March 2, 2018

CooperSurgical, Inc
% Tove Kjær
Director Corporate Regulatory Affairs
ORIGIO a/s
Knardrupvej 2
DK-2760 Målov
Denmark

Re: K173731
Trade/Device Name: SAGE Vitrification Kit (ART-8025 and ART-8026)
SAGE Vitrification Warming Kit (ART-8030 and ART-8031)
Regulation Number: 21 CFR 884.6180
Regulation Name: Reproductive Media and Supplements
Regulatory Class: Class II
Product Code: MQL
Dated: November 23, 2017
Received: December 6, 2017

Dear Tove Kjær:

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,

Benjamin R. Fisher -S

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)*
K173731

Device Name
SAGE Vitrification Kit (ART-8025 and ART-8026)
SAGE Vitrification Warming Kit (ART-8030 and ART-8031)

Indications for Use *(Describe)*
SAGE Vitrification Kit is intended for use in the vitrification of oocytes (MII), pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.

SAGE Vitrification Warming Kit is intended for use in the thawing of vitrified oocytes (MII), 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
K173731

I. Submitter information

Submitted on behalf of: Mr. James Keller
Vice President, Regulatory Affairs and Quality Assurance
CooperSurgical, Inc.
95 Corporate Drive
Trumbull, CT 06611
USA
e-mail: James.Keller@coopersurgical.com
Phone: +1 (203) – 601 - 5200

Contact person: Ms. Tove Kjær
Director Corporate Regulatory Affairs
ORIGIO a/s
Knardrupvej 2
DK-2760 Måløv
Denmark
e-mail: tkjaer@origio.com
Phone: +45 4679 0220

II. Date prepared

March 2, 2018

III. Device Information:

Device name: SAGE Vitrification Kit (ART-8025 and ART-8026)
SAGE Vitrification Warming Kit (ART-8030 and ART-8031)

Common name: Vitrification Kit and Vitrification Warming Kit

Classification name: Reproductive media and supplements
Classification Number: 21 CFR 884.6180
Product Code: MQL (Media, Reproductive)
Regulatory Class: II

IV. Predicate device:

Vit Kit - Freeze (Vitrification Freeze Kit)
Vit Kit - Thaw (Vitrification Thaw Kit)
K160006

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

V. Indication for use

SAGE Vitrification Kit is intended for use in the vitrification of oocytes (MII), pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.

SAGE Vitrification Warming Kit is intended for use in the thawing of vitrified oocytes (MII), pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.

VI. Device Description:

SAGE Vitrification Kit (ART-8025 and ART-8026):

This kit includes two solutions (Equilibration Solution and Vitrification Solution). Both solutions in the kit consist of a MOPS-buffered media containing non-essential and essential amino acids, gentamicin sulfate, and human serum albumin. These solutions also contain the cryoprotectants ethylene glycol, dimethyl sulfoxide (DMSO) and sucrose as described below:

Equilibration Solution (ES): 7.5% (v/v) each of DMSO and ethylene glycol.
Vitrification Solution (VS): 15% (v/v) each of DMSO and ethylene glycol, and 0.6 M sucrose

SAGE Vitrification Warming Kit (ART-8030 and ART 8031):

This kit includes three solutions (1.0M Sucrose Warming Solution [1.0 M WS], 0.5M Sucrose Warming Solution [0.5 M WS], and MOPS Solution [MS]). All solutions in the kit consist of a MOPS-buffered media containing non-essential and essential amino acids, gentamicin sulfate, and human serum albumin. These solutions contain the cryoprotectant sucrose at the level described in their names (i.e., 1.0M, 0.5M, or no sucrose).

Solutions in the SAGE Vitrification Kit and SAGE Vitrification Warming Kit are aseptically-filtered and are provided to users in either 5 ml Type 1 borosilicate glass vials with a rubber closure and an aluminum seal (ART-8025 and ART-8030) or 2 ml polypropylene vials with cap (ART-8026 and ART-8031). The solutions in ART-8025 and ART-8030 are single-use only devices, whereas solution in ART-8026 and ART-8031 are to be used within 7 days after opening.

VII. Comparison of Intended Use and Technological Characteristics of Subject and Predicate Devices

	Subject device		**Predicate device (K160006)**		**Comparison**
Parameter	**SAGE Vitrification Kit ART8025/ ART8026**	**SAGE Vitrification Warming Kit ART8030/ ART8031**	**Vit-Kit Freeze**	**Vit-Kit Thaw**	**N/A**
Indication for Use	SAGE Vitrification Kit is intended for use in the vitrification of oocytes (MII), pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.	SAGE Vitrification Warming Kit is intended for use in the thawing of oocytes (MII), pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.	Vit Kit-Freeze (Vitrification Freeze Kit) is intended for use in the vitrification of oocytes (MII), pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.	Vit Kit- Thaw (Vitrification Thaw Kit) is intended for use in the thawing of oocytes (MII), pronuclear (PN) zygotes through day 3 cleavage stage embryos and blastocyst stage embryos.	Same
Product and performance specification					
pH	7.20-7.40	7.20-7.40	7.05-7.54	7.05-7.44	**Different –** The pH range is larger for the

