Study Protocol

POST–APPROVAL STUDY OF THE TECNIS® TORIC IOL EXTENDED CYLINDER RANGE (ECR), MODELS ZCT450, ZCT525 AND ZCT600

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POST–APPROVAL STUDY OF THE TECNIS® TORIC IOL EXTENDED CYLINDER RANGE (ECR), MODELS ZCT450, ZCT525 AND ZCT600

PROTOCOL NUMBER: TIOL-204-EPAS

SPONSOR: Abbott Medical Optics Inc.
1700 E. St. Andrew Place
Santa Ana, CA 92705
714-247-8200

Investigator Agreement

As an Investigator, I agree to:

- Implement and conduct this study diligently and in strict compliance with this agreement; the protocol; Good Clinical Practices; 21CFR812, ISO 14155 and all other applicable FDA regulations; conditions of approval imposed by the reviewing Institutional Review Board (IRB), FDA or other regulatory authorities; and all other applicable laws and regulations.
- Supervise all testing of the device where human subjects are involved.
- Ensure that the requirements for obtaining informed consent are met.
- Obtain authorization for use/disclosure of health information (e.g., HIPAA authorization or equivalent).
- Maintain all information supplied by Abbott Medical Optics in confidence and, when this information is submitted to an independent IRB or any other group, it will be submitted with a designation that the material is confidential.

I have read this protocol in its entirety and I agree to all aspects.

Investigator Printed Name	Signature	Date
Subinvestigator Printed Name	Signature	Date

Acknowledged By:

Signature of Sponsor's Representative	Date

Printed Name and Title

TABLE OF CONTENTS

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PROTOCOL CHANGE HISTORY

Version	Section(s)	Page(s)	Description of Change(s)	Rationale for Change(s)
1.0	N/A	N/A	Original	N/A
2.0	Personnel and Facilities	4	Updated name of Clinical Operations contact	Personnel changes
	Footer	All	Changed to DDMMM2016/v2.0	New version of document
	Table of Contents	2 –3	Updated contents of table	Changes in protocol
	Protocol Change History	5-6	Added change history	Explain why changes were made
	1.0 Synopsis, Overall Study Design 4.0 Study Design 8.0 Study Population 11.1 Overview	7 11 15 20	Updated enrollment to 120 subjects at up to 20 sites. Additionally decreased the target site enrollment number to 6 from 8. Removed “75” from additional implants.	Enrollment has proven to be more difficult than anticipated and there is a need to add more sites and allow for additional enrollment for screen failures. Correction and consistency with pg. 15.
	8.0 Study Population	15	Changed wording of “implant” to “enroll”.	Correction; consistency with synopsis.
	10.0 Study Timeline, Table 3 Expected Study Timeline	19	Updated to reflect enrollment difficulty for this patient population Modify wording relative to clinical study final report	Enrollment has been more difficult than anticipated. Edit per FDA request.
	10.0 Study Timeline, 20.5 Interim Reports	19 41	Correction to when PAS study reports will be submitted (based on PMA approval date, not study initiation)	Correction to be in compliance with FDA Guidance on “Procedures for Handling Post-Approval Studies Imposed by PMA Order” dated June 15, 2009 (4A).

1. SYNOPSIS

PROTOCOL:

Post-Approval Study of the TECNIS® Toric 1-Piece IOL Extended Cylinder Range, Models ZCT450, ZCT525 and ZCT600.

Protocol: TIOL-204-EPAS

STUDY TREATMENTS:

Study Product: TECNIS Toric 1-Piece IOLs

TECNIS Toric Extended Cylinder Range Study Lenses:

- TECNIS Toric 1-Piece IOL, Model ZCT450
- TECNIS Toric 1-Piece IOL, Model ZCT525
- TECNIS Toric 1-Piece IOL, Model ZCT600

The ZCT450, ZCT525 and ZCT600 lens models are designed for cataract patients with pre-existing corneal astigmatism that, when surgically induced astigmatism (SIA) is taken into account, have approximately 3.00 D to 4.75 D of predicted corneal astigmatism to be corrected.

Other TECNIS Toric Study Lenses:

- TECNIS Toric 1-Piece IOL, Model ZCT300
- TECNIS Toric 1-Piece IOL, Model ZCT375
- TECNIS Toric 1-Piece IOL, Model ZCT400

*The ZCT375 IOL may replace the ZCT400 IOL in this study following FDA-approval.

Control Product: No control product will be used in this study

STUDY OBJECTIVE:

The purpose of this post-approval study is to evaluate the rates of severe visual distortions for the TECNIS Toric 1-Piece IOLs with Extended Cylinder Range of approximately 3.00 D to 4.75 D of cylinder correction at the corneal plane (Models ZCT450, ZCT525 and ZCT600) in clinical practice to ensure continued safety of these FDA-approved devices.

CLINICAL HYPOTHESIS:

Severe visual distortions for the TECNIS Toric IOL Models ZCT450, ZCT525 and ZCT600 will be reported in less than 10 percent of the study population.

OVERALL STUDY DESIGN:

Structure:	Prospective, multicenter, bilateral, non-randomized, open-label clinical study
Number of sites:	Up to 20 sites in the USA
Duration:	6 months; however, any subjects that undergo a lens repositioning procedure due to IOL misalignment or that report a severe visual distortion at six months, will be followed through 1 year postoperatively.
Administration:	Surgeons will perform standardized, small-incision, cataract surgery and implant the study lenses using an AMO-validated, insertion system qualified for use with the study lenses. Refractive target outcomes will be emmetropia for both eyes.
Visit Schedule:	All subjects will undergo a minimum of 5 visits: Preoperative for both eyes, Operative 1st eye, Operative 2nd eye, 1-month and 6-month visits for both eyes together. If a subject experiences a lens repositioning procedure for IOL misalignment or if a subject reports a severe visual distortion at 6 months, the subject will also undergo a final visit at 1 year.

STUDY POPULATION CHARACTERISTICS:

Condition:	Bilateral cataracts with corneal astigmatism of approximately 2.00 D to 4.75 D (with 3.00 D to 4.75 D in at least one eye) based on the combination of preoperative keratometric cylinder and the expected effect of surgically-induced astigmatism (SIA).
Number of Subjects:	Up to 120 subjects will be enrolled to achieve bilateral implantation in approximately 80 subjects; a minimum of 15 subjects will be implanted with a TECNIS Toric ZCT600 in at least one eye, and the remaining subjects will be implanted with either a TECNIS Toric ZCT450, ZCT525 or ZCT600 in at least one eye. This is a bilateral study; both eyes must be implanted with a TECNIS Toric IOL (ZCT300 – ZCT600); however, each eye may have a different TECNIS Toric IOL implanted as determined by the surgeon however as stated above, at least one eye must be implanted with a TECNIS Toric ECR IOL (ZCT450-ZCT600). The eye with the highest toric power IOL will determine the model group. Each site should enroll approximately 6 subjects and no site may enroll more than 20% of the enrollment total.

Inclusion Criteria (all criteria apply to each study eye):

- Minimum 22 years of age
- Bilateral cataracts for which phacoemulsification extraction and posterior chamber IOL implantation have been planned
- Preoperative keratometric cylinder of at least 2.00 D in both eyes. At least one eye, when taking surgically induced astigmatism into account, must have approximately 3.00 D to 4.75 D of predicted corneal astigmatism to be corrected and qualify for implantation of ZCT450, ZCT525 or ZCT600 IOLs as determined by the web-based AMO Toric IOL Calculator
    - Most appropriate toric IOL model choice (ZCT450, ZCT525 or ZCT600) is to be based on the associated residual refractive cylinder (lowest) and axis
- Clear intraocular media other than cataract in each eye
- Availability, willingness, ability and sufficient cognitive awareness to comply with examination procedures and study visits
- Ability to understand, read and write English in order to consent to study participation and complete a study questionnaire
- Signed informed consent and HIPAA authorization

Exclusion Criteria (all criteria apply to each study eye):

- Irregular corneal astigmatism
- Any corneal pathology/abnormality other than regular corneal astigmatism
- Previous corneal surgery
- Recent ocular trauma or intraocular surgery that is not resolved/stable or may affect visual outcomes
- Any pupil abnormalities (non-reactive, fixed pupils, or abnormally shaped pupils)
- Subjects with conditions associated with increased risk of zonular rupture, including capsular or zonular abnormalities that may lead to IOL decentration, including pseudoexfoliation, trauma, or posterior capsule defects
- Known ocular disease or pathology that may affect visual acuity or that may require surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, uncontrolled glaucoma, etc.)
- Concurrent participation or participation during 30 days prior to preoperative visit in any other clinical study
- Planned monovision correction
- Patient is pregnant, plans to become pregnant, is lactating or has another condition associated with the fluctuation of hormones that could lead to refractive changes

EVALUATION CRITERIA:

The purpose of this post-approval study is to evaluate the rates of severe visual distortions for the TECNIS Toric 1-Piece IOLs with Extended Cylinder Range of approximately 3.00 D to 4.75 D of cylinder correction at the corneal plane (Models ZCT450, ZCT525 and ZCT600). The primary endpoint is the rate of severe visual distortions reported by subjects under overall circumstances at 6 months for any of the 5 items of interest contained in the visual distortion questionnaire (PRVDQ). Other endpoints are individual visual distortion ratings, mean percent reduction in absolute cylinder, percent of eyes with cylinder and spherical equivalent (MRSE) within 0.50 D and within 1.00 D of intended, mean difference between IOL axis marker location and postoperative steep keratometry meridian, uncorrected and best corrected distance visual acuity (monocular and binocular), rates of medical and/or lens findings, rates of IOL repositioning procedures (secondary surgical intervention) due to IOL misalignment and rates of other adverse events.

DATA ANALYSIS:

The key timeframe for reporting results is the 6-month visit. The rate of severe visual distortions is defined as the percentage of subjects who report one or more severe visual distortions under overall circumstances at 6 months for any of the 5 items of interest visual distortion items listed under the primary endpoint. The frequency, proportion and 95% Confidence Interval (CI) of those with severe visual distortions will be reported for all bilateral subjects. In addition, the frequency and proportion of bilateral subjects with each response to individual visual distortion items from the questionnaire will also be reported for bilateral subjects in the overall and with and without correction circumstances.

