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

July 15, 2016

Abbott Medical Optics Inc.
Ms. Ophelia Biggs
Associate Director Regulatory Affairs
1700 E. St. Andrew Place
Santa Ana, CA 92705

Re: P980040/S065
TECNIS® Sym*f*ony Extended Range of Vision Intraocular Lens; Models ZXR00;
Toric Models, ZXT150, ZXT225, ZXT300, and ZXT375
Filed: January 19, 2016
Procode: POE

Dear Ms. Biggs:

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) supplement for the TECNIS® Sym*f*ony Extended Range of Vision Intraocular Lens. The TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00, is indicated for primary implantation for the visual correction of aphakia, in adult patients with less than 1 diopter of pre-existing corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. The Model ZXR00 IOL is intended for capsular bag placement only. The TECNIS® Symfony Toric Extended Range of Vision IOLs, Models ZXT150, ZXT225, ZXT300, and ZXT375, are indicated for primary implantation for the visual correction of aphakia and for reduction of residual refractive astigmatism in adult patients with greater than or equal to 1 diopter of preoperative corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. The Model Series ZXT IOLs are intended for capsular bag placement only. We are pleased to inform you that the PMA supplement is approved. You may begin commercial distribution of the device as modified 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 five 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" 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. 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. You will submit a final report within 3 months of the last subject visit. Two (2) copies of each report, identified as an "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.

OSB Lead PMA Post-Approval Study – TECNIS® Symfony Toric New-Enrollment Study: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. The TECNIS® Symfony Toric New-Enrollment Study is a study designed to evaluate the rate of visual symptoms and distortions experienced with the TECNIS® Symfony Toric

Intraocular Lenses (IOLs) with greater than 2.0 D of cylinder correction at the corneal plane (Models ZXT300 and ZXT375, "higher-cylinder group") in comparison to the rate of visual symptoms and distortions experienced with the TECNIS® Symfony Toric IOL with approximately 1.0 D of cylinder correction at the corneal plane (Model ZXT150, "lower-cylinder group"). The study is intended to ensure the safety of the approved devices and will be conducted in three phases.

Phase One:

Phase one of the study is comprised of the development of the *Patient Reported Visual Symptoms Questionnaire* (PRVSQ) and further development of the existing *Patient Reported Visual Distortions Questionnaire* (PRVDQ). Using an iterative process, the questionnaires will be modified and evaluated through patient interviews; final versions will undergo cognitive debriefing processes for further qualitative assessment.

Results of the development work for both questionnaires will be submitted to and must be accepted by the FDA prior to the initiation of Phase two.

Phase Two:

Phase two involves the quantitative assessment and validation of the aforementioned questionnaires. The design of the validation studies will be submitted to FDA for review and approval prior to initiation. If the PRVDQ is modified, the validation will involve the assessment of visual distortions with and without induced astigmatism (similar to the processes performed under P980040/S039 and P980040/S044). For the PRVSQ, quantitative evaluation will be performed using an existing population of multifocal and monofocal patients to assess the ability of the questionnaire to discriminate known differences between populations, as well as the repeatability of responses.

The results of this validation work will be submitted to the FDA for review and approval prior to the initiation of Phase three. Additionally, if determined to be necessary based on the results from phases one and two, a protocol revision for Phase three will also be submitted and must be approved by the FDA prior to Phase three initiation.

Phase Three:

Phase three, or the Post-Approval Study Phase, consists of a prospective, multicenter (up to 50 sites), bilateral, non-randomized, open-label comparative clinical study of TECNIS Symfony Toric patients in the higher-cylinder group (models ZXT300 and ZXT375) in comparison to patients in the lower-cylinder group (model ZXT150).

The primary endpoint is the rate of bothersome visual symptoms at six months postoperatively, defined as the percentage of patients that either have a 'severe' visual *distortion*:

- Lines that slant, tilt, split, or separate
- Flat surfaces appearing curved
- Objects appearing further away or closer than they actually are
- Objects appearing to have a different size or shape

- Physical discomfort related to vision

or a visual *symptom* that 'extremely bothered' them and impacted daily activity (determined by a 'yes' response to the question 'Is there anything you have a lot of difficulty with, or do not do, because of {the symptom}'):

- Halos
- Glare
- Starbursts

The study hypothesis associated with this endpoint is that the rate of bothersome visual symptoms for the higher-cylinder group will be less than eight percentage points above the rate of bothersome visual symptoms for the lower-cylinder group.

Results for bothersome visual symptoms will be evaluated using a non-inferiority approach with a non-inferiority margin of eight percentage points. The upper limit of the 95% confidence interval of the difference in bothersome visual symptom rates (lower-cylinder group subtracted from higher-cylinder group) will be used to evaluate the primary endpoint.

Other endpoints to be collected in this study include:

1. Ratings of individual items included on the PRVDQ.
2. The rates of 'very bothersome' glare, halos, and starbursts.
3. Rates of IOL repositioning procedures (secondary surgical intervention) due to IOL misalignment.
4. The rate of explants related to visual symptoms for both the higher and lower-cylinder groups.
5. The rates of other adverse events.

Based on the study hypothesis, 298 adult patients in the higher-cylinder group and 298 adult patients in the lower-cylinder group will need to be enrolled to ensure that 240 patients in each group are available at 6 months postoperatively; the sample size allows for an anticipated screen failure rate of 15% and an overall attrition rate of 5%. The 240 subjects in each group will provide over 90% power to evaluate the rate of bothersome visual symptoms for the higher-cylinder group as being non-inferior to the lower-cylinder group.

Patients will be followed for six months after the second-eye surgery. Study visits/assessments will occur at one month and six months postoperatively. Any subject who undergoes a lens repositioning procedure due to IOL misalignment, or reports a bothersome visual symptom at six months, however, will be followed through one year postoperatively.

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 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 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" (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 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 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 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 six copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

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If you have any minor clarification questions concerning the contents of the letter, please contact Bennett Walker at 301-796-6860 or Bennett.Walker@fda.hhs.gov.

Sincerely yours,

William H. Maisel -S

William H. Maisel, MD, MPH
Deputy Center Director for Science
Center for Devices and Radiological Health