DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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January 23, 2017

Research Instruments Ltd.
Wendy Hassan
Regulatory Affairs Executive
Bickland Industrial Park
Falmouth, Cornwall TR11 4TA
United Kingdom

Re: K161275
Trade/Device Name: EZ-Tip Singles, EZ-Tip Vial of 20, EZ-Grip
Regulation Number: 21 CFR 884.6130
Regulation Name: Assisted reproduction microtools
Regulatory Class: Class II
Product Code: MQH
Dated: December 14, 2016
Received: December 19, 2016

Dear Wendy Hassan,

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,

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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K161275

Device Name
EZ-Tip Vial of 20
EZ-Tip Singles
EZ-Grip

Indications for Use *(Describe)*
EZ-Tip pipettes are for denudation, i.e. removing the cumulus from an oocyte prior to Intracytoplasmic Sperm Injection (ICSI) and In Vitro Fertilization (IVF) and for handling gametes, embryos and biopsied cells (polar bodies, blastomeres and trophectoderm) during assisted reproductive techniques (ART). EZ-Tips are not intended for biopsy of cells from oocytes or embryos.

The EZ-Grip provides aspiration and expulsion capabilities to plastic pipettes when fitted during assisted reproduction procedures.

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

Date prepared
January 16, 2017

Submitter's information

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Device Names

Trade Name:	EZ-Tip Vial of 20, EZ-Tip Singles, EZ-Grip
Common name:	IVF micropipette and micropipetter
Classification Number:	884.6130
Classification Name:	Assisted Reproduction Microtools
Product Code:	MQH (Microtools, Assisted Reproduction)
Classification Panel:	Obstetrics/Gynecology
Regulatory Class:	II

Predicate Device

Trade Name:	The Stripper micropipet and micropipeter tips
Common name:	IVF micropipet and micropipeter
Manufacturer:	Mid-Atlantic Diagnostics, Inc
Classification Name:	Microtools, Assisted Reproduction (21CFR 884.6130, 85 MQH)
510(K)	K993699

The Stripper micopipet and micropipeter tips have not been subject to a design-related recall.

Device Description
The EZ-Tip pipette is an extruded medical grade polycarbonate capillary that is pulled at one end to form a tapered tip. It has an outer diameter (OD) of 0.9 mm at the proximal end and fits to an actuating device such as the EZ-Grip. All tips are approximately 90 mm in length and depending on the size of the tip they have a volumetric capacity of 15.9 - 25.4 µl.

Pipette Tips are supplied in a range of inner diameter (ID) sizes at the distal end as shown below:

- Size 75 µm, 200 µm, 250 µm, 290 µm, 600 µm are suitable for specimen handling
- Sizes 125 µm, 135 µm, 145 µm, 155 µm, 170 µm are suitable for denudation

The EZ-Tip is supplied sterile in one of two packaging options; individually blister packed or pouch packed in a vial containing 20 tips. All pipettes are intended single use and disposable.

The EZ-Grip is a hand held, reusable actuator or pipeter for plastic pipettes. It consists of a machined aluminium barrel containing stainless steel and PTFE internal working mechanisms, a titanium plunger wire and medical grade silicone and nylon seals. The plunger mechanism is designed to be compatible with 0.9 mm OD plastic pipettes and it has an aspiration volume range of 0.2 µl to 3 µl with a blow-out volume of 1.4 µl above the adjusted aspiration volume setting.

The EZ-Grip is supplied non-sterile with validated protocols for cleaning and sterilization included in the Instructions for Use.

Indications for Use
EZ-Tip pipettes are for denudation, i.e. removing the cumulus from an oocyte prior to Intracytoplasmic Sperm Injection (ICSI) and In Vitro Fertilization (IVF) and for handling gametes, embryos and biopsied cells (polar bodies, blastomeres and trophectoderm) during assisted reproductive techniques (ART). EZ-Tips are not intended for biopsy of cells from oocytes or embryos.

The EZ-Grip provides aspiration and expulsion capabilities to plastic pipettes when fitted during assisted reproduction procedures.

Comparison to Predicate Indication for Use
The Stripper tips indications for use is as follows:
- The Stripper micropipette family's indication for use is to manipulate and transfer zygotes and embryos during IVF and ICSI procedures.
- The Stripper micropipets are used in the tissue culture techniques performed by embryologists when preparing oocytes for IVF, ICSI and assisted hatching techniques prior to implantation.
- The Stripper micropipets are tools used in procedures that have been developed to aid infertile couples achieve pregnancy
- Removes cumulus and corona cells from oocytes for confirmation of fertility during IVF.
- Removes cumulus and corona cells from oocytes prior to ICSI procedures
- Used to transfer embryos and oocytes through various media and solutions during IVF procedures

Although differences in indications exist, the overall intended use is the same i.e. both subject and predicate devices are used to remove the cumulus and corona cells from oocytes and to manipulate or handle human reproductive cells through various media and solutions during ART procedures.

The EZ-Grip is used in the same manner as intended by the Stripper predicate device i.e. to provide aspiration and expulsion capabilities to pipettes when fitted during assisted reproduction procedures.

Technological Assessment

Table 1: Comparison of the EZ-Tip and the Stripper micropipette.

