



Food and Drug Administration  
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October 7, 2016

KITAZATO BioPharma Co., Ltd.  
% Richard Vincins, CBA, CQA, RAC (US,EU)  
Vice President, QA/RA  
Emergo Global Consulting, LLC  
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Re: K160864  
Trade/Device Name: Cryotop® Vitrification Kit and Cryotop® Thawing Kit  
Regulation Number: 21 CFR§ 884.6180  
Regulation Name: Reproductive Media and Supplements  
Regulatory Class: II  
Product Code: MQL, MQK  
Dated: September 2, 2016  
Received: September 7, 2016

Dear Richard Vincins:

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.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. 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.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

**Joyce M. Whang -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

## Indications for Use

510(k) Number (if known)

K160864

Device Name

Cryotop® Vitrification Kit and Cryotop® Thawing Kit

Indications for Use (Describe)

The Cryotop® Vitrification Kit 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 is indicated for use in the preparation and thawing of vitrified pronuclear (PN) zygotes through day 3 cleavage stage embryos and 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

## Cryotop Vitrification and Thawing Kit

### K160864

#### 1. Submission Sponsor

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#### 3. Date Prepared

6 October 2016

#### 4. Device Identification

Trade/Proprietary Name: Cryotop® Vitrification Kit  
Cryotop® Thawing Kit

Common/Usual Name: Vitrification Cryopreservation Media

Classification Name: Reproductive Media and Supplements

Regulation Number: 884.6180

Product Code: MQL, Media, Reproductive  
MQK, Labware, Assisted Reproduction

Device Class: Class II

Classification Panel: Obstetrics/Gynecology

#### 5. Legally Marketed Predicate Device(s)

K093273, Vit Kit® - Vitrification Freeze Kit/ Vitrification Thaw Kit, Irvine Scientific Sales Co., Inc.

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

#### 6. Device Description

The Cryotop® Vitrification and Thawing Kits are composed of a set of five media to vitrify and warm pronuclear (PN) through blastocyst stage embryos for Assisted Reproductive Technologies (ART) procedures.

The Cryotop® Vitrification Kit includes two media components, Equilibration Solution (ES) and Vitrification Solution (VS), containing the cryoprotectants ethylene glycol and dimethyl sulfoxide. During the vitrification process, embryos are first exposed to ES and then in VS. Using this methodology, the permeating cryoprotectants can replace water in the PN through blastocyst stage embryos prior to vitrification and storage in liquid nitrogen. The Cryotop® Vitrification Kit comes pre-packaged with one 1.5 ml vial of ES, two 1.5 ml vials of VS, 4 Cryotop devices (Cryotop CL, Cryotop SC, or Cryotop US), and two Repro Plates.

The Cryotop® Thawing Kit is composed of three media used stepwise for thawing and removing cryoprotectants from vitrified PN through blastocyst stage embryos. The Cryotop® Thawing Kit is composed of TS (Thawing Solution), DS (Dilution Solution) and WS (Wash Solution). The Cryotop Thawing Kit comes pre-packaged with two 4.0 ml vials of thawing solution, one 4.0 ml vial of dilution solution, one 4.0 ml vial of washing solution, one Repro Plate, and two 35 mm dishes.

All of the media in the Cryotop® Vitrification Kit and Cryotop® Thawing Kit contain Gentamicin. The media in these kits undergo aseptic filtration, while storage devices and plates are sterilized by radiation. The specifications for the Cryotop Vitrification and Thawing Kits are listed in Table 1 below.

**7. Indication for Use Statement**

The Cryotop® Vitrification Kit 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 is indicated for use in the preparation and thawing of vitrified pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.

**8. Substantial Equivalence Discussion**

The following table compares the Cryotop® Vitrification and Thawing Kits to the predicate device with respect to indications for use, principles of operation, technological characteristics, materials, and performance testing. The comparison of the devices provides more detailed information regarding the basis for the determination of substantial equivalence. Based on the information below, the proposed and predicate device have comparable intended uses, and differences in technology noted do not raise different questions of safety or effectiveness as compared to the predicate.

