SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:

Toric Monofocal One-Piece Posterior Chamber Intraocular Lens (IOL)

Device Trade Name:

TECNIS® Toric 1-Piece Intraocular Lens, Models ZCT150, ZCT225, ZCT300, ZCT400 and TECNIS® Toric Calculator System

Device Procode: MJP

Applicant's Name and Address:

Abbott Medical Optics Inc.
1700 East. Saint. Andrew Place
Santa Ana, CA 92705

Date(s) of Panel Recommendation: none

Premarket Approval (PMA) Application Number: P980040/S039

Date of FDA Notice of Approval to Applicant: April 15, 2013

Expedited: Not applicable

TECNIS® Toric 1-Piece Intraocular Lenses (IOLs) are a modification to the parent lens, SENSAR® 1-Piece IOL (Model AAB00), which was approved under PMA P980040/S015 on October 30, 2007. SENSAR® 1-Piece lenses are indicated for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed by phacoemulsification. These devices are intended to be placed in the capsular bag. The purpose of this PMA Supplement is to obtain FDA approval for the TECNIS® Toric 1-Piece IOLs, which shares the same material and manufacturing processes as the parent lens, but has the following different design characteristics: 1) a modified prolate (aspheric) anterior surface, 2) perpendicular maximum and minimum radii of curvature, and 3) two sets of four (8) axis orientation marks located on the anterior optic of the lens. The different design features of the TECNIS® Toric 1-Piece IOLs allows for the visual correction of aphakia and pre-existing corneal astigmatism in adult patients with or without presbyopia.

II. INDICATIONS FOR USE

The TECNIS® Toric 1-piece posterior chamber lenses 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 in residual refractive cylinder and increased spectacle independence for distance vision. The device is intended to be placed in the capsular bag.

III. CONTRAINDICATIONS

None

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the TECNIS® Toric 1-Piece IOL labeling.

V. DEVICE DESCRIPTION

The TECNIS® Toric 1-Piece IOL is an ultraviolet light (UV)-absorbing posterior chamber intraocular lens on a one-piece enhanced monofocal platform. The lens is designed for the visual correction of aphakia and pre-existing corneal astigmatism in adult patients with or without presbyopia. The lens is available in various cylinder powers, which are reflected in the model numbers; ZCT150 (1.50 D), ZCT225 (2.25 D), ZCT300 (3.00 D) and ZCT400 (4.00 D). All models of the TECNIS® Toric 1-Piece IOL are available in the spherical equivalent diopter (D) range of +5.0 D to +34.0 D in 0.5 D increments.

The TECNIS® Toric 1-Piece IOL is an extension of AMO's SENSAR® 1-Piece IOL, Model AAB00 and its optic and haptics are both made of the same hydrophobic SENSAR acrylic material. The TECNIS® Toric 1-Piece IOL is similar to its parent lens, Model AAB00, with the addition of 1) a modified prolate (aspheric) surface, 2) perpendicular maximum and minimum radii of curvature, and 3) two sets of four axis orientation marks, all located on the anterior optic of the lens. The axis orientation marks are located in the periphery of the anterior optic and indicate the meridian of the lowest power (flat meridian) for proper alignment of the flat meridian of the IOL with the steep meridian of the corneal curvature.

The aspheric design of the lens optic is identical to the aspheric design of the commercially available TECNIS® 1-Piece IOL, Model ZCB00 (PMA P980040/S015). The TECNIS® Toric 1-Piece IOL has a biconvex optic shape with additional cylinder power on the anterior surface,

and similar to the TECNIS® 1-Piece IOL, Model ZCB00, a 6mm squared posterior optic and an overall length of 13mm. A summary of the physical characteristics of the TECNIS® Toric 1-Piece IOL is provided in **Table 1**.

The new TECNIS® Toric 1-Piece IOL is designed to provide aphakic cataract patients with corneal astigmatism improved uncorrected distance vision, reduction in residual refractive cylinder and increased spectacle independence for distance vision. This lens model was validated in accordance with American National Standards Institute (ANSI) Z80.30 standard for toric IOLs dated March 24, 2010, and applicable International Organization for Standardization (ISO) test requirements.