	Subject device		Predicate device (K160006)		Comparison
Parameter	**SAGE Vitrification Kit ART8025/ ART8026**	**SAGE Vitrification Warming Kit ART8030/ ART8031**	**Vit-Kit Freeze**	**Vit-Kit Thaw**	**N/A**
					predicate devices than the subject devices. Differences in pH do not raise different Safety and effectiveness (S&E) questions.
Osmolality (mOsm/kg)	ES: 2331-2849 VS: 5603-6849	1.0M WS 1255-1535 0.5 M WS 745-911 MS: 257-273	ES: 1005-1445 VS: 1100-1588	TS: 1732-1912 DS: 857-910 WS: 268-292	**Different –** Osmolality is higher in the subject vitrification kit solutions as compared to the predicate, while the warming solutions of the subject and predicate devices are similar. Differences in osmolality do not raise different S&E questions.
Endotoxin (EU/mL)	<0.5	<0.5	≤0.6	≤0.6	Similar
MEA 1-cell (% blastocysts at 96h)	≥80%	≥80%	≥80%	≥80%	Same
Sterilization	Aseptic Filtration	Aseptic Filtration	Aseptic Filtration	Aseptic Filtration	Same
Components					
Cryoprotectants	Ethylene glycol DMSO Sucrose	Sucrose	Ethylene glycol DMSO Sucrose	Sucrose	Same
Amino Acids	Yes		Yes		Same
Antibiotics	Gentamicin	Gentamicin	Gentamicin	Gentamicin	Same
Protein	Human Serum Albumin	Human Serum Albumin	Dextran Serum Supplement	Dextran Serum Supplement	**Different –** Serum used in the subject and

	Subject device		Predicate device (K160006)		Comparison
Parameter	**SAGE Vitrification Kit ART8025/ ART8026**	**SAGE Vitrification Warming Kit ART8030/ ART8031**	**Vit-Kit Freeze**	**Vit-Kit Thaw**	**N/A**
					predicate media are not the same. Differences in serum do not raise different questions of S&E.
Base medium	Modified Human Tubal Fluid (MOPS-Buffered)	Modified Human Tubal Fluid (MOPS-Buffered)	Medium 199 (HEPES-Buffered)	Medium 199 (HEPES-Buffered)	**Different –** The base media of the subject and predicate media are not the same. Differences in base media do not raise different questions of S&E.

As noted in the table above, the subject and predicate devices have the same intended use and are technologically comparable. Differences in technological characteristics noted above do not raise different questions of safety or effectiveness.

VIII. Summary of Non-Clinical Performance Testing

The following studies have been performed to support substantial equivalence to the predicate devices:

- pH (USP<791>)– 7.2-7.4
- Osmolality (USP<785>)
    - ES: 2331-2849
    - VS: 5603-6849
    - 1.0 M WS: 1255-1535
    - 0.5 M WS: 745-911
    - MS: 257-273

- Endotoxin testing (USP<85>) - <0.5 EU/ml
- Mouse Embryo Assay (MEA) – 1-Cell MEA: ≥80% blastocysts at 96h
- Aseptic process validation testing meeting the requirements of EN ISO 13408-1:2015 and EN ISO 13408-2:2011.
- Sterility testing (USP<71>) – No microbial growth
- Shelf-life testing - ART-8025 and ART-8030 relied on testing provided in K073522 supporting a 52-week shelf-life as the media and media packaging remained unchanged. Real-time shelf-life testing was conducted on ART-8026 and ART-8031 to ensure that the following product specifications were met at time zero and at the end of shelf-life (52 weeks) in closed vials and in vials that were opened and underwent simulated use procedures over the seven days prior to testing:
    - pH

- o Osmolality
- o Endotoxin
- o MEA
- o Sterility

IX. Clinical Performance Data

Published journal articles assessing vitrification and warming media that were identical or similar to the subject devices were provided to support extension of the current indication for vitrifying and warming blastocyst stage embryos to also include vitrification and warming of human MII oocytes, pronuclear (PN) zygotes, and day 3 cleavage-stage embryos. In addition, literature was also provided to support use of the subject media for vitrification and warming of collapsed blastocysts in support of methods included in device labeling. The results included in these studies demonstrated that the subject media was capable of vitrifying and warming the oocytes and embryos as shown by their rates of survival, fertilization, and pregnancy/live birth rates. A summary of the supporting journal articles is shown below:

Oocytes

- Literature 1: Reports results after oocyte vitrification/warming using SAGE™ Vitrification Kit and SAGE™ Vitrification Warming Kit. This study included 11 subjects who had their surplus MII oocytes vitrified. Post-warming results showed a survival rate of 94.1%, fertilization rate of 67.0%, and a clinical pregnancy rate of 36.4%.

