



May 30, 2018

Clinical Research Consultants, Inc.
Barbara Fant, Pharm.D.
President
3308 Jefferson Avenue, Upper Level
Cincinnati, OH 45220

Re: P170039
Trade/Device Name: CustomFlex™ Artificial Iris
Filed: December 1, 2017
Product Code: QBT

Dear Dr. Fant:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the CustomFlex™ Artificial Iris. This device is indicated for use in children and adults for the treatment of full or partial aniridia resulting from congenital aniridia, acquired defects, or other conditions associated with full or partial aniridia.

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 4 years. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of the PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR

814.84. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final UDI rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). For more information on these requirements, please see the UDI website, <http://www.fda.gov/udi>.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the PMA device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Two (2) copies of each report, identified as an "ODE Lead PMA Post-Approval Study Report" or "OSB Lead PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. ODE Lead PMA Post-Approval Study – Post-Approval Study of Adult and Pediatric Subjects Implanted with the CustomFlex™ Artificial Iris: The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. This study will be conducted as per the protocol outlined in our May 17, 2018 email. On May 17, 2018, you agreed to conduct a study as follows:

The study is a prospective, nonrandomized, multi-center, safety study in adults and pediatric subjects in which the postoperative outcomes are compared to its preoperative baseline. The study is designed to evaluate the long term safety (up to postoperative 3 years for adults and 5 years for pediatrics) of the CustomFlex™ Artificial Iris for the treatment of iris defects in adult and pediatric subjects. The study is limited to adult and pediatric subjects who participated in the 12-month AI-001 clinical trial and are implanted with the CustomFlex™ Artificial Iris for less than 36 months (adults) or less than 60 months (pediatrics). Up to 580 subjects (180 subjects of the PMA cohort, 250 subjects of the Continued Access, and 150 subjects of the Compassionate Use cohort) enrolled in one of four AI-001 study cohorts will be evaluated through 36 months for adults and 60 months for pediatrics for safety. Eligible subjects who are enrolled in the study will be followed postoperatively for 3 years for adults and 5 years for pediatrics, with the following frequency of assessments: postoperative at 12, 24, and 36 months for adults, and postoperative 3, 12, 24, 36, 48, 60 months for pediatrics.

The study will evaluate: secondary surgical interventions, implant position, device or surgery related complications, and device malfunction or defects. Specifically, the primary safety outcome is to evaluate

device related adverse events at postoperative 12 months (i.e., <5% experience a >2 lines best spectacle-corrected visual acuity (BSCVA) loss that is device related, and <5% experience BSCVA worse than 20/40, if preoperative BSCVA was 20/40 or better). The secondary safety outcome is to evaluate cumulative rate of lens (IOL) related adverse events at 12 months (i.e., anisometropia, glare/halos, diplopia, and IOL removal or replacement due to lens power calculation error <1%). Other study outcomes include: cumulative rate of surgery related adverse events, endothelial cell density (ECD) changes, device malfunction or defects, and device related complications.

2. OSB Lead PMA Post-Approval Study - Pediatric Artificial Iris New Enrollment PAS: The Office of Surveillance and Biometrics (OSB) will have the lead for the study initiated after device approval. This study will be conducted as per the protocol outlined in our May 17, 2018 email. On May 17, 2018, you agreed to conduct a study as follows:

You will conduct a prospective, single-arm, multi-center, new enrollment, safety study, in which the postoperative outcomes of the subjects are compared to their preoperative baselines. The study is designed to evaluate the long-term safety of the CustomFlex™ Artificial Iris in pediatric subjects for the treatment of full or partial aniridia resulting from congenital and acquired iris defects, including but not limited to traumatic iris defects, traumatic mydriasis, and post inflammatory iris sequelae. A total of 125 pediatric eyes are to be enrolled, where 77 eyes are from the new enrollment PAS and 48 eyes are from the AI-001 compassionate use study. The sample size is based on an 80% follow-up rate to ensure that there are 100 evaluable eyes at 5 years post-operative. The study sites will be the same sites as those in the AI-001 study with the possibility of the additional non-IDE sites. A minimum of 7 sites with pediatric subjects is required for the study. Eligible subjects will be followed for five years post implantation with the following frequency of assessments: preoperative, the operative day and postoperative at 3, 12, 24, 36, 48, 60 months.

The study will evaluate: secondary surgical interventions, implant position, device or surgery related complications, and device malfunction or defects. Specifically, the primary safety outcome is to evaluate device related adverse events at postoperative 12 months (i.e., <5% experience a >2 lines best spectacle-corrected visual acuity (BSCVA) loss that is device related, and <5% experience BSCVA worse than 20/40, if preoperative BSCVA was 20/40 or better). The secondary safety outcome is to evaluate cumulative rate of lens (IOL) related adverse events at 12 months (i.e., anisometropia, glare/halos, diplopia, and IOL removal or replacement due to lens power calculation error <1%). Other study outcomes include: cumulative rate of surgery related adverse events, endothelial cell density (ECD) changes, device malfunction or defects, and device related complications.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage <http://www.fda.gov/devicepostapproval>.

In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more

information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm>).

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies described above. Your PMA supplements should be clearly labeled as an "ODE Lead PMA Post-Approval Study Protocol" or "OSB Lead PMA Post-Approval Study Protocol" as noted above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Before making any change affecting the safety or effectiveness of the PMA device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm>.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52 for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> and on combination product postmarketing safety reporting is available at (see <https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at <http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm>.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve

your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at

<http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm>. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in 6 copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Simona Bancos, Ph.D., at 301-796-2243 or Simona.Bancos@fda.hhs.gov.

Sincerely,


Randall G. Brockman -S

for William H. Maisel, MD, MPH
Director, Office of Device Evaluation
Center for Devices and Radiological Health