Mean percent reduction in cylinder, mean absolute cylinder, mean spherical equivalent and mean cylinder and spherical equivalent compared to intended values will be reported for primary eyes (the eye with the higher cylinder Toric IOL) and fellow eyes. The frequency and proportion of eyes within 0.50 D and within 1.00 D of intended refractive cylinder and spherical equivalent will also be determined. The frequency and proportion of eyes/subjects achieving each acuity level for uncorrected and best corrected distance visual acuity will also be reported.

The frequency and proportion of primary and fellow eyes with medical/lens findings or adverse events will also be reported.

STUDY VISITS AND PROCEDURES:

Inclusion and exclusion qualifications will be assessed at the preoperative visit according to the inclusion/exclusion criteria. The Informed Consent Document and Authorization

for Use/Disclosure of Health Information form (HIPAA authorization or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries) must be signed by any patients who agree to participate in the study prior to undergoing any study-specific procedures.

Each subject will have bilateral implantation of high cylinder TECNIS toric IOLs (Models ZCT300, ZCT375, ZCT400, ZCT450, ZCT525, ZCT600) in which at least one eye will be implanted with TECNIS toric IOLs Model ZCT450, ZCT525 or ZCT600. The fellow eye will be implanted with the high cylinder TECNIS toric IOL Model ZCT as chosen by the surgeon.

All subjects are intended to have bilateral cataract surgery with the second-eye surgery occurring within approximately 1 month of the first-eye surgery (≤60 days). Two postoperative study visits will be conducted; at 1 month (30-60 days after the second-eye surgery) and at 6 months (120-180 days after the second-eye surgery) for both eyes together. However, subjects who underwent an IOL repositioning procedure due to IOL misalignment or who reported a severe visual distortion at 6 months will return for a final visit at 1 year (330-420 days after the second-eye surgery) postoperatively.

2. BACKGROUND/INTRODUCTION

Amongst patients undergoing cataract surgery, approximately 35-41% of cataract patients have ≥ 0.75 diopter of corneal astigmatism[1] and about 3% have corneal astigmatism of 3.25 D or greater[1]. Although there are various modalities to reduce the amount of astigmatism during cataract surgery (e.g., limbal relaxing incisions, etc.), toric IOLs are now commonly used for correction of aphakia and pre-existing ocular astigmatism. Additionally, corneal treatments for astigmatism reduction are limited in the amount and reproducibility of the reduction attained. In April 2013, Abbott Medical Optics (AMO) received USA FDA approval (P980040/S039) of the TECNIS Toric 1-Piece IOL, Models ZCT150, ZCT225, ZCT300 and ZCT400 for the correction of aphakia and pre-existing corneal astigmatism of one diopter or greater. In the IDE registration trial of the TECNIS Toric IOL, rotational stability was demonstrated and there were minimal subject complaints of visual distortions; however, there is the potential, particularly in the case of toric IOLs that correct for higher amounts of corneal astigmatism, that patients may experience spatial distortions related to axis misalignment, e.g., whether objects appear tilted or misshapen, etc. As a condition of approval, a post-approval study is being conducted to evaluate visual distortions of the TECNIS Toric IOLs with ≥2.0 D of cylinder correction at the corneal plane,

[1] Ferrer-Blasco, T. et al. Prevalence of corneal astigmatism before cataract surgery. J Cataract Refract Surg 2009; 35: 70-75

Models ZCT300 and ZCT400 (or ZCT375 upon FDA-approval) (P980040/S043) and to ensure the continued safety of the approved devices. This post-approval study will be conducted to evaluate visual distortions of the TECNIS Toric IOLs with ≥3.0 D of cylinder correction at the corneal plane (Models ZCT450, ZCT525, and ZCT600) and to also ensure the continued safety of these devices.

3. CLINICAL HYPOTHESIS

Severe visual distortions for the TECNIS Toric IOL Models ZCT450, ZCT525 and ZCT600 will be reported in less than 10 percent of the study population.

4. STUDY DESIGN

This study is a prospective, multicenter, bilateral, non-randomized, open-label, clinical study conducted at up to 20 sites in the USA. Subjects will be bilaterally implanted with the high cylinder TECNIS Toric IOLs, Model ZCT300-ZCT600 with at least one eye of each subject implanted with TECNIS Toric IOL, Models ZCT450 or ZCT525 or ZCT600. The fellow eye will be implanted with a high cylinder TECNIS Toric IOL, Model ZCT300-ZCT600 as chosen by the surgeon.

JUSTIFICATION OF STUDY DESIGN

The study is being conducted as a condition of approval in the USA to ensure the continued safety of the approved devices.

5. ACRONYMS

The following acronyms are used throughout the document:

- UCDVA: uncorrected distance visual acuity
- BCDVA: best corrected distance visual acuity
- D: diopters
- IRB: Institutional Review Board

6. STUDY OBJECTIVES AND ENDPOINTS

The objective of this post-approval study is to evaluate the rates of severe visual distortions for the TECNIS Toric IOLs with ≥ 3.0 D of cylinder correction at the corneal plane (Models ZCT450, ZCT525 and ZCT600) in clinical practice and to ensure the continued safety of the approved devices.

6.1 PRIMARY ENDPOINT

The primary endpoint is the rate of severe visual distortions based on data collected from a self-administered subject questionnaire (PRVDQ).

The rate of severe visual distortions is defined as the percentage of subjects who report a severe visual distortion under overall circumstances at 6 months postoperative for any of the following 5 visual distortion items of interest:

- 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

Distortions will be assessed using the overall circumstance reply at the 6-month visit. The frequency and proportion of subjects reporting one or more of these items as severe will be used to determine the rate of severe visual distortions.

6.2 OTHER ENDPOINTS

- Ratings of individual items included in the visual distortion questionnaire (PRVDQ)
- Mean percent reduction in absolute cylinder
- Mean refractive cylinder, mean refractive cylinder compared to intended, mean spherical equivalent and mean spherical equivalent compared to intended
- Percent of eyes with absolute cylinder within 0.50 D and within 1.00 D of intended
- Percent of eyes with spherical equivalent within 0.50 D and within 1.00 D of intended
- Uncorrected distance visual acuity (monocular and binocular)
- Best corrected distance visual acuity (monocular and binocular)
- Rates of medical and/or lens findings
- Rates of IOL repositioning procedures (secondary surgical intervention) due to IOL misalignment
- Mean difference between IOL axis marker location and postoperative steep keratometry meridian
- Rates of other adverse events

7. STUDY PRODUCTS

7.1 INTRAOCULAR LENSES

The TECNIS Toric 1-Piece IOL, Models ZCT450, ZCT525 and ZCT600 are posterior chamber, 1-piece, aspheric, hydrophobic acrylic foldable IOLs and are to be implanted in

the capsular bag following cataract extraction. The TECNIS Toric Models ZCT450, ZCT525 and ZCT600 are similar to the TECNIS Toric Models, ZCT150, ZCT225, ZCT300, ZCT375 and ZCT400 with the exception of increased amounts of cylinder correction. All TECNIS Toric IOLs have an anterior aspheric optic surface and a spherical posterior optic surface with a toric feature on the anterior optic surface to correct for astigmatism.

INDICATION

The TECNIS® Toric 1-Piece IOLs are indicated for the visual correction of aphakia and pre-existing corneal astigmatism of one diopter or greater in adult patients with or without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire improved uncorrected distance vision, reduction of residual refractive cylinder, and increased spectacle independence for distance vision. The devices are intended to be placed in the capsular bag.

The ZCT450, ZCT525 and ZCT600 lens models, in particular, are intended for cataract patients with pre-existing corneal astigmatism that, when taking surgically induced astigmatism into account, have approximately 3.00 D to 4.75 D of predicted corneal astigmatism to be corrected (Table 1).

TABLE 1
TECNIS Toric IOL, Models ZCT150- ZCT600 Astigmatism Correction Range

ZCT IOL Model	Cylinder Power (D)		Correction Range Based on Combined Corneal Astigmatism (Preoperative Kcyl[a] + SIA[b])
	IOL Plane	Corneal Plane	
ZCT150[c]	1.50 D	1.03 D	0.75 – 1.50 D
ZCT225[c]	2.25 D	1.54 D	1.50 – 2.00 D
ZCT300	3.00D	2.06 D	2.00 – 2.50 D
ZCT375[d]	3.75 D	2.57 D	2.50 – 3.00 D
ZCT400	4.00 D	2.74 D	2.75 – 3.25 D
ZCT450	4.50 D	3.08 D	3.00 – 3.50 D
ZCT525	5.25 D	3.60 D	3.50 – 4.00 D
ZCT600	6.00 D	4.11 D	4.00 – 4.75 D

[a] Keratometric cylinder
[b] Surgically induced astigmatism
[c] IOL Model is not being used in this study
[d] ZCT375 will be used in place of the ZCT400 model following FDA-approval

The TECNIS Toric IOLs have two sets of four axis (8 total) orientation marks 180° apart in the outer periphery of the anterior optic surface (**Figure 1**) to indicate the meridian of the lowest power (flat meridian). These axis orientation marks are for proper alignment of the flat meridian of the IOL with the steep meridian of the corneal curvature.

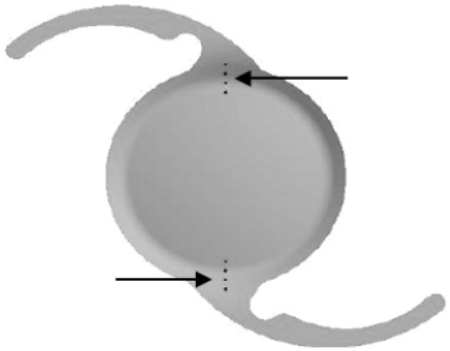

FIGURE 1
TECNIS Toric IOL Illustration of Axis Orientation Marks

Table 2 lists the general design characteristics of the TECNIS Toric IOLs:

TABLE 2
Lens Characteristics of the TECNIS Toric Model ZCT

CHARACTERISTICS	TECNIS® Toric 1-Piece IOL Model ZCT
Lens Design	1-piece acrylic monofocal with an aspheric anterior surface and a maximum and a minimum radii of curvature perpendicular to each other
Lens Model	Surface-treated SENSAR® soft acrylic (acrylic with covalently bound UV absorber)
DIMENSIONAL FEATURES	
Overall Diameter	13.0 mm
Optical Center Thickness	0.722 mm (20.0 D Lens)
Haptic Angle	No angulation, but offset from the optic body
Optic Body Diameter	6.0 mm
Haptic Material	Same as optic
Haptic Width	0.39 mm
Haptic Thickness	0.46 mm
Haptic Style	TRI-FIX Design Modified C, integral with optic
Other Features	Axis orientation marks
OPTICAL FEATURES	
Optic Shape	Biconvex
Anterior Optic Profile	Aspheric with a maximum and a minimum radii of curvature perpendicular to each other Aspheric
Posterior Optic Profile	Spherical
Optic Edge Design	PROTEC™ squared edge
Dioptric Power Range	+5.0 to +34.0 D in 0.50 D increments
Cylinder Power Range	1.50 D, 2.25 D, 3.00 D, 3.75 D, 4.00 D, 4.75 D, 5.25 D, and 6.00 D (at the IOL plane)
Refractive Index	1.470 (35° C)
Theoretical A-constant[a]	118.8 for ultrasound biometry 119.3 for optical biometry

[a] For lens power calculations, the investigator's personalized A-Constant for the TECNIS Toric ZCT IOLs is to be used.