Table 1: Summary of Physical Characteristics

TECNIS® Toric 1-Piece IOL				
Model Numbers	ZCT150	ZCT225	ZCT300	ZCT400
Optic Type	Biconvex Aspheric Toric Optic			
Optic/Haptic Material * Measured in Water	Hydrophobic SENSAR soft acrylic material with polyethylene glycol surface treatment UV cutoff at 10% Transmittance: 375nm* (5.00 diopter lens) 380nm* (34.00 diopter lens)			
IOL Spherical Equivalent Power (Diopter)	+5.00 D to +34.00 D in +0.50 D increments			
IOL Cylinder Power (Diopter)	1.50 D	2.25 D	3.00 D	4.00 D
Index of Refraction	1.47 at 35°C			
Haptic Configuration	TRI-FIX design Modified C, integral with optic			
Optic Diameter	6.0mm			
Overall Length	13.0mm			
Haptic Angle	0°			

The TECNIS® Toric Calculator System is an online service comprised of a centrally hosted database application accessed by the surgeon and system administrators through the Internet using a personal computer and common web browser software.

The TECNIS® Toric Calculator System helps select the appropriate TECNIS® Toric 1-Piece lens for each patient. It considers the preoperative corneal astigmatism of the patient, as well as any anticipated surgically induced astigmatism (SIA) in determining the resultant postoperative corneal astigmatism correction. The anticipated SIA in predicting the postoperative corneal astigmatism is used with other biometric parameter data to calculate the optimum intraocular lens toricity of the patient. The TECNIS® Toric Calculator System calculates different cylinder lens power options as well as the orientation in which the lens should be implanted to achieve optimum results. In addition, predicted postoperative residual astigmatism is calculated for each suggested lens model when placed into the indicated orientation to facilitate the surgeon's lens selection.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

A cataract is a condition typically caused by aging of the human eye, in which the crystalline lens of the eye becomes increasingly less transparent. It is a progressive condition that gradually impairs the function of the eye by increasing light scatter and preventing a clear image from forming on the retina, thereby decreasing visual acuity. Surgical removal of the cataractous lens may be necessary if visual loss is significant. Absence of the natural lens (aphakia) results in the inadequacy of the refracting power of the eye. Normal vision cannot be obtained due to the inability of the eye to focus on any object within the visual field. Thus, cataract extraction must be followed by some form of optical correction such as eye glasses, contact lenses, or intraocular lenses.

1. Cataract spectacles are an effective means of correction, but may result in some visual distortion because of the high plus power of the lens. The image of the object being viewed is highly magnified (15% to 20%) and confined to the center of the field, so that peripheral vision is highly restricted. In addition, a monocular cataract lens induces such retinal image size disparity between the phakic and aphakic eyes that this method is essentially inappropriate for the monocular aphake.

2. Contact lenses are another available method. They have reduced image magnification and improved visual field compared to cataract spectacles, but they are not tolerated by all patients. In particular, elderly patients are frequently reluctant or unable to manipulate contact lenses or to undertake the cleaning and disinfection processes.

Approximately one-fourth of cataract patients have more than 1.00 diopter of refractive astigmatism (either corneal or lenticular). For those patients, several methods can be employed to reduce the amount of astigmatism; including surgical and non-surgical methods.

3. Other approved intraocular lenses may be used for visual correction after cataract surgery, including non-toric lens implantation. Implantation of non-toric IOLs will require supplemental astigmatism correction such as spectacles, toric contact lenses and refractive surgery.

4. Limbal relaxing incisions, peripheral corneal relaxing incisions, or intraoperative surgical incision(s) on the steep axis of the cornea can reduce residual astigmatism. However, alteration of the corneal shape to correct astigmatism requires a predictable healing response, which is not always possible, especially when high levels of astigmatic correction are involved.

VII. MARKETING HISTORY

The TECNIS® Toric 1-Piece IOL is currently available outside of the United States in Australia, European Union, Egypt, Hong Kong, Norway, New Zealand, Saudi Arabia, South Africa and Taiwan. The lenses have not been withdrawn or recalled from any country for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events and complications accompanying cataract or implant surgery may include, but are not limited to the following: corneal endothelial damage, infection (endophthalmitis), retinal detachment, vitritis, cystoid macular edema, corneal edema, pupillary block, iris prolapse, hypopyon, elevated IOP requiring treatment, and secondary surgical intervention.

Secondary surgical interventions include, but are not limited to, lens repositioning (due to decentration, rotation, subluxation, etc.), lens replacement, vitreous aspirations or iridectomy for pupillary block, wound leak repair, retinal detachment repair, corneal transplant, and lens replacement due to refractive error or severe inflammation.

For the specific adverse events that occurred during the TECNIS® Toric 1-Piece IOL clinical study, please see the *Summary of Primary Clinical Study* section below.

IX. SUMMARY OF PRECLINICAL STUDIES

Preclinical studies performed demonstrate the safety and effectiveness of the TECNIS® Toric 1-Piece IOLs and the TECNIS® Toric Calculator System. The results of these studies are summarized below.

