October 23, 2018

Kitazato Corporation
℅ Audrey Swearingen
Manager, Regulatory Affairs
Emergo Global Consulting, LLC
2500 Bee Cave Road
Building 1, Suite 300
Austin, TX 78746

Re: K182002
Trade/Device Name: Cumulus Remover
Regulation Number: 21 CFR 884.6180
Regulation Name: Reproductive media and supplements
Regulatory Class: Class II
Product Code: MQL
Dated: July 25, 2018
Received: July 26, 2018

Dear Audrey Swearingen:

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,

Michael T. Bailey -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
510(k) Number (if known)
K182002

Device Name
Cumulus Remover

Indications for Use (Describe)
Cumulus Remover is for the removal of the cumulus complex and corona radiata surrounding the oocyte in preparation for ICSI.

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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“An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number.”
510(k) Summary
Cumulus Remover
K182002

1. Submission Sponsor

Kitazato Corporation
81 Fuji
Shizuoka 416-0907
JAPAN
Phone number: +(81) 545-66-2202
Contact: Mr. Futoshi Inoue
Title: President

2. Submission Correspondent

Emergo Global Consulting, LLC
2500 Bee Cave Road
Building 1, Suite 300
Austin, TX 78746
Office Phone: (512) 327-9997
Contact: Audrey Swearingen, RAC
Title: Director, Regulatory Affairs

3. Date Prepared

October 23, 2018

4. Device Identification

Trade name: Cumulus Remover
Common name: Hyaluronidase Solution
Regulation name: Reproductive Media and Supplements
Regulation number: 21 CFR 884.6180
Product code: MQL (Media, Reproductive)
Regulatory class: II

5. Predicate Device

ICSI Cumulase (K081639) manufactured by MediCult a/s. This predicate device is now branded by Origio a/s and has not been subject to any design related recalls.
6. Device Description

Cumulus Remover is an enzyme solution containing recombinant human hyaluronidase that digests hyaluronic acid that binds the cumulus and corona cells surrounding oocytes together. This function of hyaluronidase can be used for denuding cumulus and coronal cells from oocytes prior to performing Intracytoplasmic Sperm Injection (ICSI) fertilization procedures. Cumulus Remover is provided in a polypropylene vial (package size 0.5 mL), and five vials are packaged together in a box. This product is aseptically processed and has a shelf-life of six months when stored at 2-8°C. Cumulus Remover is tested for pH, osmolality, endotoxin, sterility, embryotoxicity, and hyaluronidase activity before lot release.

7. Indication for Use

Cumulus Remover is for the removal of the cumulus complex and corona radiata surrounding the oocyte in preparation for ICSI.

8. Substantial Equivalence Discussion

<table>
<thead>
<tr>
<th>Device</th>
<th>K182002 (subject device)</th>
<th>K081639 (predicate device)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications for Use</td>
<td>Cumulus Remover is for the removal of the cumulus complex and corona radiata surrounding the oocyte in preparation for ICSI.</td>
<td>ICSI Cumulase is for the removal of cumulus complex and corona radiata surrounding the oocyte in preparation for ICSI.</td>
</tr>
<tr>
<td>pH</td>
<td>7.2-7.6</td>
<td>Information is not available</td>
</tr>
<tr>
<td>Osmolality</td>
<td>270-295 mOsm</td>
<td>Information is not available</td>
</tr>
<tr>
<td>Hyaluronidase activity</td>
<td>70-90 units/ml (average 80 units/ml)</td>
<td>40-120 units/ml (average 80 units/ml)</td>
</tr>
<tr>
<td>Formulation</td>
<td>Physiological salts</td>
<td>Physiological salts</td>
</tr>
<tr>
<td></td>
<td>Energy substance</td>
<td>Energy substance</td>
</tr>
<tr>
<td></td>
<td>Buffering substance (HEPES)</td>
<td>Buffering substance (HEPES)</td>
</tr>
<tr>
<td></td>
<td>Recombinant human hyaluronidase</td>
<td>Recombinant human hyaluronidase</td>
</tr>
<tr>
<td></td>
<td>Human albumin</td>
<td>Human albumin</td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
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<tr>
<td></td>
<td>Dextran</td>
<td></td>
</tr>
</tbody>
</table>

The subject and predicate devices have the same indications for use/intended use; however, there are differences in technological characteristics. Although the subject and predicate devices possess different ranges of hyaluronidase activity, the activity range of the subject device falls within the activity range of the predicate and both devices have the same average hyaluronidase activity (80 units/ml). Regarding formulation, the subject and predicate devices have the same or comparable salts, energy substance, and buffering agents. The subject device is different from the predicate device in that it contains gentamicin and dextran. These differences in formulation do not raise different questions of safety and effectiveness. In addition, the pH and osmolality values for the predicate device are not known; however, differences in pH and osmolality are common in assisted reproduction media products and do not raise different questions of safety and effectiveness. Also, the subject device pH and osmolality ranges are comparable to other assisted reproduction media products.

9. Summary of Non-Clinical Performance Testing

The following studies have been performed to support substantial equivalence to the predicate devices:
• pH testing per USP <791> - See table above
• Osmolality per USP <785> - See table above
• Aseptic Processing Validation per ISO 13408-1:2015 and ISO 13408-2:2003
• Sterility testing per USP <71> - No microbial growth
• Endotoxin testing per USP <85> - <0.25 EU/ml
• Mouse embryo assay (MEA)
  One-cell mouse embryos were exposed to subject devices and cultured at 37°C in an atmosphere containing 5% CO₂. The percent of embryos developed to the expanded blastocyst stage within 96 hours were assessed in comparison with the control group. The acceptance specification is that ≥80% of embryos expand to the blastocyst stage by 96h.
• Hyaluronidase activity – 70-90 units/ml (per Japanese Pharmacopoeia, JP17)
• Shelf-life testing was conducted to ensure that the following product specifications are met at time zero and end of shelf-life (six months).
  * pH
  * Osmolality
  * 1-cell MEA
  * Endotoxin
  * Sterility
  * Hyaluronidase activity

10. Conclusion

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