DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

April 17, 2015

AcuFocus™, Inc.
% Ms. Jone Hsia
Director, RA
32 Discovery, Suite 200
Irvine, California 92618

Re: P120023
Trade/Device Name: KAMRA® inlay
Filed: February 1, 2013
Amended: February 15, 2013; January 13, February 18, 21, May 14, September 2 and 9, 2014
Product Code: LQE

Dear Ms. Hsia:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its evaluation of your premarket approval application (PMA) for the KAMRA® inlay. The KAMRA® inlay is indicated for intrastromal corneal implantation to improve near vision by extending the depth of focus in the non-dominant eye of phakic, presbyopic patients between the ages of 45 and 60 years old who have cycloplegic refractive spherical equivalent of +0.50 D to -0.75 D with less than or equal to 0.75 D of refractive cylinder, who do not require glasses or contact lenses for clear distance vision, and who require near correction of +1.00 D to +2.50 D of reading add. 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 this restriction on sale and distribution is 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 2 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 this 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" (please use this title even if the specified interval is more frequent than one year) 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. 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 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. You are asked to submit separate PAS Progress Reports every six months until the end of the second year and annually thereafter. Two (2) copies of each report, identified as an “ODE Lead IDE Post-Approval Study Report" and “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 – Continuation Study: The Office of Device Evaluation (ODE) will have the lead for clinical studies initiated prior to device approval. The Continuation Study is described as follows:

   The continuation study, conducted per protocol ACU-P012-020C approved under IDE G080184, is an ongoing prospective multi-center observational study designed to monitor the safety of patients who participated in the pivotal trial (ACU-P08-020/020A) and are still implanted with the KAMRA Inlay. Patients will be followed for an additional two years (a total of 5 years post implantation). Thirteen of the 15 US sites and 6 of the 9

OUS sites that participated in the pivotal trial are participating in the continuation study. Clinical evaluations are scheduled at 48 and 60 months post implantation. Eligible patients are those that completed the pivotal trial with the inlay still implanted at those sites participating in the continuation study and are considered enrolled in the study when the informed consent is signed. Both eyes of each patient are to be evaluated during the study.

The clinical parameters to be evaluated in this study are as follows:

- Specular Microscopy: all visits (implanted and fellow eyes)
- Slit lamp examination with fluorescein: all visits (implanted and fellow eyes)
- Fundus examination: all visits (implanted and fellow eye)
- Adverse Events and Complications: all visits
- Manifest refraction (mid-point, no auto-refraction): all visits (implanted and fellow eyes)
- Uncorrected distance visual acuity (ETDRS): all visits (implanted eyes, fellow eyes, and both eyes together [OU]) at a testing distance of 6m/20 ft
- Uncorrected near visual acuity: all visits (implanted eyes, fellow eyes, and OU) at a testing distance of 40 cm
- Distance-corrected distance visual acuity (ETDRS): all visits (implanted eyes, fellow eyes, and OU)
- Computerized corneal topography: all visits (implanted and fellow eyes)
- Dry eye assessment (tear break-up time and anesthetisized Schirmer's test): all visits (implanted and fellow eyes)
- Mesopic & Photopic Contrast Sensitivity: all visits (implanted eye and OU)

Patients will be examined and evaluated according to the following schedule of visits:

- Visit 1 Month 48 (46 to 52 months post-op)
- Visit 2 Month 60 (58 to 64 months post-op)

Each of the clinical parameters will be evaluated at each visit.

2. OSB Lead PMA Post-Approval Study – New Enrollment Study: The Office of Surveillance and Biometrics (OSB) will have the lead for clinical studies initiated after device approval. The New Enrollment Study is described as follows:

   The specific questions the study will address are: (1) What is the percentage of implanted eyes with uncorrected near visual acuity (UCNVA) of 20/40 or better through 5 years after implantation?; (2) What is the percentage of implanted eyes with a persistent loss of 2 lines or more in best-corrected distance visual acuity (BCDVA) through 5 years after implantation or 2 years after removal, whichever is longer?; and (3) What is the percentage of patient symptoms in the KAMRA patient population?

This study will include 529 participants, which allows for a 20% dropout rate resulting in 423 participants with 60-month data. All 529 participants will take both the preoperative and postoperative version of the modified questionnaire.

This study will be conducted in two phases:

Phase 1: Questionnaire Development. Before starting enrollment for Phase 2 of the PAS, you will develop a questionnaire for the New Enrollment PAS by refining your prior Patient Reported Outcome (PRO) questionnaire. You will conduct concept elicitation interviews to ensure measurement of relevant concepts, including Pulfrich's phenomenon, which is not addressed in the current version of the PRO questionnaire.