A. Laboratory Studies

1. Physicochemical Testing

All physicochemical reports pertaining to the SENSAR soft acrylic material were previously submitted to FDA in 2007 as part of the 180-Day PMA Supplement for the parent SENSAR® 1-Piece IOL (P980040/S015). Testing of the SENSAR® 1-Piece IOL was performed to demonstrate equivalence to the material parent, SENSAR® Model AR40e, approved in P980040. The physicochemical characterization of the TECNIS® Toric 1-Piece IOL material met the requirements of the International Standards, ISO 11979-5, *Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility*. The physicochemical tests are summarized in **Table 2**. All acceptance criteria for physicochemical testing were met.

Table 2: Physicochemical Test Summary, Surface-Treated Acrylic 1-Piece IOL, Indicating Relationship to the SENSAR® AR40e IOL

Physicochemical Tests	Purpose	Acceptance Criteria	Results of Testing
Exhaustive Extraction	Evaluate extractable components to assess the risk for potentially harmful effects	Qualitative and quantitive analysis of extractable components equivalent to clinically studied material parent lens	Equivalent to AR40e* approved under PMA P980040
Leachables	Evaluate extractable components under simulated physiological conditions to assess the risk for potentially harmful effects	Qualitative and quantitive analysis of extractable components equivalent to clinically studied material parent lens	Equivalent to AR40e approved under PMA P980040
Insoluble Inorganics	Evaluate the presence of residual insoluble inorganics on and in the lens to assess the risk of potentially harmful effects	No hazardous components identified	Passed
Hydrolytic Stability	Evaluate the stability of the material in an aqueous environment to assess the risk for potentially harmful effects	Stable to 5 years equivalent age	Passed
Photostability	Evaluate degradation products following simulated *in* situ exposure to UV radiation to assess the risk of potential harmful effects	Stable to 20 years equivalent age	Passed
Nd-YAG Laser	Evaluate release of cytotoxic substances due to Nd-YAG laser exposure	Analysis of exposure medium equivalent to clinically studied material parent lens	Equivalent to AR40e approved under PMA P980040

*The SENSAR® AR40e IOL has the OptiEdge design and was approved in the same PMA (P980040) as the SENSAR® AR40 IOL, which has a rounded optic edge design.

2. Dimensional, Optical, and Mechanical Testing

Dimensional, optical, and mechanical testing was performed on finished, sterilized, TECNIS® Toric 1-Piece IOLs to verify the conformance of the design to the ANSI Standard for Toric IOLs, ANSI Z80.30 *Ophthalmics – Toric Intraocular Lenses,* as well as the International Standards ISO 11979-2 - *Part 2: Optical properties and test methods*, and ISO 11979-3, *Part 3: Mechanical properties and test methods*, and internal specifications. Folding and insertion testing was also performed to verify recovery of lens properties following simulated insertion. The TECNIS® Toric 1-Piece IOLs passed all requirements established in ANSI Z80.30, ISO 11979-2, ISO 11979-3 standards, and product specifications. A summary of the results of the

dimensional, optical and mechanical testing performed on the TECNIS® Toric 1-Piece IOLs are summarized in **Table 3**.

Table 3: Dimensional, Optical and Mechanical Test Requirements Summary

Requirement	Result		
Optical Requirements			
Dioptric Power	Power Range (D)	Spherical Acceptance Criteria	Cylinder Acceptance Criteria
	≤ 15.0	±0.3D	±0.4D
	15.0 < P ≤ 25.0	±0.4D	±0.4D
	25.0 < P ≤ 30.0	±0.5D	±0.5D
	>30.0	±1.0D	±0.5D
Image Quality (Post-Folding)	Greater or equal to 0.43 or 70% of maximal theoretical MTF value		
Axis Orientation Mark(s)	Combined angular errors of the cylindrical axis mark and any deviation from orthogonality between the meridians of highest and lowest dioptric power within ±5°		
Spectral Transmittance (20 D lens)	% T > 90% at 600nm % T=10% at ~380nm		
Mechanical Requirements			
Overall Diameter	13.00 ± 0.20mm		
Vault Height	± 0.25mm from nominal		
Sagitta	± 0.35mm from nominal		
Clear Optic Diameter	>4.50mm		
Optic Body Diameter	6.00 ± 0.10mm		
Axial Displacement in Compression	0.11 mm ± 0.062mm		
Optic Decentration	Mean + 2SD= 0.076mm < 0.60mm (10% clear optic)		
Optic Tilt	Mean + 2SD = 2.98° < 5°		
Angle of Contact	42° ± 1.0°		
Compression Force and Decay	0.39 mN ± 0.05		
Dynamic Fatigue Durability	No breakage or damage after 250,000 cycles of haptic compression		
Loop Pull Strength	0.79 N ± 0.143		
Surface and Bulk Homogeneity	Essentially free from defects and deviations from intended features of design when inspected under 10x magnification		