STORAGE AND DISTRIBUTION

All lenses will be obtained from the site's own inventory. All study lenses should be stored in the original packaging and kept in a dry place. Lenses should not be stored in direct sunlight or at temperatures greater than 45° C (113°F). Each lens is packaged in a lens tray and sealed in a peel-pouch. The lens is sterile as long as the package has not been opened or damaged and the shelf-life expiration date has not been exceeded.

7.2 IOL IMPLANTATION SYSTEMS

All lenses are to be implanted using either the UNFOLDER Platinum 1 Series Implantation System (DK7796 handpiece with the Platinum 1 Series cartridge, Model 1MTEC30) or the ONE SERIES Ultra Implantation System (DK7786 [plunger] or the DK7791 [twist] handpieces in combination with the ONE SERIES Ultra cartridge, Model 1VIPR30).

8. STUDY POPULATION

All subjects will be enrolled from the normal surgical cataract population at up to 20 sites in the U.S.A. This study will include only subjects intended to undergo bilateral primary phacoemulsification cataract extraction and IOL implantation who have approximately 3.00 D to 4.75 D of corneal astigmatism in at least one eye requiring correction based on the combination of preoperative keratometric cylinder and the expected effect of SIA. Up to 120 subjects will be enrolled to achieve approximately 80 bilaterally implanted subjects. A minimum of 15 subjects will be implanted with the TECNIS Toric ZCT600 in at least one eye; the remaining subjects are to be implanted with the TECNIS Toric ZCT450, ZCT525 or ZCT600 in at least one eye. The eye with the highest toric power will define the toric group. Both eyes will be implanted with a high cylinder TECNIS Toric IOL (Models ZCT300-ZCT600), but the fellow eye may have a lower cylinder correction toric IOL implanted (i.e. ZCT300, ZCT375 and ZCT400). Each site should enroll approximately 6 subjects, and no site may enroll more than 20% of the enrollment total.

This study will include only subjects who meet all of the study inclusion and exclusion criteria in both eyes. All subjects who meet the inclusion/exclusion criteria will be offered enrollment in the study. Eligibility criteria may not be waived by the investigator. Any questions regarding patient eligibility are to be discussed with AMO prior to subject enrollment.

8.1 INCLUSION CRITERIA

Note: All criteria apply to each eye

- Minimum 22 years of age

- Bilateral cataracts for which phacoemulsification extraction and posterior chamber IOL implantation have been planned
- Preoperative keratometric cylinder of at least 2.00 D in both eyes. At least one eye, when taking surgically induced astigmatism into account, must have approximately 3.00 D to 4.75 D of predicted corneal astigmatism to be corrected and qualify for implantation of ZCT450, ZCT525 or ZCT600 IOLs as determined by the web-based AMO Toric IOL Calculator
    - Most appropriate toric IOL model choice (ZCT450, ZCT525 or ZCT600) is to be based on the associated residual refractive cylinder (lowest) and axis
- Clear intraocular media other than cataract
- Availability, willingness, ability and sufficient cognitive awareness to comply with examination procedures and study visits
- Ability to understand, read and write English in order to consent to study participation and complete a study questionnaire
- Signed informed consent and HIPAA authorization

8.2 EXCLUSION CRITERIA

Note: All criteria apply to each eye

- Irregular corneal astigmatism
- Any corneal pathology/abnormality other than regular corneal astigmatism
- Previous corneal surgery
- Recent ocular trauma or intraocular surgery that is not resolved/stable or may affect visual outcomes
- Any pupil abnormalities (non-reactive, fixed pupils, or abnormally shaped pupils)
- Subjects with conditions associated with increased risk of zonular rupture, including capsular or zonular abnormalities that may lead to IOL decentration, including pseudoexfoliation, trauma, or posterior capsule defects
- Known ocular disease or pathology that may affect visual acuity or that may require surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, uncontrolled glaucoma, etc.)
- Concurrent participation or participation during 30 days prior to preoperative visit in any other clinical study
- Planned monovision correction
- Patient is pregnant, plans to become pregnant, is lactating or has another condition associated with the fluctuation of hormones that could lead to refractive changes

9. INVESTIGATOR SELECTION

9.1 INVESTIGATOR QUALIFICATIONS

AMO will select ophthalmic surgeons who have completed a residency in ophthalmology (or its documented equivalent), and are licensed to practice medicine and perform surgery at his/her investigative site. Each site will have one designated principal investigator; some sites may have additional implanting sub-investigators/surgeons.

Investigators will be selected from surgeons who are experienced in small-incision, phacoemulsification and toric IOL implantation in cataract patients. Additionally, investigators should have established their personalized A-constant for the TECNIS Toric ZCT. All sites are required to have adequate staff support for reporting and subject follow-up, as well as the necessary instrumentation to conduct study testing.

9.2 INVESTIGATOR OBLIGATIONS

Investigators are required to fulfill the following obligations:

- Conduct the study in accordance with the relevant and current protocol. Investigator will only make changes to a protocol after notifying and obtaining approval from AMO, the FDA or other governing agencies, and the Institutional Review Board (IRB), except when necessary to protect the safety, rights or welfare of subjects
- Personally conduct and supervise the study
- Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties
- Be responsible for protecting the rights, safety and welfare of subjects under the investigator's care and be responsible for the control and documentation of the devices under investigation
- Inform patients that the device(s) are being used for regulatory post-approval purposes and that requirements relating to obtaining informed consent and IRB approval are met according to 21CFR50, 21CFR56, 21CFR812 and all other applicable laws and regulations
- Maintain confidentiality as required by HIPAA or similar laws and regulations
- Shall not obtain written informed consent from any subject to participate or allow any subject to participate before obtaining FDA and IRB approval
- Document in each subject's case history that informed consent was obtained prior to participation in the study as required by 21CFR812
- Report to AMO and the reviewing IRB any adverse experiences that occur during the course of the study in accordance with applicable laws and regulations
- Maintain adequate and accurate records in accordance with applicable laws and regulations and make available all study documents and subject medical records for inspection by either AMO, duly authorized regulatory agencies (e.g., FDA) and/or the IRB

- Submit progress reports on the investigation to AMO and the reviewing IRB at regular intervals, but no less often than yearly as required by 21CFR812.150
- Ensure the IRB that is responsible for initial and continuing review of the study complies with applicable laws and regulations
- Report all changes in research activity and all unanticipated problems involving risks to patients to the IRB and AMO
- Provide sufficient accurate financial information to AMO to allow AMO to submit complete and accurate certification or disclosure statements as required by 21CFR54. Promptly update this information if any relevant changes occur during the course of the study or for up to one year following completion of the study
- Comply with all other obligations of clinical investigators and requirements according to all applicable FDA regulations (e.g., 21CFR812), all other applicable laws and regulations, and all conditions of approval imposed by the reviewing IRB, the FDA and the regulatory agency of the country in which the study is being conducted
- Ensure that all associates, colleagues and employees assisting in the conduct of the study are adequately informed about the protocol, the study device, their study-related duties and functions and agree to fulfill their obligations in meeting the above commitments.

Investigators shall provide adequate time and resources to conduct and report on the study. The Investigator, or delegate, shall notify AMO of any change in the conduct of the study including changes in study personnel assigned to the study project, location of the study device(s), or maintenance of study records, etc.

9.3 INVESTIGATOR APPROVAL

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB. All correspondence with the IRB should be retained in the Investigator Study Files/Notebook. Copies of IRB submissions and approvals should be forwarded to AMO. Study sites will obtain IRB approvals and fulfill any other site-specific regulatory requirements. The investigator is required to report to AMO within five working days any withdrawal of approval by the reviewing IRB for his/her participation in the investigation.

Prior to the start of subject enrollment, the following documents must be signed and returned to AMO:

- Confidentiality Agreement
- Clinical Trial Agreement
- Investigator Agreement/Protocol Signature page
- Financial Disclosure form
- Signed and dated copy of investigator's current curriculum vitae
- Copy of the investigator's current medical license

- Hospital/Ambulatory Surgery Center Clinical Study Acknowledgement, if required

By signing the study documents, the investigator agrees to conduct this study according to the obligations above and all other applicable regulatory and legal requirements.

10. STUDY TIMELINE

This study will be initiated following the USA FDA approval of the TECNIS Toric IOL, Models ZCT450, ZCT525, and ZCT600 for the correction of aphakia and pre-existing corneal astigmatism of three diopters or greater (P980040/S058) and FDA approval of this protocol. The expected study timeline is presented in **Table 3**.

TABLE 3
Expected Study Timeline

Study Activity	Expected Timing
Begin IRB approvals, site initiations and subject enrollment	JAN 2016: Following FDA approval of Post-Approval Study protocol and PMA approval of TECNIS Toric IOL Models ZCT 450, ZCT525 and ZCT600
Complete Site IRB approvals and initiations for initial 10 sites	JUL 2016: 6 months (~1-2 sites/month)
Complete Site IRB approval and initiations for additional sites	JUN 2017
Complete subject enrollment	SEP 2018: (~1 subject/site/3 months)
Complete subject follow-up	APR 2019: 6 months NOV 2019: 12 months[a]
Complete primary-analysis, 6-month clinical study report	JUL 2019: 3 months following completion of 6-month exams
Complete 1-year clinical study report	FEB 2020: 3 months following completion of 1-year exams

[a] An additional 6 months may be necessary depending upon the number and timing of subjects returning for 1 year visits (due to reports of severe visual distortions at 6 months or the occurrence of an IOL repositioning procedure)

Additionally, AMO will provide interim study reports every 6 months for the first two years following FDA approval of the lens models (July 31, 2015) and then annually thereafter until completion of the post-approval study. Further details on interim reports are provided in Section 20.5 Interim Reports.