Feature	***EZ-Tip*** K161275	***Stripper Tips*** K993699	**Comparison**
Geometry and dimensions	Proximal OD 0.9 mm Distal ID size range - 75µm to 600 µm Length 90 mm	Information unknown	Different: The specific dimensions of tips cleared in K993699 is not known; however, differences in tip dimensions do not raise different safety and effectiveness questions (e.g., tip size appropriate to handle reproductive cells of interest).
Materials used	Polycarbonate	Polycarbonate	Same
Manufacture	Extruded plastic capillary Cut to provide different ID dimensions Sealed in packaging to retain sterile barrier	Extruded plastic capillary Cut to provide different ID dimensions Sealed in packaging to retain sterile barrier	Same
Sterility	Sterile (SAL 10^{-6}) gamma irradiated	Sterile (SAL 10^{-6}) gamma irradiated	Same
Use	Single Use	Single Use	Same
Mouse Embryo Assay (MEA)	1-Cell MEA: ≥80% hatched blastocysts at 120 h.	1-Cell MEA: ≥ 70%, to blastocyst at 96 h	Different: The Mouse Embryo Assay (MEA) specification is lower in the predicate device; however this does not raise different S & E questions.
Endotoxin (LAL)	< 20 EU/device	<0.03 EU/ml	Different: The Endotoxin (LAL) specification for the predicate device is different; however this does not raise different S & E questions.

As noted in the table above, the subject and predicate tips are similar in that they are both polycarbonate tips with similar designs and are provided sterile and single-use only. The differences identified do not raise different questions of safety and effectiveness as discussed in Table 1 above.

Table 2: Comparison of the EZ-Grip with the Stripper device.

Feature	***EZ-Grip*** K161275	***The Stripper*** K993699	**Comparison**
Usage	Reusable – supplied not sterile	Reusable – supplied not sterile	Same
Handling	Hand-held device with thumb operated plunger	Hand-held device with thumb operated plunger	Same
OD of the plastic pipette tip	0.9 mm	Unknown	Different: The specific OD dimension of tips cleared in K993699 is not known; however, differences in OD do not raise different questions of S & E (e.g. ability to hold pipettes used for aspiration and expulsion procedures).
Material - of barrel	Machined aluminium	Aluminium	Same
Material - of plunger wire	Titanium	Stainless steel	Different: The material of the plunger wire in the predicate device is different however this does not raise different S & E questions.
Maintenance	Seals and plunger wire	Seals and plunger wire	Same
Aspiration Volume	Maximum adjustable aspiration volume up to 3 µl with 1.4 µl blow out capacity above the maximum aspiration volume	Unknown	Different: The blow out capacity of the predicate device is different however this does not raise different S & E questions.

In summary, the similarities between the EZ-Grip and the predicate Stripper are that both are hand held devices with thumb operated plungers that are used to aspirate and expel fluids in support of assisted reproduction laboratory procedures. Both devices are provided non-sterile, are reusable, and require periodic maintenance to replace the seals and plunger wire components. The differences identified do not raise different questions of safety and effectiveness as discussed in Table 2 above.

Non-Clinical Assessment of the EZ-Tip

- **Mouse Embryo Assay (MEA) Testing -** One-cell MEA testing was performed on three lots of EZ-Tip, demonstrating that devices met the acceptance specification of ≥80% hatched blastocysts at 120 h. Test articles passed all MEA testing conducted. MEA testing is performed on each lot of EZ-Tip.
- **Endotoxin Testing -** Bacterial Endotoxin (Limulus Amoebocyte Lysate) Assay testing (FDA recognized consensus standard USP<85> "Bacterial Endotoxins Test" and ANSI/AAMI ST72:2011 "Bacterial endotoxins test methods, routine monitoring, and alternatives to batch testing") was performed on three lots of product demonstrating that devices met the acceptance specification of ≤20 EU/device. Endotoxin testing is performed on each lot of EZ-Tip.
- **Sterilization Validation -** The sterilization validation was performed in compliance with requirements in the applicable standards for gamma irradiation sterilization ISO11137-1:2006 "Sterilization of health care products. Radiation. Requirements for development, validation and routine control of a sterilization process for medical devices" and ISO11137-2:2012 "Sterilization of health care products - Radiation - Part 2: Establishing the sterilization dose".
- **Packaging Validation -** Package integrity validation studies were conducted per ISO11607-2:2006 "Packaging for terminally sterilized medical devices Part 2: Validation requirements for forming, sealing and assembly processes", ASTM F1886/F1886M - 09 "Standard Test Method for Seal Strength of Flexible Packaging by Visual Inspection", ASTM F1929-12 "Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration" and ASTM F1140-07 "Standard Test Methods for Internal Pressurization Failure Resistance of the Unrestrained Packages." These studies used accelerated aged samples conditioned in accordance with ASTMF1980:07(2011) "Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices".
- **Shelf-Life -** The proposed shelf-life of EZ-Tip Vial of 20 (three years) and Singles (five years) is supported by packaging and performance tests conducted on samples exposed to real-time and accelerated aging conditions pursuant to ASTMF1980:07(2011) "Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices". The parameters assessed before and after aging included endotoxin (LAL) and MEA testing.

Non-Clinical Assessment of the EZ-Grip

- **Mouse Embryo Assay (MEA) Testing -** One-cell MEA testing was performed on three lots of EZ-Grip plunger wires demonstrating that devices met the acceptance specification of ≥80% hatched blastocysts at 120 h. Test articles passed all MEA testing conducted. MEA testing is performed on each lot of EZ-Grip plunger wires.
- **Reprocessing Validation -** Reprocessing validation of the EZ-Grip was in accordance with the procedures outlined in the FDA guidance document titled "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling" issued on March 17, 2015.
- **Device Life -** Bench testing confirmed that the EZ-Grip performs according to the product specifications after routine maintenance and reprocessing during one year of simulated use consisting 16,000 actuations of the device set to aspirate 3 µl. Device evaluation consisted of measuring aspirated volume at each device setting, assessment of delivered volume and the force required to actuate the 3µl default setting and 1.4 µl blow-out function.

Conclusion

The intended use, technological characteristics and non-clinical test data supports a conclusion that the EZ-Tip and EZ-Grip devices are substantially equivalent to the predicate devices.