Recovery of Properties Following Simulated Surgical Manipulation			
Dioptric Power	Power Range (D)	Spherical Acceptance Criteria	Cylinder Acceptance Criteria
	≤ 15.0	±0.3D	±0.4D
	15.0 < P ≤ 25.0	±0.4D	±0.4D
	25.0 < P ≤ 30.0	±0.5D	±0.5D
	>30.0	±1.0D	±0.5D
Image Quality	Greater or equal to 0.43 or 70% of maximal theoretical MTF value		
Overall Diameter	13.00 ± 0.20mm		
Sagitta	± 0.35mm from nominal		
Surface and Bulk Homogeneity	Essentially free from defects and deviations from intended features of design when inspected under 10x magnification		

SD=standard deviation

3. Sterilization, Packaging, Shelf Life and Transport Stability Testing

The TECNIS® Toric 1-Piece IOLs are packaged in a polycarbonate lens case, sealed with a Tyvek lid, and placed in a Tyvek/Mylar pouch. Pouched lenses are sterilized using ethylene oxide (EO). Testing performed in association with the EO sterilization process demonstrates that lenses meet the requirements for sterility assurance, bacterial endotoxin levels, and ethylene oxide residual levels. Testing conducted in support of the package integrity, shelf life, and transport stability demonstrates that the packaging configuration maintains its sterile barrier and protects the lens during transport. These tests were conducted in accordance with the following Standards and United States Pharmacopoeial chapters:

- ANSI/AAMI/ISO 11135-1, *Sterilization of Healthcare Products – Ethylene Oxide – Part 1: Requirements for Development, Validation, and Routine Control of a Sterilization Process*
- ISO 10993-7, *Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals*
- 34/29 USP 2011, *Bacterial Endotoxin Testing*
- ISO 11979-6, *Ophthalmic Implants – Intraocular Lenses – Part 6: Shelf-life and transport stability*

The results of the sterilization, packaging, shelf life and transport stability studies are summarized in **Table 4**.

Table 4: Sterilization, Packaging, Shelf Life and Transport Stability Test Results

Test	Results
Sterility Testing	No microbial growth detected
Bacterial Endotoxin	Endotoxin levels were below the Agency's recommended limit for medical devices of 0.02 EU/ml
Ethylene Oxide Residuals	EO ≤ 0.5µg per lens per day EO ≤ 25ppm per lens ECH ≤ 2µg per lens per day ECH ≤ 25ppm per lens
Package Integrity	Results demonstrate no leak in the package seals
Shelf Life	Results support a 4 year shelf-life
Transport Stability	The results showed that the lenses would not be damaged during shipping

EU=endotoxin units

B. Animal Studies

1. Biocompatibility Testing

The TECNIS® Toric 1-Piece IOL is made of the same SENSAR soft acrylic material and has the same manufacturing contact materials previously qualified with the parent model, the SENSAR® 1-Piece IOL, Model AAB00. With the exception of genotoxicity testing, all other biocompatibility tests conducted on the SENSAR® 1-Piece IOL parent model were previously submitted to FDA in 2007 as part of the PMA Supplement, P980040/S015. The biocompatibility studies were performed in accordance with the requirements in ISO 10993, *Biological Evaluation of Medical Devices*, and 11979-5 *Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility* guidelines to establish a complete profile of the IOL material. The results are summarized in **Table 5.** All acceptance criteria for biocompatibility were met.

Table 5: Biocompatibility Test Summary for the TECNIS® Toric 1-Piece IOL

Biological Tests	Results of Testing
Cytotoxicity: MEM	Non-cytotoxic
Agar Diffusion solid & saline extract	Non-cytotoxic
Percent Inhibition of Cell Growth Method (%ICG)	Non-inhibitory to cell growth
Guinea Pig Maximization a. Saline Extract b. Sesame Oil Extract	Non-sensitizing Non-sensitizing
Non-ocular Implant Study (Six-Week Subcutaneous Implantation in Rabbits)	No macroscopic signs of inflammation. Histology showed no differences in biological response between non-treated and treated samples or the USP negative control. No appreciable changes in UV transmittance. No material degradation (including calcification) was noted.
Six-Month Rabbit Intraocular Study	No mortality or test article-related decrease in body weight was observed. There were no differences in the type and incidence of ocular reactions with the eyes implanted with the test or control lens. No appreciable changes in UV transmittance. No material degradation (including calcification) noted.
Genotoxicity Testing (*Salmonella typhimurium* and *Escherichia coli* reverse mutation assay)	Non-genotoxic, non-mutagenic
Genotoxicity Testing (Chromosomal aberration assay in Chinese hamster ovary [CHO] cells)	Non-clastogenic