11. STUDY PLAN

11.1 OVERVIEW

This study will be conducted in accordance with U.S. Code of Federal Regulations, the Declaration of Helsinki, ISO 14155 and all other applicable laws and regulations. The study will not begin until regulatory and IRB approvals have been obtained

This study is a prospective, multicenter, bilateral, non-randomized, open-label, clinical study conducted at up to 20 US sites. Subjects will be bilaterally implanted with high cylinder TECNIS Toric IOLs, Models ZCT300-ZCT600 in both eyes with at least one eye implanted with a Model ZCT450, ZCT525 or ZCT600. The eye with the highest toric power lens will determine the lens group. Second-eye surgeries are to be performed within approximately 1 month (no more than 60 days) of the first-eye surgery, as second-eye cataract surgeries are typically performed within 2 months of the first-eye surgery. Subjects will be examined postoperatively at 1 and 6 months following the second-eye surgery. If a subject requires a lens repositioning procedure due to IOL misalignment or if a subject reports a severe visual distortion at 6 months, the subject will undergo a final visit at 1 year. Additional visit schedule details are provided in Section 11.2 Visit Schedule.

At the 1-month visit, a spectacle and/or contact lens prescription will be offered to each subject. Postoperative procedures will include uncorrected and best corrected visual acuities, manifest refraction, intraocular pressure and biomicroscopic slit-lamp examination. In addition, if the subject has a spontaneous report of any of the 5 visual distortion items of interest or of blurred or hazy vision, the questionnaire will be administered and keratometry and toric IOL axis measurements will be performed.

At the 6-month visit, the postoperative procedures will include a subject questionnaire for determination of visual distortions, keratometry, uncorrected and best corrected visual acuities, manifest refraction, intraocular pressure and a biomicroscopic slit-lamp examination for determination of toric IOL axis position and for any adverse events.

If outside of a scheduled study visit, a subject has a spontaneous report of; 1) any of the 5 visual distortion items of interest or 2) blurred or hazy vision at one month postoperatively or later, the PRVDQ questionnaire will be administered and keratometry and toric IOL axis measurements will be performed. Exam details will be documented on an unscheduled visit form.

If a subject reported a severe visual distortion in the questionnaire or experienced a serious or device-related adverse event at any unscheduled study visit, uncorrected distance visual acuity, best corrected distance visual acuity, manifest refraction, keratometry, intraocular pressure and biomicroscopic slit-lam examinations will also be performed.

A 1-year examination will be required only if the subject reports a severe visual distortion at the 6-month examination or experienced an IOL repositioning procedure (due to IOL misalignment during the study).

If a serious or device-related adverse event occurs at or prior to the 6-month visit, details of the event will be collected at the time of the event using an adverse event form. If the adverse event results in an IOL repositioning procedure due to misalignment, the questionnaire should be administered prior to the procedure to collect information regarding visual distortions. Keratometry and toric IOL axis measurements will be performed prior to the repositioning procedure to collect data regarding the IOL misalignment.

A chart summary of all examination procedures required at each study visit is provided in Appendix A.

11.2 VISIT SCHEDULE

The study visit schedule for all study subjects is outlined below in **Table 4**. Additional visits may be conducted at the discretion of the investigator; however routine follow-up visits without reports of serious or device-related adverse event(s) or spontaneous reports of visual distortion(s) are not considered study visits. Note that second-eye surgeries are intended to be performed within approximately 1 month (≤60 days) of the first-eye surgery.

TABLE 4
Study Visit Schedule

VISIT	EYES EVALUATED	EXAM	VISIT WINDOW
1	Both Eyes	Preoperative Exam	N/A
First Eye Surgery			N/A
Second Eye Surgery			Within approximately 1 month (≤60 days) of 1st eye surgery
2	Both Eyes	1 month	30-60 days postoperative from 2nd implant
3	Both Eyes	6 months	120-180 days postoperative from 2nd implant
4[a]	Both Eyes	1 year[a]	330-420 days postoperative from 2nd implant

[a] The 1-year exam is only required if a severe visual distortion was reported by the subject at the 6-month visit or if the subject underwent an IOL repositioning procedure during the study as a result of axis misalignment.

11.3 PREOPERATIVE PROCEDURES

All subjects enrolled in the study must sign the current IRB-approved informed consent document and meet the inclusion/exclusion criteria. The informed consent must be signed before any study-specific examinations are performed, and this must be documented in the source documents. An Authorization for Use/Disclosure of Health Information Form (HIPAA authorization) or similar medical treatment privacy law documentation must also be signed.

As the Informed Consent Form is signed at the beginning of the preoperative study exam, some subjects may not qualify after study-specific testing is performed. Subjects will be considered screen-failures if they do not qualify or if they qualify but decide not to proceed with surgery. These subjects will be exited from the study.

Study-specific preoperative testing for this protocol includes the administration of the subject questionnaire assessing visual distortions as well as any other preoperative procedures that are not already performed during the investigator's routine cataract evaluation for astigmatic patients (e.g., potential visual acuity). Documentation via the AMO Toric IOL Calculator options of toric power lens choice for each eye of each subject is required.

Preoperative testing to be performed for each eye includes the following:

- Informed consent documentation
- Subject demographic information
- Ocular history, including presence of ocular pathology for each eye
- Potential best-corrected distance visual acuity for each eye (Note: 20/30 or better is recommended for study inclusion; may be performed by surgeon estimation)
- Monocular uncorrected distance visual acuity (Snellen)
- Monocular best corrected distance visual acuity (Snellen)
- Manifest refraction (Snellen) for each eye
- Keratometry for each eye
- Intraocular pressure for each eye
- Ocular medications
- Cataract type and density for each eye
- Dilated fundus exam results for each eye (recommended)
- Medical and lens findings from a biomicroscopic slit-lamp exam for each eye
- Axial length, vertex distance, spherical equivalent IOL power and spherical equivalent targeted refraction (emmetropia, within ±0.50 D) for each eye using the investigator's preferred biometry method
- A-constant used for spherical equivalent IOL power determination
- Surgeon-estimated surgically induced astigmatism (SIA) and planned incision location
- Documentation of the AMO Toric IOL Calculator choice of ZCT toric power for each eye and corresponding residual refractive cylinder and axis for each eye
  - Investigator to determine the most appropriate toric IOL model (ZCT450, ZCT525 or ZCT600 in at least one eye of each subject) based on the associated residual refractive cylinder (lowest) and axis
- Subject Questionnaire

LENS POWER CALCULATIONS AND IOL SELECTION:

For lens power calculations, the investigator's personalized A-Constant for the TECNIS Toric ZCT lens is to be used. The spherical equivalent lens power, as determined by the investigator's standard biometry methods, should be calculated to achieve emmetropia (± 0.50 D) at distance for all eyes. Intentional overcorrection or under-correction (i.e., monovision or outside ± 0.50 D) should NOT be planned for either eye; however, surgeons may adjust the targeted refraction as necessary to achieve emmetropia based on their surgeon factor, study subject experience and/or subject first-eye outcomes.

In order to verify subject eligibility and to optimize toric IOL selection and axis placement, investigators will use the web-based AMO Toric IOL Calculator (www.TecnisToricCalc.com) to determine the appropriate TECNIS Toric IOL model for each eye (ZCT450, ZCT525 and/or ZCT600 must be implanted in at least one eye per subject for this study). Note that the AMO Toric IOL calculator provides toric IOL options based on predicted astigmatism, i.e., the vector sum of pre-existing corneal astigmatism and the expected effect of SIA. For this study, subjects are to have corneal astigmatism that, when taking SIA into account, have approximately 3.00 D to 4.75 D of predicted corneal astigmatism to be corrected and qualify for implantation of a ZCT450, ZCT525 and/or ZCT600 IOL in at least one eye (with the fellow eye also qualifying for implantation of ZCT300-ZCT600) as determined by the web-based AMO Toric IOL Calculator. Therefore, toric IOL calculations are to be performed for all subjects in this study and the toric IOL model selections chosen by the investigator via the AMO Toric IOL Calculator are to be printed and maintained as source documentation.

Note: Because lenticular astigmatism in the crystalline lens may influence the determination of the amount of astigmatism to be corrected, it is vital that corneal astigmatism (keratometry readings) and not refractive cylinder data be used for toric IOL calculations.

11.4 STUDY LENS SUPPLY

All lenses will be pulled from the site's own inventory and re-ordered per the standard practice at the site. Two lenses should be available for each case, a primary and a back-up lens.

11.5 OPERATIVE PROCEDURES

The investigator should use his or her standard, small-incision, phacoemulsification, cataract extraction surgical technique. Lenses should be folded for implantation and inserted into the capsular bag using one of the AMO-validated insertion systems. **No additional refractive procedures are to be performed during the operative**

procedure or throughout the postoperative study period (e.g., LRI, OCCI, CRI, AK, PRK, LASIK or LASEK).

Following lens insertion, the TECNIS Toric 1-Piece IOL is to be precisely aligned with the intended axis of placement using the imaginary line formed by the axis orientation marks at each of the haptic/optic junctions of the IOL, identifying the flat meridian of the optic. Carefully remove all viscoelastic from the capsular bag. Special care should be taken to ensure proper positioning of the TECNIS Toric IOL at the intended axis following viscoelastic removal and/or inflation of the capsular bag at the end of the surgical case. Residual viscoelastic and/or over-inflation of the bag may allow the lens to rotate, causing misalignment of the TECNIS Toric IOL from the intended axis.

Operative case report forms will include the following information:

- Date of surgery
- Operative eye
- IOL model, power and serial number
- Incision location
- Surgical complications
- Other surgical procedures
- IOL placement (e.g., within capsular bag, proper alignment, etc.)
- Wound closure (e.g., suture required)
- Adverse events

11.6 POSTOPERATIVE PROCEDURES

Postoperatively, subjects will be examined according to the schedule in Section 11.2, Visit Schedule. All subjects will be examined at the 1- and 6-month study visits. If a subject requires a lens repositioning procedure due to IOL misalignment or if a subject reports a severe visual distortion at 6 months, the subject will also undergo a final visit at 1 year.