- Literature 2: Reports results after oocyte vitrification/warming using SAGE™ Vitrification Kit and SAGE™ Vitrification Warming Kit. The study included six subjects with tubal factor infertility where surplus MII oocytes were vitrified. Post-warming results showed a survival rate of 75.0%, fertilization rate of 77.7%, and a 33.3% clinical pregnancy rate.

- Literature 3: The performance of SAGE™ Vitrification Kit and SAGE™ Vitrification Warming Kit for vitrification and warming of oocytes was shown to be in-line with general results reported after transfer of frozen/thawed oocytes showing a pregnancy rate of 33.6%.

- Literature 4: The control arm in this study used media and vitrification/warming procedures determined to be comparable to the subject devices. Results for subjects in the control arm of this study that assessed outcomes following vitrification and warming of 2353 MII oocytes showed an oocyte survival rate of 92.1%, clinical pregnancy rate per embryo transfer of 56.4%, and a live birth rate per cycle of 45.3%.

- Literature 5: This study used media and vitrification procedures determined to be comparable to the subject devices. Clinical oocyte vitrification and warming using a closed vitrification device (54 study subjects and 413 MII oocytes) resulted in a survival rate of 90.5%, fertilization rate of 64.2%, and a clinical pregnancy rate of 40.9%.

Pronuclear (PN) Zygotes

- Literature 6: This study assessed the effectiveness of two vitrification and warming media systems. The primary media was determined to be comparable to the subject devices, while the second media assessed was a commercially available media (RapidVit-Cleave) that included different cryoprotectants than the subject devices. Post-warming in the primary media group including 37 subjects and 74 embryos showed a survival rate of 98.6%, with 97% of surviving embryos reaching the cleavage stage. The clinical pregnancy rate was 21.6%. The clinical pregnancy rate for the primary media system was comparable to that observed for the commercially-available comparator media (23.1%).

- Literature 7: This study used media and vitrification procedures determined to be comparable to the subject devices. A total of 849 pronuclear-stage (PN) zygotes were vitrified during the study period. During this period, 103 cycles of cryopreserved embryo transfer were completed. In total, 339 PN zygotes were thawed resulting in an 89.0% survival rate. The clinical pregnancy rate obtained was 28.2%, resulting in 9 live birth events (18 infants) with 15 ongoing pregnancies.

Cleavage –Stage Embryos

- Literature 8: Reported prospective outcomes following vitrification and warming of cleavage stage embryos using the SAGE™ Vitrification Kit and SAGE™ Vitrification Warming Kit. The study included 24 warming cycles after fresh cycle cancellation due to risk of Ovarian Hyperstimulation Syndrome (OHSS). Results showed a post-warming survival rate of 97.1%, a clinical pregnancy rate of 41.6% and an implantation rate of 18.0%.

Vitrification of Collapsed Blastocysts

- Literature 9: Reports data after vitrification/warming of collapsed blastocysts generated from lower grade cleavage-stage embryos using the SAGE™ Vitrification Kit and SAGE™ Vitrification Warming Kit. Results from the control group (102 warming cycles) in this randomized controlled trial where blastocyst collapse was performed without additional zonal thinning showed a post-warming survival rate of 98.0% and a clinical pregnancy rate of 35.3%.

X. Conclusion

The results of the performance information summarized above demonstrated that the subject devices are as safe and effective as the predicate devices and supports substantial equivalence.

XI. References

1. Pregnancies and deliveries after injection of vitrified-warded oocytes with cryopreserved testicular sperm. (Selman et al, (2010) Fertility and Sterility Vol. 94(7):2927-2929).
2. Ongoing pregnancies after vitrification of human oocytes using a combined solution of ethylene glycol and dimethyl sulfoxide. (Selman et al. (2006) Fertility and Sterility 86(4):997-1000).
3. Assisted reproductive technology in Europe, 2011: results generated from European registers by ESHRE. (Kupka et al (2016) Human Reproduction 31(2): 233-248).
4. A combination of hydroxypropyl cellulose and trehalose as supplementation for vitrification of human oocytes: a retrospective cohort study. (Coello et al (2016) Journal of Assisted Reproduction Genetics 33(3): 413-421).
5. Closed vitrification of human oocytes and blastocysts: outcomes from a series of clinical cases. (Gook et al, (2016) J Assist Reprod Genet 33: 1247-1252).
6. Comparison of two different media for vitrification and rewarming of human zygotes: Prospective randomized study. (Alcolak et al, (2011) Middle East Fertility Society Journal 16:189-193).
7. Three years of routine vitrification of human zygotes: is it still fair to advocate slow-rate freezing? (Al-Hasani et al, (2016) Reproductive BioMedicine Online 14(3):288-293).
8. Vitrification is a highly efficient method to cryopreserve human embryos in *in-vitro* fertilization patients at high risk of developing ovarian hyperstimulation syndrome (Selman et al, (2009) Fertility and Sterility 91(4):1611-1613).
9. Laser-assisted hatching improves clinical outcomes of vitrified-warmed blastocysts developed from low-grade cleavage-stage embryos: a prospective randomized study. (Wan et al, (2014) Reproductive BioMedicine Online 28:582-589).