C. Additional Testing

1. Chemical Characterization Testing

Additional chemical characterization testing was conducted, including a Cleanliness Evaluation, on specially manufactured TECNIS® Toric 1-Piece IOLs with ten times the number of axis orientation marks (80 instead of 8) as worst-case representatives. The chemical characterization studies as well as the leachables and insoluble inorganics testing for the Cleanliness Evaluation met all acceptance criteria and are summarized in **Table 6.**

Table 6: Additional Chemical Characterization Testing

Additional Testing	Purpose	Acceptance Criteria	Results of Testing
X-ray photoelectron spectroscopy (XPS/ESCA)	To ensure that materials such as process aids are not trapped within the axis orientation marks	No unexpected lens materials elements	Passed
Presterilization for bioburden, bacterial endotoxins and cytotoxicity	To ensure that materials such as process aids are not trapped within the axis orientation marks	0 CFU/lens, < 0.02 EU/lens, and 0% cell lysis	All results met acceptance criteria
Cleanliness Evaluation (Leachables and Insoluble Inorganics testing of lenses with 10x axis marks).	To ensure that materials such as process aids are not trapped within the axis orientation marks	Comparable to controls	The leachables and insoluble inorganics test results met all acceptance criteria

CFU=colony forming units
EU=endotoxin units

2. Software Validation

A software validation was performed for the TECNIS® Toric Calculator System according to the procedures described in FDA's Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices for software Level of Concern: MAJOR. The software for this device was developed under an appropriate software development program. A hazard analysis was performed from both the patient's and user's standpoint and all identified hazards were addressed. These procedures provide the foundation for assuring, to the extent possible, that the software will operate in a manner described in the specifications, and in no other way.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

A. Study Design

The clinical investigation of the TECNIS® Toric 1-Piece IOLs, Models ZCT150, ZCT225, ZCT300 and ZCT400 (Protocol TIOL-103-TCNS) was designed to evaluate the safety and effectiveness, including the ability to reduce astigmatism, of the TECNIS® Toric IOLs. This was a pivotal, prospective, multicenter, two-armed, bilateral, six-month study conducted between March 2010 and September 2011 at 14 sites in the USA and Canada. The first arm of the study was a randomized, comparative, double-masked (subject and technician) evaluation of the TECNIS® Toric Model ZCT150 versus the TECNIS® Model ZCB00 control IOL; this arm was referred to as the Randomized Control Arm (RCA). The second arm of the study was an open-label, non-comparative clinical trial of the TECNIS® Toric IOLs, Models ZCT225, ZCT300 and ZCT400; this arm was referred to as the Open Label Arm (OLA).

The four TECNIS® Toric1-Piece IOL models in the clinical study and their corresponding cylinder powers are listed below in **Table 7**. The corneal astigmatism correction ranges are for the combined corneal astigmatism based on a vector sum of preoperative corneal astigmatism (preop Kcyl) and the predicted effect of surgically induced astigmatism (SIA).

Table 7: TECNIS® Toric 1-Piece IOLs

IOL Model	Cylinder Power (D)		Correction ranges based on combined corneal astigmatism (preop Kcyl + SIA)
	IOL Plane	Corneal Plane	
ZCT150	1.50	1.03	0.75 – 1.50 D
ZCT225	2.25	1.55	1.50 – 2.00 D
ZCT300	3.00	2.06	2.00 – 2.75 D
ZCT400	4.00	2.74	2.75 – 3.62 D

1. Subject Selection and Implantation Criteria

All subjects were enrolled from the normal cataract surgical populations at the investigative sites. In general, subjects were to have healthy eyes with preoperative keratometric cylinder (Kcyl) of 0.75 D to 3.62 D in both eyes (with exception of second eyes in the RCA), and no pathology other than cataract in both eyes. The following is a summary of the subject inclusion/exclusion criteria:

Subject Inclusion Criteria

- Age 18 or greater
- Cataract(s) for which phacoemulsification extraction and posterior IOL implantation have been planned for both eyes
- Preoperative best corrected distance visual acuity (BCDVA) of 20/40 or worse, with or without a glare source
- Visual potential of 20/30 or better in each eye
- Preoperative keratometric cylinder of 0.75 D to 3.62 D (with exception of second eyes in the RCA with <0.75 D)