At the 1-month visit, a spectacle and/or contact lens prescription will be offered to each subject. Postoperative procedures will include uncorrected and best corrected visual acuities, manifest refraction, intraocular pressure and biomicroscopic slit-lamp examination. In addition, if the subject has a spontaneous report of any of the 5 visual distortion items of interest or of blurred or hazy vision, the questionnaire will be administered and keratometry and toric IOL axis measurements will be performed.

Primary 6-month postoperative data collection consists of administration of a subject questionnaire for determination of visual distortion reports, manifest refraction, distance visual acuities, intraocular pressure, keratometry, and a biomicroscopic slit-lamp exam for determination of toric IOL axis position and for any adverse events.

If outside of a scheduled study visit, a subject has a spontaneous report of; 1) any of the 5 visual distortion items of interest or 2) blurred or hazy vision at one month postoperatively or later,, the PRVDQ questionnaire will be administered and keratometry and toric IOL axis measurements will be performed. Exam details will be documented on an unscheduled visit form.

If a subject reports a severe visual distortion or has experienced a serious or device-related adverse event at any unscheduled study visit, uncorrected distance visual acuity, best corrected distance visual acuity, manifest refraction, keratometry, intraocular pressure and biomicroscopic slit-lam examinations will be performed.

Subjects should be assessed at each visit for occurrence of and/or change in status of any adverse events, particularly serious and/or device-related adverse events. If a serious or device-related adverse event occurs, details of the event are to be captured on an adverse event CRF and the exam details are to be captured on the appropriate visit CRF (i.e., 1-month, 6-month, 1-year or unscheduled). The event will be followed up as necessary and details captured on adverse event follow-up CRFs until resolution. See Section 12.0, Adverse Events, and **Appendix D** Adverse Event Reporting Instructions, for further information.

If a serious or device-related adverse event occurs at or prior to the 6-month visit, details of the event will be collected at the time of the event using an adverse event form. If the adverse event results in an IOL repositioning procedure due to misalignment, the questionnaire should be administered prior to the procedure to collect information regarding visual distortions. Keratometry and toric IOL axis measurements will be performed prior to the repositioning procedure to collect data regarding the IOL misalignment.

If correction is required during the study postoperatively, spectacles or contact lenses will be prescribed; however, no additional refractive procedures (LRI, AK, etc.) are allowed until after completion of the 6-month study visit. If a subject is required to return for a 1-year exam (due to a severe visual distortion at 6 months or an IOL repositioning procedure during the study), a refractive enhancement (LRI, AK, etc.) may be performed prior to the 1-year exam but must be reported on the 1-year case report form; this enhancement will not be considered a secondary surgical intervention at this time.

The postoperative case report form will include the following information (Appendix A):

- Confirmation of offering of spectacle and/or contact lens prescription: 1-month visit only
- Questionnaire: (Following completion of the questionnaire by the subject, the questionnaire is to be reviewed by the site personnel for reports of severe visual distortions), 6-month and 1-year visits and also at 1-month or unscheduled visits only

if there is a spontaneous report of visual distortion or prior to an IOL repositioning procedure at that visit.

- Keratometry: 6-month and 1-year visits; also at 1-month and unscheduled visits if there is a spontaneous report of visual distortion or prior to an IOL repositioning procedure at that visit.
- Monocular uncorrected distance visual acuity, Snellen: all scheduled postoperative visits and unscheduled visits if a severe visual distortion or a serious or device-related adverse event is reported at that visit.
- Binocular uncorrected distance visual acuity, Snellen: 1- month, 6-month and 1-year visits; also at unscheduled visits if a severe visual distortion or a serious or device-related adverse event is reported at that visit.
- Manifest refraction (Snellen): 1- month, 6-month and 1-year visits; also at unscheduled visits if a severe visual distortion or a serious or device-related adverse event is reported at that visit.
- Monocular best corrected distance visual acuity, Snellen: 1- month, 6-month and 1-year visits; also at unscheduled visits if a severe visual distortion or a serious or device-related adverse event is reported at that visit.
- Binocular best corrected distance visual acuity, Snellen: 1- month, 6-month and 1-year visits; also at unscheduled visits if a severe visual distortion or a serious or device-related adverse event is reported at that visit.
- Toric IOL axis measurement by dilated slit-lamp examination (Refer to Appendix B for measurement instructions): 6-month and 1-year visits; also at 1-month and unscheduled visits if there is a spontaneous report of visual distortion or prior to an IOL repositioning procedure at that visit.
- Medical and lens findings from biomicroscopic slit-lamp exam: 1- month, 6-month and 1-year visits; also at unscheduled visits if a severe visual distortion or a serious or device-related adverse event is reported at that visit. Findings of aqueous cells and flare, corneal edema, posterior capsule striae, posterior capsular opacification and IOL glistenings are to be rated using a standardized grading scales provided in Appendix C.
- Ocular medications
- Intraocular pressure
- Dilated fundus exam, if medically indicated
- Occurrence of Nd:YAG capsulotomy(ies)
- Occurrence of any adverse events

11.7 UNSCHEDULED VISITS

A visit is considered an unscheduled study visit when it occurs other than at the specified 1- or 6-month study visits AND at which a serious or device-related adverse event is reported OR if the subject has a spontaneous report of any of the 5 visual distortion items of interest (lines that slant, tilt 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, or physical discomfort related to vision as defined in Section 6.1) or of blurred or hazy vision at 1 month postoperatively or later.

For example, if the subject is seen for a routine (non-study) 3-month follow-up visit and there are no serious or device-related adverse events or any spontaneous report of visual distortion(s) of interest or of blurred or hazy vision at 1 month postoperatively or later, this would NOT be captured on an unscheduled visit form. If however, the subject commented on a visual distortion as listed above or a serious or device-related adverse event was noted at this visit, this visit would be captured on an unscheduled visit form. If a subject reports a visual distortion at an unscheduled visit, the PRVDQ questionnaire is to be administered, and keratometry and toric IOL axis measurements are to be performed.

If the subject reported a severe visual distortion in the questionnaire or if a serious or device-related adverse event was reported at any unscheduled visit, uncorrected and best corrected visual acuities, manifest refraction, keratometry, intraocular pressure and biomicroscopic slit-lam examinations will be performed. If the event results in an IOL repositioning procedure (secondary surgical procedure), the PRVDQ questionnaire is to be administered and keratometry and toric IOL axis measurements are to be performed PRIOR to the IOL repositioning procedure for evaluation of visual distortions arising from IOL misalignment.

Data to be collected on unscheduled visit forms (due to serious or device-related adverse event or spontaneous report of visual distortion) include, as applicable:

- Questionnaire - in the event of a spontaneous report of visual distortion or prior to an IOL repositioning procedure
- Snellen manifest refraction
- Uncorrected and best corrected distance visual acuity using Snellen
- Intraocular pressure
- Slit-lamp examination for medical and/or lens findings
- Keratometry
- Toric IOL axis measurement
- Dilated fundus exam, if medically indicated
- Ocular symptoms
- Adverse events
- Medications

11.8 EXIT OF SUBJECTS

An Exit Case Report Form will be completed for all subjects, either when they complete the study or if they exit early.

It is the responsibility of the investigator to provide complete follow-up data to AMO for each subject, and every attempt will be made to gather that complete follow-up data for all subjects enrolled as missing data can have a negative effect on the study results.. Patients who would be traveling, relocating or otherwise unavailable for postoperative follow-up visits should not be chosen for this clinical study.

SUBJECT FOLLOW-UP

To minimize subjects lost to follow-up, subjects will be provided compensation for their time and participation in the study at the 1- and 6-month postoperative exams. Additionally, sites will be compensated for completion of the 1- and 6-month exams and will be provided frequent listings of upcoming 1- and 6-month subject examinations as well as follow-up reminder cards to send to the subjects. It is anticipated that at least 90% of subjects will be available for the 6-month study visit (i.e., no more than a 10% lost-to-follow-up rate at 6 months postoperatively). If a subject has a confirmed report of severe visual distortion(s) per the questionnaire, prior to the 6-month exam, every effort is to be made to ensure that subject returns for the 6-month exam. The investigative site shall make a minimum of at least three attempts (phone calls/emails and/or letters) to locate missing subjects.

SUBJECT DISCONTINUATION

Subjects will be discontinued from the study if the study lens is removed or if the subject dies. Subjects will be considered “lost-to-follow-up” from the study only if irretrievably lost for unavoidable reasons such as: subject moved/unable to locate, subject uncooperative/refuses further study participation, subject ill/unable to travel. The site shall document at least three attempts (phone calls/emails and/or letters) to locate lost-to-follow-up subjects and the investigator should notify AMO prior to exiting a subject from the study. If a subject is exited from the study, the investigator will, if at all possible, have the subject return for a final study visit. In the event of subject relocation, efforts must be made by the investigator to secure follow-up information (i.e., slit-lamp findings and general visual acuity, etc.) from the subject’s new physician.

If a subject is exited early from the study, the investigator will complete an Exit Case Report Form indicating the reason for study exit. In the event of a lens removal or other serious adverse event, the subject may be exited from the study; however, efforts must be made by the investigator to follow the subject until resolution of the adverse event.

Note: A subject may be exited from the study if complications occur during the first-eye surgery and the planned study lens is not implanted; however, the eye will be followed until the resolution of the complication prior to exiting the subject from the study. If a complication occurs during the second-eye surgery and the planned study lens is not implanted in the second eye, the subject is to be followed according to the protocol for

the first eye (although data may be analyzed separately), and the second eye will be followed for safety until resolution of the complication.

11.9 PROTOCOL DEVIATIONS

Any departure from the protocol procedures represents a protocol deviation. Protocol deviations may be subject-based (e.g., inclusion/exclusion criteria, informed consent deviation, etc.) or procedural-based (e.g., out-of-interval visits, non-compliance with testing procedures, etc.). All protocol deviations will be documented using protocol deviation case report forms. Any deviation made to protect the life or physical well-being of a subject in an emergency as well as any use of the study device without obtaining informed consent must be reported to AMO within 5 working days. Protocol deviations will be monitored by AMO, and if the non-compliance is persistent or egregious, AMO may take action, including but not limited to termination of the investigator's participation in the study. The investigator is also responsible for informing the reviewing IRB of instances of protocol non-compliance in accordance with the IRB requirements.

12. ADVERSE EVENTS AND PRODUCT COMPLAINTS

12.1 ADVERSE EVENT DEFINITIONS

Adverse Event (AE)

An adverse event is defined (following ISO 14155) as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the study device.