Cognitive debriefing interviews of the revised questionnaire should be performed with needed revisions being completed prior to starting the New Enrollment PAS. The qualitative evaluation of the PRO questionnaire, to be completed within six months of PMA approval, will consist of concept elicitation interviews and cognitive debriefing interviews. The cognitive debriefing interviews should be conducted with a minimum of 20 patients (a minimum of 5 patients per item). The process will continue with up to 50 patients recruited from up to 5 investigative sites (or until concept saturation has been reached). The qualitative assessment will evaluate (1) the clarity of the items within the instrument; (2) how the respondents interpret the item(s); (3) ease of completion of the PROs; (4) the comprehensiveness of the PROs; and (5) the appropriateness of the format, response scales, and recall period used in the PROs.

Results of the cognitive debriefing findings will be evaluated after 50% of patients in each item group have been interviewed. After this phase, modifications (if needed) will be made to the questionnaire with the remaining 50% of the sample being debriefed on the revised questionnaire or taking the prior version of the questionnaire if no revisions are recommended. The findings including the transcripts, saturation grid, and all revisions with the data supporting those revisions should be included as part of your PAS interim reports.

Phase 2: New Enrollment. This Phase will begin after results from Phase 1 are accepted by FDA. Phase 2 will be a multicenter, prospective, single-arm study consisting of presbyopic patients with emmetropia (defined as having +0.50 D to -0.75 D refractive error) in both eyes, enrolled from 20-30 study sites in the USA for unilateral implantation of the KAMRA inlay.

The quantitative questionnaire assessment, to be completed within nine months of initiating the Phase 2: New Enrollment study, will evaluate the psychometric properties of the revised questionnaire including evaluations of the:

1. preoperative questionnaire with a minimum of 100 patients composed of a balanced number of patients (approximately 15) in up to 12 clinical investigative sites, tested at baseline and screening (preoperative), to include and evaluation of the following: (a) Internal consistency reliability, (b)Test-retest reliability (in stable patients), (c)

Clinical validity, (d) Known groups validity (differences in scores between patient reported severity and between those with and without known eye co-morbidities), (e) Item Response Theory and/or Factor Analysis to understand the factor structure and determine if scores would be more appropriate; and

2. postoperative questionnaire at the 3-month visit with a repeat administration performed between 7-14 days after the first administration with a minimum of 100 patients to examine all the aforementioned characteristics.

The primary effectiveness endpoint is the percentage of eyes with monocular photopic UCNVA of 20/40 or better (measured at 40cm/16in) at 60 months after implant must be ≥75% of best-case eyes with successful KAMRA Inlay implantation.

The primary safety endpoint tests whether fewer than 5% of eyes have a persistent loss of two lines or more of BCDVA at 60 months after inlay implantation or 24 months after removal, whichever is longer, with a one-sided alpha level of 0.05, 80% power, and a minimum detectable difference of 2.5%. Persistent loss of BCDVA is defined as a loss of two lines or more of BCDVA present at the subject's last visit. The secondary safety endpoints will: (1) assess if less than 1% of eyes with preoperative best spectacle corrected distance visual acuity of 20/20 have BCDVA worse than 20/40 at 60 months and (2) assess whether ocular adverse events related to the device occur in no more than 10% of eyes and any single ocular adverse event related to the device should occur in no more than 2.5% of eyes.

Additional clinical outcomes include: change in distance-corrected near visual acuity (DCNVA), within participant change in UCNVA vs. uncorrected distance visual acuity (UCDVA), accommodative amplitude, stereoacuity (Randot Stereo test), refractive stability (Manifest refractive spherical equivalent – MRSE), change in topography over time, detailed ocular surface examination, assessment of dry eye syndrome, rate of corneal edema, retinal examination (dilated fundus exam; PI assessment of ease of examination), rate of adverse events, rate of device removals, information about cataract development and management, and visual symptoms (measured by PRO).

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. 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 a complete protocol of your post-approval study described above. Your PMA supplement should be clearly labeled as an "ODE Lead PMA Post-Approval Study Report" or "OSB Lead PMA Post-Approval Study Report" 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 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, 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

In accordance with the recall requirements specified in 21 CFR 806.10, 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 approved labeling in final printed form. Final printed 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 printed labeling is identical to the labeling approved in draft form. If the final printed 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
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10903 New Hampshire Avenue
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If you have any questions concerning this approval order, please contact Jennifer Brown at (301) 796-5626 or Jennifer.Brown@fda.hhs.gov.

Sincerely yours,

William H. Maisel -S

William H. Maisel, MD, MPH
Director (Acting)
Office of Device Evaluation
Deputy Center Director for Science
Center for Devices and Radiological Health