Subject Exclusion Criteria

- Requiring an intraocular lens outside the spherical power range of +15.0 to +28.0 D
- Pharmacologically dilated pupil size less than 5.5 mm *(for lens axis analyses)*
- Use of systemic or ocular medications that may affect vision or likely to impact pupil dilation or iris structure
- Acute or chronic disease or illness that would increase the operative risk or confound study outcome(s) (e.g., poorly controlled diabetes)
- Uncontrolled systemic or ocular disease
- History of ocular trauma or prior ocular surgery or subjects expected to require retinal laser treatment or other surgical intervention
- Presence of ocular pathology other than cataract such as:
    - Amblyopia or strabismus
    - Corneal abnormalities (including irregular astigmatism)
    - Pupil abnormalities
    - Capsule or zonule abnormalities
    - Intraocular inflammation
    - Known pathology that may affect visual acuity and/or are predicted to cause future acuity losses to a level of 20/30 or worse (e.g., macular degeneration
- Inability to achieve keratometric stability for contact lens wearers

Subjects were assigned to a study arm based on each eye's preoperative Kcyl and the toric lens calculator output to achieve emmetropia (±0.25 D) and were to be implanted as follows in **Table 8**.

Table 8: Summary of Study Arm Groups

Study Arm	Study IOLs	Preoperative Keratometric Cylinder	Planned Implantation
Randomized Control Arm: RCA	Toric ZCT150 Control ZCB00	Both Eyes: 0.75 – 1.50 D	Bilateral implantation with toric ZCT150 or ZCB00 control IOLs per randomization
		First Eye: 0.75 – 1.50 D Second Eye: 0.00 – 0.74 D	First eye implantation with toric ZCT150 or ZCB00 control IOL per randomization; Second eye implantation with ZCB00 control lens
Open Label Arm: OLA	Toric ZCT225, ZCT300, ZCT400	Both Eyes: 1.50 – 3.62 D	Highest cylinder eye to be implanted first
		First eye: 1.50 – 3.62 D Second Eye: 0.75 – 1.50 D	Highest cylinder eye to be implanted first; Second eye implantation with ZCT150

2. Follow-up Schedule

The clinical study visit schedule is presented in **Table 9**.

Table 9: Summary of Clinical Study Visit Schedule

Visit	Exam	Eyes Evaluated	Visit Window
1	Preoperative Exam	Both Eyes	Within 30 days prior to 1st surgery
2	Operative	1st Eye	0-30 days following preoperative exam
3	Postop 1 (1 day)	1st Eye	1-2 days postoperative
4	Postop 2 (1 week)*	1st Eye	7-14 days postoperative
5	Operative	2nd Eye	Within 1 month after 1st eye surgery
6	Postop 1 (1 day)	2nd Eye	1-2 days postoperative
7	Postop 2 (1 week)	2nd Eye	7-14 days postoperative
8	Postop 3 (1 months)	Both Eyes	30-60 days postop from 2nd eye surgery
9	Postop 4 (3 months)	Both Eyes	80-100 days postop from 2nd eye surgery
10	Postop 5 (6 months)	Both Eyes	120-180 days postop from 2nd eye surgery

* Postop 2 for the first eye was to be completed prior to surgery on the second eye.

3. Clinical Endpoints

The primary effectiveness endpoint was the mean percent reduction in cylinder, which is the achieved reduction in cylinder (postoperative refractive cylinder - preoperative Kcyl) as a percentage of the intended reduction in cylinder (target refractive cylinder - preoperative Kcyl). Secondary effectiveness endpoints were mean uncorrected distance visual acuity and the percent of eyes 20/20 or better, as well as spectacle independence at distance. The primary safety endpoints were the percent of eyes achieving best corrected distance visual acuity of 20/40 or better vs. ISO 11979-7 Safety and Performance Endpoint (SPE) rates, lens axis misalignment of toric IOLs (specifically the percent of eyes with $\leq 5^{o}$ of rotation at two consecutive visits), visual disturbances, and complication and adverse events rates vs. ISO 11979-7 SPE rates. The critical time point for analyses was the 6-month visit and the primary analysis group was first eyes from both study arms. Endpoints were analyzed for three population groups: safety (all implanted eyes), intent-to-treat with data imputation for missing

values (ITT; included all implanted eyes and all subjects randomized but not necessarily implanted), and per-protocol (subjects/eyes without any protocol deviations).

Statistical Methods

For the primary effectiveness endpoint (mean percent reduction in cylinder) and the secondary effectiveness endpoint (mean UCDVA), superiority testing was performed in the RCA with comparisons between toric and control first eyes evaluated using one-sided, two-sample t-tests. For the secondary effectiveness endpoint of spectacle independence, superiority testing was also performed in the RCA with comparisons between IOL groups using a one-sided Fisher's exact test. For the ITT analyses of these endpoints, missing data were imputed using propensity analyses followed by the t-test for reduction in cylinder and UCDVA and by logistic regression for spectacle independence. For the OLA, the achieved proportions (UCDVA 20/20 or better and spectacle independence) were compared to target proportions (6% and 15%, respectively) using a one-sided Fisher's exact test. For the mean percent reduction in cylinder for the OLA, the mean value was compared to a target mean of 25% reduction using a one-sided, one-sample t-test.