Serious Adverse Event (SAE)

An adverse event is considered serious (following ISO 14155) if it is an untoward occurrence which may or may not be related to use of the study device that

- is sight- or life-threatening,
- results in death,
- requires inpatient hospitalization or prolongation of hospitalization (a planned hospitalization for a pre-existing condition is not considered a serious adverse event),
- results in permanent impairment of a body structure or body function,
- necessitates medical or surgical intervention to prevent permanent impairment to a body structure or function, or
- results in fetal distress, fetal death or a congenital abnormality or birth defect

Device-Related Adverse Event

A device-related adverse event is defined as any adverse event that is believed to be definitely, probably or possibly related to the study device (following the guidelines in Section 12.4, Causal Relationship). A device-related event is considered an adverse

device effect (ADE; following ISO 14155) resulting from any untoward or unintended response to the study device.

Study-Specific Serious Anticipated Adverse Events

The following is a list including, but not limited to, ocular adverse events that are anticipated and must be reported to AMO for this study. Any events that are unlikely but anticipated (i.e., endophthalmitis) will be reported to the FDA and other appropriate regulatory agencies.

- Endophthalmitis/Intraocular infection
- Hypopyon
- Hyphema
- IOL dislocation
- Cystoid macular edema
- Pupillary block
- Retinal detachment/tear
- Persistent corneal edema
- Persistent iritis
- Persistent raised IOP requiring treatment
- Axis misalignment requiring secondary surgical intervention (e.g., repositioning)
- Tilt and decentration requiring secondary surgical intervention (e.g., repositioning)
- Residual refractive error resulting in a secondary surgical intervention
- Residual lens remnants resulting in a secondary surgical intervention
- Visual symptoms requiring secondary surgical intervention

NOTE 1: Wound burps during the first week postoperatively, suture removal, planned blepharoplasty and Nd:YAG capsulotomy (for PCO) are not considered adverse events for this study.

NOTE 2: Raised IOP requiring treatment, cornea edema, and iritis will only be considered serious if persistent at the final study visit (120-180 days postoperative) or sight-threatening at the time of occurrence. Treatment merely to hasten the resolution of such conditions (and not intended to prevent permanent damage to the eye) will not be reported as serious adverse events.

Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE)

Any UADE (USA 21CFR 812.3(s)) or USADE (ISO 14155) is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan (i.e., this protocol),

application (including a supplementary plan or application), or risk assessment, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

12.2 PRODUCT COMPLAINT/DEVICE DEFICIENCY DEFINITION

A product complaint/device deficiency is defined (21 CFR 820.3(b) and ISO 14155) as any alleged deficiency related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device. Product complaints can pertain to any marketed AMO device being used in the study. The investigator is to assess whether the deficiency could have led to a serious adverse event without suitable action or intervention or under less fortunate circumstances.

12.3 ADVERSE EVENT AND COMPLAINT REPORTING REQUIREMENTS

All adverse events and any complaint encountered using any AMO product, regardless of severity and whether or not attributed to the study device(s), are to be reported to AMO and recorded on the case report form corresponding to the visit during which awareness of the event occurred. All serious adverse events, whether anticipated or unanticipated, and all adverse device effects shall be reported using a serious or device related adverse event case report form and forwarded to AMO. Adverse events are also to be reported to the reviewing IRB as per the IRB's reporting requirements. If required, adverse events will be reported to the appropriate regulatory agencies (e.g., FDA) according to all applicable laws and regulations. Specific instructions on notification procedures to AMO are included in **Appendix D**, Adverse Event Reporting.

Reporting of adverse events shall follow the USA Code of Federal Regulations (21CFR812) for sites in the USA. General guidelines are provided below:

Adverse Event Reporting

An adverse event that is not serious or device-related is to be reported to AMO in a timely manner. Notification of non-serious and non-device related adverse events will occur by recording events on the CRF when noted. Such adverse events are also to be reported to the reviewing IRB per their reporting requirements.

Complaints/Device Deficiency Reporting

A general product complaint or device deficiency is to be reported to AMO in a timely manner. Notification of complaints/device deficiencies will occur by either recording complaints on the CRF when the complaint occurred (e.g. operative form) or by a phone call to the Sponsor. Any device deficiency that could have led to a serious adverse event without suitable action or intervention, or under less fortunate circumstances, must be reported to the sponsor immediately (no later than 48 hours after detection). Device

deficiencies that could have led to a serious adverse event should also be reported to the investigator's IRB per their reporting requirements.

Serious and/or Device-Related Adverse Event Reporting

In the event of a serious adverse event (SAE), which may or may not be related to use of the study device, or a device-related adverse event, AMO must be notified immediately (no later than 48 hours after detection). Any SAE and/or device-related AE is to be reported by phone and by submitting a completed Serious and/or Device-Related Adverse Event CRF. Any SAE or device-related AE should also be reported to the investigator's IRB per their reporting requirements.

Unanticipated Adverse Device Effect (UADE)/Unanticipated Serious Adverse Device Effect (USADE) Reporting

If during the study, a serious adverse event occurs that may reasonably be regarded as study-device-related and was not previously expected in nature, severity, or degree of incidence, the investigator is to report the UADE/USADE to AMO within 48 hours, and to the investigator's IRB as soon as possible (and no later than 10 working days after learning of the event for sites in the USA as required by 21CFR812).

12.4 CAUSAL RELATIONSHIP

The investigator should always be alert to adverse events that may be related to the study device or use of the study device (in the implantation procedure). An attempt should be made in every case to determine if the event may be device-related.

The following definitions are to be used as guidelines in determining the relationship between the event and the study devices: .

Definitely related:	There is a definite causal relationship between the adverse event and the device or implantation procedure.
Probably related:	There is a reasonable possibility of a causal relationship between the adverse event and the device or implantation procedure.
Possibly related:	The adverse event has not been determined to be related to the device or implantation procedure, but no other cause has been definitively identified and the device or implantation procedure cannot be ruled out as a possible cause.
Unlikely to be related:	The possibility of a potential causal relationship between adverse event and the device or implantation procedure could exist, but the adverse event is most likely explained by causes other than the device or implantation procedure.
Not related:	There is no possibility of a causal relationship between the adverse event and the device or implantation procedure.

If an adverse event is believed to be definitely, probably or possibly related to the study device, the event will be considered device-related.

12.5 ADVERSE EVENT FOLLOW-UP

For every serious or device-related adverse event, appropriate measures should be undertaken to treat and/or monitor the subject until resolution occurs. Obtain and maintain in the subject's files all pertinent medical data relating to the event including the subject's medical records and medical reports and/or judgments from colleagues or outside specialists who assisted in the treatment and follow-up of the subject. The investigator should keep AMO closely informed as to the outcome of serious and/or device-related adverse events, thereby allowing AMO to comply with the appropriate regulatory reporting requirements. A Serious and/or Device-Related Adverse Event Update CRF should be completed each time the subject returns to the investigator or other specialist(s) for follow-up of serious and/or device-related adverse event until resolution of the event. Any subject who is exited from the study due to a serious and/or device-related adverse event will be followed until the outcome is determined.

13. PROTOCOL CHANGES/AMENDMENTS

If the investigator desires to modify any procedure and/or the design of the study, he or she must contact and obtain consent from AMO regarding the proposed changes prior to implementation. Any modifications (including additional data collection) require approval by the FDA and all other appropriate regulatory agencies, as well as approval of the governing IRBs prior to implementation.

14. ETHICS REVIEW AND PATIENT WELFARE

14.1 INSTITUTIONAL REVIEW BOARD (IRB)

It is the responsibility of the investigator to obtain prospective approval of the study protocol, protocol amendments or changes, informed consent forms and other relevant documents (e.g., advertisements) from the IRB. All correspondence with the IRB should be retained in the Investigator Notebook. Copies of IRB submissions and approvals should be forwarded to AMO.

The investigator is responsible for notifying the IRB of reportable adverse events as well as any other circumstance in which additional procedures outside the protocol were conducted to eliminate apparent hazards to subjects.

14.2 INFORMED CONSENT

The current version of the IRB-approved study informed consent must be signed by each study subject prior to any study-specific examinations being performed. The IRB-approved informed consent is to be signed and dated by the subject as well as by

the person who conducted the informed consent discussion. The signed informed consent will be maintained by the investigator as a permanent part of the subject's medical records. A copy of the signed and dated form is to be provided to the subject. The investigator will provide AMO acknowledgement on the preoperative case report form that a signed agreement of informed consent has been obtained and is in the investigator's possession for each subject. As required by 21CFR812 Part G, the site shall document in the source documents that informed consent was obtained prior to participation in the study for each subject enrolled.

NOTE: The informed consent process also includes obtaining the subject's signature on an Authorization for Use/Disclosure of Health Information for Research Form.

NOTE: The sponsor will secure appropriate insurance for study subjects prior to study start.

15. DOCUMENTATION

15.1 SOURCE DOCUMENTS

Source documents must be kept for all study subjects. Source documents may include a subject's medical records, hospital charts, clinic charts, the investigator's subject study files, as well as results of any diagnostic tests or procedures such as topographies or laboratory tests with photographs or instrument printouts.

Each site is expected to adhere to the clinic's own standard documentation requirements for medical charts/clinic notes. However, for the purposes of this clinical study, the medical charts/clinic notes must also include, at a minimum, the following data that will be considered source data and will be reviewed by AMO:

- Subject's name and study identification number
- Subject's contact information
- Study protocol number and the Sponsor name (AMO)
- A statement that informed consent was obtained prior to participation in the study (including the date)
- Dates of all subject visits and surgeries throughout the duration of the study
- Implant serial number identification
- Concurrent medications
- Corrected and uncorrected distance visual acuity
- Manifest refraction
- Occurrence and status of any operative complications, postoperative medical or lens findings and adverse events
- Occurrence and status of any subject complaints, e.g., ocular/visual symptoms

- The date the subject exited the study, and a notation as to whether the subject completed the study or reason for early exit.

15.2 SUBJECT CONFIDENTIALITY

Subjects will be assigned a site/subject number to maintain subject confidentiality. Subject names may possibly be disclosed to AMO or regulatory agencies during inspection of medical records related to the study, but reasonable precautions will be taken to maintain confidentiality of personal information to the extent permitted by applicable laws and regulations.

15.3 CASE REPORT FORM COMPLETION

This study will use an electronic data capture system using electronic case report forms.. Case report forms will be completed in accordance with instructions provided to the site prior to study start. The investigator is responsible for ensuring that data are properly recorded on each subject's case report forms and related documents. Prior to database lock, the investigator will verify completeness and accuracy of data submitted to AMO.