**Table 1 – Comparison of Characteristics**

<b>Manufacturer</b>	<b>Kitazato BioPharma Co, Ltd.</b>	<b>Irvine Scientific Sales Co., Inc.</b>	<b>Significant Differences</b>
<b>Trade Name</b>	<b>Cryotop® Vitrification and Thawing Kits</b>	<b>Vit Kit® - Vitrification Freeze Kit and Vitrification Thaw Kit</b>	
<b>510(k) Number</b>	K160864	K093273	N/A
<b>Product Code</b>	MQL, MQK	MQL	Similar
<b>Regulation Number</b>	884.6180	884.6180	Same
<b>Regulation Name</b>	Reproductive Media and Supplements	Reproductive Media and Supplements	Same
<b>Indications for Use</b>	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	Vit Kit® - Freeze, Vitrification Freeze Kit for Embryos (PN through Blastocyst Stage) is intended for use in the vitrification of pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage	Similar indications – same intended use

Manufacturer	Kitazato BioPharma Co, Ltd.	Irvine Scientific Sales Co., Inc.	Significant Differences
Trade Name	<b>Cryotop® Vitrification and Thawing Kits</b>	<b>Vit Kit® - Vitrification Freeze Kit and Vitrification Thaw Kit</b>	
	<p>blastocyst stage embryos.</p> <p>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.</p>	<p>embryos.</p> <p>Vit Kit® - Thaw, Vitrification Thaw Kit for Embryos (PN through Blastocyst Stage) is intended for use in the thawing of pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.</p>	
Components of Kit	<p>Vitrification Media</p> <p>Thawing Media</p> <p>Cryotop</p> <p>35 mm dish</p> <p>Repro Plate</p>	<p>Freeze Kit</p> <p>Vitrification Thaw Kit</p>	<p>Different. During a standard procedure, users would obtain these components separately to complete the procedure. These accessories have been included in this kit as a convenience to complete the procedure. Inclusion of these components does not represent a different question of safety and effectiveness.</p>
Embryo Stage	PN through Blastocyst	PN through Blastocyst	Same
Principal of Operation	Provides users with the ability to cryopreserve supernumerary embryos created during the in vitro fertilization	Provides users with the ability to cryopreserve supernumerary embryos created during the in vitro fertilization	Same

Manufacturer	Kitazato BioPharma Co, Ltd.	Irvine Scientific Sales Co., Inc.	Significant Differences
Trade Name	Cryotop® Vitrification and Thawing Kits	Vit Kit® - Vitrification Freeze Kit and Vitrification Thaw Kit	
	procedure and then to re-warm them for use at a future point in time	procedure and then to re-warm them for use at a future point in time	
Vitrification Formulation	Medium 199 (HEPES buffered Medium)	Medium 199 (HEPES buffered Medium)	Similar; the subject device utilizes trehalose instead of sucrose and HPC instead of DSS in the formulation. However, differences in these components do not raise different questions of safety and effectiveness (e.g., material safety, embryotoxicity, post-thaw survival, etc.).
	Ethylene glycol	Ethylene glycol	
	DMSO	DMSO	
	Trehalose	Sucrose	
	Hydroxypropyl Cellulose (HPC)	Dextran Serum Supplement (DSS)	
	Gentamicin	Gentamicin	
Vitrification Steps	2 Step	2 Step	Same
Vitrification Media Component	Equilibration Solution (ES) 1.5mL x 1 Vial	Equilibration Solution (ES) 1.0mL x 1 Vial	Similar
	Vitrification Solution (VS) 1.5mL x 2 Vials	Vitrification Solution (VS) 1.0mL x 2 Vials	
Thawing Formulation	Medium 199 (HEPES buffered Medium)	Medium 199 (HEPES buffered Medium)	Similar; the subject device utilizes trehalose instead of sucrose and HPC instead of DSS in the formulation. However, differences in these components do not raise different questions of safety and effectiveness
	Hydroxypropyl Cellulose (HPC) (v/v)	Dextran Serum Supplement (DSS) (v/v)	
	Gentamicin	Gentamicin	
	Trehalose	Sucrose	

<b>Manufacturer</b>	<b>Kitazato BioPharma Co, Ltd.</b>	<b>Irvine Scientific Sales Co., Inc.</b>	<b>Significant Differences</b>
<b>Trade Name</b>	<b>Cryotop® Vitrification and Thawing Kits</b>	<b>Vit Kit® - Vitrification Freeze Kit and Vitrification Thaw Kit</b>	
			(e.g., material safety, embryotoxicity, post-thaw survival, etc.).
<b>Thawing Steps</b>	3 Step	3 Step	Same
<b>Thawing Media Component</b>	Thawing Solution (TS) 4.0mL x 2 Vials	Thawing Solution (TS) 1.0mL x 4 Vials	Similar
	Diluent Solution (DS) 4.0mL x 1 Vial	Diluent Solution (DS) 1.0mL x 1 Vial	
	Washing Solution (WS) 4.0mL x 1 Vial	Washing Solution (WS) 2.0mL x 1 Vial	
<b>Carton Packaging</b>	Each solution is contained in plastic vials. Vials are packed in a card board outer box with partition.	Each solution is contained in plastic vials. Vials are packed in a card board outer box with partition.	Same
<b>Cryopreservation Storage Device Used With</b>	Kitazato BioPharma, Cryotop®CL– K112695 Cryotop®SC – K140072 Cryotop®US – K153027	None are provided with the kit	Different. During a standard procedure, users would obtain cleared storage devices separately to complete the procedure. Storage devices have been included in this kit as a convenience to complete the procedure. Inclusion of storage devices does not represent a different question of safety and effectiveness.
<b>Sterile</b>	Solutions sterilized using aseptic processing	Solutions sterilized using aseptic processing	Same