For the safety endpoints of BCDVA and complications/adverse events, study rates for the toric IOLs were compared to ISO SPE rates using a one-sided exact test based on the binomial distribution. For rotational stability, the proportion of the toric eyes with $\leq 5^{o}$ of rotation between consecutive visits was reported in accordance with the ANSI Standard for Toric IOLs, Z80.30.

Study sample size was based on the ANSI Standard for Toric IOLs, Z80.30, as well as the requirements for a modification of a parent lens.

B. Subject Enrollment and Accountability

A total of 269 subjects were enrolled in the study; 197 were in the Randomized Control Arm (RCA) and 72 in the Open Label Arm (OLA). Of the 197 in the RCA, 95 were implanted in the first eye with the control ZCB00 lens and 102 with a ZCT150 toric lens. Of the 72 subjects in the OLA, 55 were implanted in the first eye with the higher cylinder lenses, ZCT300 and ZCT400 (>2 D of cylindrical correction at the corneal plane). Overall, a total of 174 first eyes were implanted with a TECNIS® Toric 1-Piece IOL (102 ZCT150, 17 ZCT225, 25 ZCT300 and 30 ZCT400). These enrollment numbers meet the ANSI Standard for Toric IOLs, Z80.30, for enrollment requirements. Six additional subjects in the RCA were also consented and

randomized but not implanted; these subjects were included in the intent-to-treat (ITT) population only.

Subject accountability at six months is presented in **Table 10**. Compliance was excellent with 98.5% (265/269) of all subjects completing the 6-month visit and 96.3% (259/269) of all subjects completed the 6-month exam in interval. Only four subjects (1.5%; 4/269) were lost-to-follow-up during the 6-month study due to reasons unrelated to vision (three subjects died and one moved out-of-state).

Table 10:
Subject Accountability (based on First Eyes) by IOL Model at Six Months
Randomized Control Arm and Open Label Arm
Safety, ITT and Per-Protocol Populations

		Randomized Control Arm				Open Label Arm					
		ZCT150		ZCB00		ZCT225		ZCT300		ZCT400	
Population	**Subject Status**	n	%	n	%	n	%	n	%	n	%
Safety	**N Total**	**102**		**95**		**17**		**25**		**30**	
	Available for Analysis[a]	**101**	**99.0**	**93**	**97.9**	**17**	**100**	**25**	**100**	**29**	**96.7**
	Out of Interval[b]	3	2.9	2	2.1	0	0.0	0	0.0	1	3.3
	Missing Subjects	**1**	**1.0**	**2**	**2.1**	**0**	**0.0**	**0**	**0.0**	**1**	**3.3**
	Discontinued	1[c]	1.0	2[d]	2.1	0	0.0	0	0.0	1[d]	3.3
Intent-to-	**N Total**	**103**		**100**		**17**		**25**		**30**	
treat (ITT)	**Available for Analysis**[a]	**101**	**98.1**	**93**	**93.0**	**17**	**100**	**25**	**100**	**29**	**96.7**
	Out of Interval[b]	3	2.9	2	2.0	0	0.0	0	0.0	1	3.3
	Missing Subjects	**1**	**1.0**	**2**	**2.0**	**0**	**0.0**	**0**	**0.0**	**1**	**3.3**
	Discontinued	1[c]	1.0	2[d]	2.0	0	0.0	0	0.0	1[d]	3.3
	Randomized but not implanted	**1**	**1.0**	**5**	**5.0**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**
Per-	**N Total**[f]	**90**		**88**		**17**		**24**		**29**	
Protocol[e]	**Available for Analysis**[a]	**89**	**98.9**	**86**	**97.7**	**17**	**100**	**24**	**100**	**28**	**96.6**
	Out of Interval	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Missing Subjects	**1**	**1.1**	**2**	**2.3**	**0**	**0.0**	**0**	**0.0**	**1**	**3.3**
	Discontinued	1[c]	1.1	2[d]	2.3	0	0.0	0	0.0	1[d]	3.3

[a] Percent (%) Available for Analysis = n/N
[b] Included in safety and ITT analyses
[c] Subject moved out-of-state prior to 1-month study visit.
[d] Subjects died prior to the 6-month study visit.
[e] Bilateral per-protocol population (for questionnaire) includes deviations in first and second eyes; therefore, different N's
[f] N total at six months only

Table 11 presents the questionnaire accountability at six months. Note that questionnaires were analyzed for only those subjects bilaterally implanted with either toric or control lenses and with ≥0.75 D of preoperative keratometric cylinder in second eyes.

