength) to support sterile barrier maintenance over the shelf-life of the device.
- Shelf-life testing to ensure that product specifications for endotoxin, MEA, cooling/warming rate, and sealed device durability were met over the six-month shelf-life period.

8. Conclusion

The results of the performance testing described above demonstrates that the VitaVitro Vitrification Kit, VitaVitro Warming Kit, and VitaVitro Straw Set are as safe and effective as the predicate device and supports a determination of substantial equivalence.