Manufacturer	Kitazato BioPharma Co, Ltd.	Irvine Scientific Sales Co., Inc.	Significant Differences
Trade Name	Cryotop® Vitrification and Thawing Kits	Vit Kit® - Vitrification Freeze Kit and Vitrification Thaw Kit	
	techniques through filtration.  Vials, vitrification storage device, 35 mm dish, and Repro Plate are sterilized via radiation.	techniques through filtration.  Vial containers are sterilized via radiation.	
Endotoxin	Passes	Passes	Same
Mouse Embryo Assay	>80% blastocyst at 96 hours (one-cell MEA)	>80% blastocyst at 96 hours (one-cell MEA)	Same
Sterility Testing	Passes	Passes	Same
pH Test	7.20 – 7.60	Not available	n/a
Osmolarity	ES: 2,300 – 2,800  VS: 4,900 – 6,000  TS: 1,600 – 2,000  DS: 830 - 1020  WS: 240 - 300	Not available	n/a
Storage	2 – 8°C	2 – 8°C	Same
Shelf Life	6 months	1 year	Different; the subject device has a shorter shelf life period. The shorter shelf-life does not raise different questions of safety or effectiveness.

**9. Non-Clinical Performance Data**

The Cryotop® Vitrification Kit, Cryotop® Thawing Kit, Repro Plate, and 35 mm dish passed all applicable testing in accordance with internal requirements and applicable standards that are shown below to support substantial equivalence of the subject device:

- Cleanliness and appearance: Free of turbidity and sedimentation
- pH Testing: Average pH reading is from 7.2 – 7.6 passing
- Endotoxin Testing: Endotoxin values conform to the value <0.25 EU/mL
- Osmolality Testing: Passes specification for each solution
- Sterility Testing: No microbial growth from sterility testing
- Mouse Embryo Assay: ≥80% of 1-cell control embryos develop at 96 hours
- Package integrity testing

## 10. Clinical Performance Data

The clinical information presented provides published papers that specifically identify the use of the Cryotop® and Vitrification/Thawing media with HPC as the vitrification method used for the cryopreservation of embryos and blastocysts from female subjects. A summary of the results are shown below:

- Literature 1: results of the study shows clinical pregnancies of 42% from total transfer number and live births of 30% from total transfer number<sup>1</sup>
- Literature 2: results of the study shows clinical pregnancies of 59% from number of cycles and ongoing pregnancies of 48% from number of cycles<sup>2</sup>
- Literature 3: results of the study shows clinical pregnancies of 49% from number of cycles and ongoing pregnancies of 46% from number of cycles<sup>3</sup>

The birth rates of vitrified embryo/blastocyst transfer as compared to fresh embryo/blastocyst transfer described in the literature are comparable. Each of the studies reported survival rates of embryos that are consistent with normal ART procedures using similar IVF treatments and cryopreservation techniques.

## 11. Statement of Substantial Equivalence

The results of the performance testing described above demonstrates that the Cryotop® Vitrification Kit and Cryotop® Thawing Kit are as safe and effective as the predicate device and supports a determination of substantial equivalence.

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<sup>1</sup> Kato, K. Takehara, Y. Tomoya, S., Kawachiya, S. Okuno, T. Kobayashi, T. Bodri, D. Kato, O. "Minimal ovarian stimulation combined with elective single embryo transfer policy: age-specific results of a large, single-center, Japanese cohort." *Reproductive Biology and Endocrinology* 2012, 10:35

<sup>2</sup> Ku, P. Lee, R.K. Lin, S. Lin, M. Hwu, Y. "Comparison of the clinical outcomes between fresh blastocyst and vitrified-thawed blastocyst transfer." *J Assist Reprod Genet* 2012. 29:1353-56

<sup>3</sup> Inoue, F., Yelian, F.. "Efficiency of a Closed Vitrification System with Oocytes and Blastocysts." *Low Temperature Medicine* 2014. 40/3:53-59