15.4 STUDY SUMMARY

A final investigator's summary will be provided to AMO and the reviewing IRB within three months after termination or the completion of the study or the investigator's part of the investigation.

16. MONITORING

AMO will perform three types of monitoring to ensure compliance with regulations: data monitoring, administrative monitoring, and safety monitoring.

16.1 DATA MONITORING

In order to ensure a well-controlled clinical trial, AMO will follow specific data monitoring procedures.

Subject data will be entered to AMO's data management system via completion of case report forms by the investigative site. Requests for data clarification will be handled through this same data management system.

To minimize data omissions and inconsistencies on clinical reports and to ensure that data are accurately transcribed to computer data files, AMO will follow internal data processing procedures that include automated and manual quality control checks to identify any data discrepancies. Any such items will be resolved and documented as needed on the case report forms by the investigative site via AMO's data management system.

Prevention of Missing Data

Methods used to safeguard against missing data that can have deleterious effects on the study integrity and reliability of its outcomes will include training study staff with on-site programs. In addition, subjects will be encouraged at the time of informed consent to avoid missing study visits, as missing data may affect the study reliability and diminish the scientific value of their contribution to the study.

16.2 ADMINISTRATIVE MONITORING

Administrative monitoring procedures will ensure that subjects and case report forms can be traced and will allow monitoring of investigator progress and compliance.

Device Accountability

As the study IOLs are commercially available, supply records for the lenses will solely be the responsibility of the site and managed by their customary methods. However, documentation of the lenses that are implanted in study subjects will be maintained and monitored by AMO personnel.

Site Monitoring Plan

Prior to performing any study implants, the requirements of the study and reporting mechanisms will be explained to each investigator either personally at the investigative site or at a formal study investigator meeting. When necessary, a pre-study site qualification visit may be performed to assess the adequacy of the site to perform the study for sites that have not previously worked with AMO or have undergone significant changes, or have not been visited in the past year.

Throughout the duration of the study, site visits to monitor compliance to this protocol will be made at each investigative site. During a routine site monitoring visit, AMO will review informed consent documents and subject eligibility, and the data on study case report forms will be verified against subject charts and other source documents to ensure complete and accurate reporting. The subject files will also be reviewed to assure that all adverse events and any issues encountered with AMO products have been reported in a timely fashion.

AMO will also review source documents to verify that all required items have been documented in the subject medical charts. Refer to Section 15.1, Source Documents, for a list of items that are required for source documentation. In addition to subject files, study logs will be checked. Training on study-specific procedures may also be conducted during monitoring visits.

Upon study completion, a final close-out site visit to each site will be made to monitor the last of the subject data records and finalize any outstanding study issues.

A separate Study Monitoring Plan will be established prior to study start that will define the type and frequency of monitoring visits and frequency of record monitoring.

16.3 MEDICAL OVERSIGHT

The medical monitor will be available throughout the clinical trial to review study results and to answer any questions from investigators. The medical monitor will review and assess any reports of serious and/or device-related adverse events and discuss these with the reporting investigator(s) as necessary. The medical monitor, as well as any other qualified personnel designated by AMO, shall also review study reports.

17. PUBLICATIONS

Refer to the Clinical Trial Agreement for information regarding AMO publication policies.

18. RISK ANALYSIS

POTENTIAL RISKS AND RISK MANAGEMENT

RISKS OF THE TECNIS TORIC IOLS

The TECNIS Toric IOLs are designed to provide improved uncorrected distance vision, reduction in residual refractive cylinder, and increased spectacle independence for distance; however, glasses may still be needed to improve distance vision and/or to have useful vision for intermediate or near tasks. In addition, rotation of the TECNIS Toric IOLs away from its intended axis can reduce its astigmatic correction. Misalignment greater than 30° may increase postoperative refractive cylinder. If necessary, lens repositioning should occur as early as possible prior to lens encapsulation. These risks are not unlike other lenses of this kind. As the TECNIS Toric ZCT450, ZCT525 and ZCT600 IOLs have higher amounts of cylinder correction, there may be an increased risk of visual distortions arising from misalignment.

GENERAL RISKS OF CATARACT SURGERY AND IOL IMPLANTATION

There are risks and complications associated with cataract surgery and IOL implantation in general. These can include worsening of vision, hemorrhage, loss of corneal clarity, inflammation, infections, retinal detachment, pupil changes, glaucoma, etc. Complications can result in poor vision, loss of vision or loss of the eye.

RISK MANAGEMENT

Subjects will be closely monitored thought the trial duration. The occurrence of adverse events and complaints will be assessed at each study visit and reported to AMO according to Section 12 Adverse Events and Product Complaints. Additionally, AMO will monitor incoming data following the procedures outlined in Section 16, Monitoring. The Medical Monitor will ensure subjects are not exposed to additional risks by monitoring

serious adverse events, device-related adverse events, and device-deficiencies that could have led to serious adverse events (Section 16.3, Medical Oversight).

POTENTIAL BENEFITS

The clinical performance of the TECNIS Toric IOL, Models ZCT450, ZCT525 and ZCT600 are expected to be similar to the TECNIS Toric IOL, Models ZCT300, ZCT375 and ZCT400 with respect to providing good uncorrected distance vision, reduction in residual refractive cylinder, and increased spectacle independence for distance; however, the extended cylinder range will allow patients with higher preoperative corneal astigmatism access to the same benefits as those with lower preoperative corneal astigmatism.

CONCLUSION

The hazards/risks associated with the TECNIS Toric IOL, Models ZCT450, ZCT525 and ZCT600 are acceptable and within those of AMO's other Toric IOLs. The potential clinical benefits of these lenses outweigh the residual risks when the device is used as intended.

19. RECORDS RETENTION

All study-related correspondence, subject records, consent forms, Authorization for Use/Disclosure of Health Information Forms or similar medical treatment privacy law documentation, records of the distribution and use of all study products, and an electronic copy of the completed case report forms should be maintained by the investigator.

The investigator must maintain and have access to the following essential documents until notified by the Sponsor. Note: This may be for a minimum of 15 years after completion of the study unless country-specific requirements are longer. AMO requires notification if the investigator wishes to relinquish ownership of the data so that mutually agreed-upon arrangements can be made for transfer of ownership to a suitably qualified, responsible person.

- All case report forms
- All adverse event information (adverse event forms, follow-up letters, etc.)
- IRB and regulatory approval documentation
- Study correspondence
- Study agreements
- Site visit documentation
- Protocol(s) and the reason for any deviations from the protocol
- Subject log(s)

- Directions for Use
- Completed subject informed consent forms and medical privacy forms (e.g., Authorization for Use/Disclosure of Health information or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries)
- Subject medical chart/clinic notes

20. TERMINATION OF THE INVESTIGATION

The clinical investigation will be suspended in the event of high levels of complications and/or adverse events occur that are unexpected in nature and/or severity and are possibly related to use of the study device. The clinical investigation may be suspended if the Medical Monitor or IRB, upon review and evaluation of the clinical data, finds unacceptable clinical performance or the level of single or total complications and/or adverse events unacceptable for continuation of the investigation.

If causality is shown not to be related to the study device, the study may be resumed in accordance with the IRB and regulations of the FDA. The study will be terminated if causality is shown to be related to the study device.

Additionally, the investigator, or AMO, may stop a subject's participation at any time. AMO may also stop the study at any time for reasons it determines appropriate. However, no suspension of the study would be made to disadvantage the study subjects. Following suspension of the study for any reason, all study subjects who have already received treatment would continue to be followed through completion of the study visit schedule.

20.1 STATISTICAL METHODS

This section highlights the analyses to be performed for key study endpoints. The 6-month postoperative visit is the critical analysis time point for all endpoints. Descriptive statistics will typically include mean, standard deviation, minimum, maximum for continuous data with frequency and proportion reported for categorical data.

20.2 ANALYSIS POPULATION

For the primary endpoint and most visual distortion endpoints, the primary analysis population will be all bilaterally implanted subjects having available data at the 6-month visit. Data will also be reported for all subjects including bilateral subjects and those with only one eye implanted (having a phakic lens, a cataract or other IOL in the fellow eye). Data will also be reported by IOL group. If a subject does not have overall severe visual distortion data available at the 6-month visit (or had a repositioning procedure or IOL removal performed) then data for this endpoint will be carried forward from the most recent visit (for general missing data) or the visit with data taken prior to the IOL

repositioning or removal. If a subject had an IOL repositioning/removal and no questionnaire data prior to the procedure, then the subject will be considered to have had a severe visual distortion for this endpoint. An additional analysis will be performed for the primary endpoint using multiple imputation techniques for those with no questionnaire data available. Sensitivity analyses such as worst-case and best-case will also be performed.

Refraction, visual acuity, medical/lens findings, axis evaluation and adverse events will be reported for primary eyes (those having the higher cylinder IOL or the first eye implanted if the same IOL is implanted in both eyes) and fellow eyes. Data will be reported separately for ZCT450-ZCT600 eyes and ZCT 300-ZCT400 eyes.

20.3 PRIMARY ENDPOINT

The primary endpoint for this study is the rate of severe visual distortions (under overall circumstances) as measured by the 5 visual distortion items of interest in bilateral subjects at 6 months. The frequency, proportion and a two-sided 95% confidence interval will be reported for this endpoint. The frequency and proportion of subjects reporting one or more of these items as severe will be used to determine the rate of severe distortions.

20.4 OTHER ENDPOINTS

The frequency and proportion of subjects with each response will be reported for the individual visual distortion items on the visual distortion questionnaire for overall, with and without correction.

To evaluate if IOL axis misalignment changes are associated with severe visual distortions, descriptive statistics for IOL axis misalignment and mean difference between IOL axis marker location and postoperative steep keratometry meridian will be reported for subjects with and without severe visual distortions.

Descriptive statistics will be reported for mean percent reduction in cylinder, refractive cylinder, cylinder vs intended cylinder, spherical equivalent and spherical equivalent vs intended. The frequency and proportion of eyes within 0.50 D and within 1.00 D of intended values will be reported for refractive cylinder and spherical equivalent. The frequency and proportion achieving each acuity level will be reported for monocular and binocular uncorrected and best corrected distance visual acuity.

Enrollment data, demographic data, subject accountability data and operative complications/procedures will be reported using descriptive statistics. Visual distortion findings, adverse events and other key data will be reported at 1 year for subjects who experienced a repositioning procedure during the study or who were reported with severe visual distortions at the 6-month visit.

The frequency and proportion of subjects with medical/lens findings or adverse events will also be reported.

20.5 INTERIM REPORTS

Interim status study reports will be provided to FDA every 6 months for the first 2 years following FDA approval of the lens models (July 31, 2015) and annually thereafter, until completion of the post-approval study according to the guidance document entitled "Procedures for Handling Post-Approval Studies Imposed by PMA Order," dated June 15, 2009.

A primary-analysis, 6-month study report will be provided to FDA approximately 3 months following completion of the last 6-month study visit. Any 1-year data collected to date will be included.

A final study report will be provided to FDA approximately 3 months following completion of the last 1-year study visit. Note that the primary-analysis, 6-month report and the final report may be submitted at the same time depending upon when the last 6-month and 1-year exams are completed.

Interim and final study reports will include general enrollment and accountability items including the number of active sites, the number of subjects enrolled, implanted and discontinued and the number of postoperative examinations completed. Interim reports, will only include descriptive statistics (no hypothesis testing). Additional specifics on interim report items include:

- Summary of study progress milestones/timeline elements
- Stratified subject accountability data
- Explanation for any discontinued or lost to follow-up subjects, including deaths
- Summary of safety and effectiveness data using descriptive statistics of study results as of report period
- Rationale for not meeting study milestones/timeline with a revised study timeline, as applicable
- Revised reporting schedule with rationale for revision, as applicable

20.6 SAMPLE SIZE CALCULATIONS

With 80 subjects and a rate of 0.025 for severe visual distortions, this study has 86% probability of achieving a half-width of 0.05 for a 95% confidence interval for the rate of severe visual distortions.

APPENDIX A SUMMARY OF PROCEDURES REQUIRED AT EACH VISIT

Examination X= To be performed A= To be performed if a visual distortion is spontaneously reported prior to 6 month exam or prior to a required IOL repositioning (adverse event) B=To be performed if a subject reports a severe visual distortion or experiences a serious or device-related adverse event at this visit. O = Only if medically indicated	Preoperative Both eyes	Op 1 1st eye	Op 2 2nd eye	Unscheduled Visit	1 Month Both eyes	6 Months Both eyes	1 Year[a] Both eyes
Ocular history, inclusion/exclusion criteria	X						
Informed consent	X						
Potential visual acuity	X						
Targeted refraction/Targeted cylinder/IOL power calculations[b]/axial length	X						
Lens power/serial number/operative procedures		X	X				
UCDVA-photopic, monocular (Snellen)	X			B	X	X	X
UCDVA-photopic, binocular (Snellen)				B	X	X	X
Manifest refraction (Snellen)	X			B	X	X	X
BCDVA-photopic, monocular (Snellen)	X			B	X	X	X
BCDVA-photopic, binocular (Snellen)				B	X	X	X
Offer spectacle and/or contact lens prescription					X		
Keratometry	X			A/B	A	X	X
Intraocular pressure	X			B	X	X	X
Biomicroscopic slit-lamp exam[c]	X			B	X	X	X
Toric IOL axis measurement at dilated slit-lamp exam				A	A	X	X
Dilated fundus exam	X			O	O	O	O
Adverse events		X	X	X	X	X	X
Ocular medications	X			X	X	X	X
Subject questionnaire	X			A	A	X	X

[a] Examination at 1 year is to be conducted ONLY if a subject reported a severe visual distortion at 6 months or if the subject experienced an IOL repositioning procedure (due to IOL misalignment) during the study.
[b] Includes documentation of toric IOL calculations showing chosen ZCT for each eye and targeted cylinder outcome
[c] Includes determination of medical and lens findings/complications, including lens rotation

APPENDIX B TORIC IOL AXIS MEASUREMENT AT SLIT LAMP

All investigative sites will be equipped with slit lamps that fulfill the following requirements:

1) The slit lamp is capable of producing a narrow and long slit-lamp beam,

2) the slit lamp allows 180° rotation of the slit-lamp beam and

3) the slit lamp can be fitted with an angular scale with markers which allow for estimation of axis measurement to within 1° as measured by the slit-lamp beam.

Upon installation of the angular scale and leveling of the slit lamp, the angular scale will be calibrated with a spirit level to ensure that the scale is at 90° for vertical slit-beam position and 0°/180° for the horizontal slit beam position. (A.N. Mukherjee, C. So, V. Kumar. "Clinical and experimental validation of a slit lamp modification to measure toric lens position," Contact Lens & Anterior Eye, 34 (2011) 111-113)

The following instructions are to be followed for the measurement of the toric IOL axis in both eyes.

1. Dilate each eye with 2.5% phenylephrine prior to measurement. Tropicamide (1%) may be used in addition to achieve adequate dilation for visualization of the axis orientation marks.
2. Allow sufficient time to achieve adequate pupillary dilation to facilitate direct visualization of alignment marks.
3. At the slit lamp, adjust the slit-lamp beam to be as narrow and as long as possible and align the beam with at least one of the four axis orientation marks (4.5, 5.0, 5.5 and 6.0 mm diameter) on each side of the toric IOL.
    a. It is important to align the beam with the orientation marks on both sides for an accurate measurement. If both sides are not visible in the slit lamp, align the beam with at least three axis orientation marks from the visible side of the IOL.
    b. Ensure the subject's head is oriented vertically in the slit lamp with proper head position and alignment of the eye with the slit lamp.
4. Based on alignment of the narrowed slit-lamp beam with the toric IOL axis orientation marks, read the angle from the angular scale on the slit lamp.
5. Record this angle in degrees for each eye on the appropriate postoperative case report form.

APPENDIX C SLIT-LAMP EXAM RATINGS

A. Ratings of Aqueous Cells and Flare

For consistency across study sites, the SUN (Standardization of Uveitis Nomenclature) Working Group Grading Scheme is to be used for grading of anterior chamber cells and flare as reported in: Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop; The standardization of uveitis nomenclature (SUN) working group. Am J Ophthalmol 2005;140:509-516.

CELLS

Grade	Cells in Field (Field is a 1x1 mm slit beam)
0	<1
0.5+	1 - 5
1+	6 - 15
2+	16 - 25
3+	26 - 50
4+	>50

FLARE

Grade	Description
0	None
1+	Faint
2+	Moderate (iris and lens details clear)
3+	Marked (iris and lens details hazy)
4+	Intense (fibrin or plastic aqueous)

B. Ratings of Corneal Edema

Corneal edema should be classified according to the haziness of the epithelium, the number of microcysts observed, and the clouding of the stroma.

Amount	Grade	Description
None	0	Normal transparency: a. No epithelial or sub-epithelial haziness b. No microcysts c. No stromal cloudiness
Trace	+1	a. Barely discernible localized epithelial or sub-epithelial haziness, and/or b. 1 to 20 microcysts, and/or c. Barely discernible localized stromal cloudiness
Mild	+2	a. Faint but definite localized or generalized epithelial, sub-epithelial or stromal haziness/cloudiness, and/or b. 21-50 microcysts
Moderate	+3	a. Significant localized or generalized epithelial, sub-epithelial or stromal haziness/cloudiness and/or b. 51-100 microcysts
Severe	+4	a. Definite widespread epithelial or stromal cloudiness, giving dull glass appearance to cornea or numerous coalescent bullae (please note the number and location of bullae), and/or b. >100 microcysts or bullae, and/or c. Numerous striae (please note the number and location of striae or folds)

C. Posterior Capsule Striae Grading Scale

The following five-point grading scale is to be used for rating striae in the posterior capsule:

Amount	Grade	Description
None	0	None
Trace	+1	One detectable, barely noticeable striae
Mild	+2	One or two prominent striae
Moderate	+3	Three or more prominent striae, but visibility of retina is not impacted
Severe	+4	Three or more prominent striae affecting visualization of retina

D. Posterior Capsule Opacification Grading Scale

Below is the five-point grading scale to be used for PCO determination:

Amount	Grade	Description
None	0	Normal posterior capsule with no area of opacity. Red reflex bright.
Trace	+1	Some loss of transparency involving the posterior capsule. Red reflex fairly bright
Mild	+2	Mild loss of transparency with cloudiness extending through most of the posterior capsule. There may be a few Elschnig's pearls in the posterior capsule. Red reflex mildly diminished.
Moderate	+3	Moderate loss of transparency with difficulty visualizing the retina. There may be multiple Elschnig's pearls in the posterior capsule. Red reflex markedly diminished.
Severe	+4	Posterior capsule very opaque with inability to view the retina. The posterior capsule may have confluent Elschnig's pearls and fibrous scarring. Red reflex barely visible.

E. IOL Glistenings

Use the following scale to grade IOL glistenings, using a slit beam 2.0 mm wide and 10.0 mm long:

Amount	Grade	Description
None	0	No glistenings visible
Rare	+0.5	<10 glistenings visible
Trace	+1	10-19 glistenings visible
Mild	+2	20-29 glistenings visible
Moderate	+3	30-39 glistenings visible
Severe	+4	≥ 40 glistenings visible

APPENDIX D ADVERSE EVENT AND COMPLAINT REPORTING INSTRUCTIONS

All adverse events and complaints related to using AMO products must be reported to AMO.

ALL ADVERSE EVENTS AND COMPLAINTS:

For events that are not considered serious and/or related to the study device:

1. Record the event and/or complaint on the case report form that corresponds to the visit during which awareness of the event occurred. Additionally, a complaint may be reported via a telephone call to AMO.
2. Complete the case report form in AMO's data management system in a timely manner, preferably within 1 week of the study visit.

SERIOUS ADVERSE EVENTS OR DEVICE DEFICIENCIES THAT MAY HAVE LED TO A SERIOUS EVENT

In the event of a serious event (i.e., life- or sight-threatening incident), or a device deficiency that may have led to a serious event, the investigator shall:

1. Notify AMO immediately (no more than 48 hours after learning of the event) as follows:
   a. Contact the following AMO personnel by phone or email:

   b. If a serious adverse event, also complete the Serious or Device Related Adverse Event Form in AMO's data management system.

NON-SERIOUS, DEVICE-RELATED EVENTS

For events that are not considered serious but are believed related to the study device (ADEs):

1. Complete the Serious or Device Related Adverse Event Form
2. Submit the completed Serious or Device Related Adverse Event Form to AMO within a timely manner.