Table 11:
Questionnaire Accountability at Six Months
Bilateral Subjects in the Randomized Control Arm and Open Label Arm
Safety, Modified ITT and Per-Protocol Populations (Based on Both Eyes)

Subject/Questionnaire Status	Randomized Control Arm		Open Label Arm
	ZCT150	ZCB00	ZCT225, ZCT300, ZCT400
Available for Analysis	101	93	71
Excluded Subjects[a]	<29>	<15>	<0>
SAFETY ANALYZED	**72**[b]	**78**[b]	**71**
MODIFIED ITT ANALYZED[d]	**73**[b]	**80**[b]	**72**
PER-PROTOCOL ANALYZED[e]	**58**[b]	**66**[b]	**68**

[a] Subjects excluded if same lens type not in both eyes, if <0.75 D preoperative Kcyl in the second eye, or if second eye not implanted.
[b] Bilateral toric or control subjects with ≥0.75 D preoperative Kcyl in second eyes
[d] Same as analyzed preoperative questionnaires; missing data at six months imputed
[e] Subjects excluded with deviations in either or both eyes

C. Study Population Demographics and Baseline Parameters

Subject demographics are presented for both study arms in **Table 12**. In the RCA, females outnumbered males in both the ZCT150 and ZCB00 lens groups, mean ages were similar between lens groups and most subjects were Caucasian. Comparable demographics were noted in the OLA. Overall, lens groups were similar for evaluation of toric outcomes and comparison to the control.

Table 12:
Subject Demographics
Randomized Control Arm and Open Label Arm
Safety Population

Variable		Randomized Control Arm					Open Label Arm	
		ZCT150 N=102		ZCB00 N=95		P-Value	ZCT255, ZCT300, & ZCT400 N=72	
Age (years)	Mean	69.9		71.3		0.2205	68.8	
	Std	7.6		9.1			8.6	
	Min	49.0		42.0			41.0	
	Max	87.0		95.0			85.0	
Age Group	<60	10	(9.8%)	5	(5.3%)	N/A	7	(9.7%)
	60-69	39	(38.2%)	36	(37.9%)		33	(45.8%)
	70-79	41	(40.2%)	36	(37.9%)		25	(34.7%)
	>=80	12	(11.8%)	18	(18.9%)		7	(9.7%)
Sex	Male	47	(46.1%)	40	(42.1%)	0.6668	32	(44.4%)
	Female	55	(53.9%)	55	(57.9%)		40	(55.6%)
Race	Asian	2	(2.0%)	1	(1.1%)	1.0000	1	(1.4%)
	African American	4	(3.9%)	3	(3.2%)		3	(4.2%)
	Caucasian	96	(94.1%)	91	(95.8%)		68	(94.4%)
	Other	0	(0.0%)	0	(0.0%)		0	(0.0%)
Iris Color	Blue/Gray	40	(39.2%)	42	(44.2%)	0.0989	27	(37.5%)
	Brown/Black	41	(40.2%)	25	(26.3%)		24	(33.3%)
	Green/Hazel	21	(20.6%)	28	(29.5%)		21	(29.2%)

%=n/N

There were no statistically significant differences between the ZCT150 and ZCB00 first eyes in the RCA for demographics, preoperative parameters (inclusion/exclusion criteria, refractive,

biometric, and preoperative ocular symptoms) or operative parameters (surgical procedures, operative complications, etc.). In addition, demographics, preoperative and operative parameters for subjects in the OLA were comparable to those of the RCA.

D. Safety and Effectiveness Results

1. Safety Results

Best Corrected Distance Visual Acuity (BCDVA)

The primary safety endpoint of this study was the proportion of toric first eyes achieving BCDVA of 20/40 or better vs. ISO 11979-7 SPE rates at six months. All toric eyes (100%; 172/172) achieved BCDVA of 20/40 or better at six months exceeding the ISO SPE rates for posterior chamber lenses (92.5% overall and 96.7% best-case). Note: Additional BCDVA details are provided in the "Distance Visual Acuity" section of Effectiveness in conjunction with uncorrected distance visual acuity (UCDVA) results.

Complications and Adverse Events

The incidences of cumulative complications and adverse events for TECNIS® Toric 1-Piece first eyes compared to the ISO 11979-7 SPE rates are presented in **Table 13**. The incidence rates for the TECNIS® Toric ZCT first eyes compared favorably to the ISO SPE rates. Only the rate of surgical re-intervention (3.4%; 6/174) was statistically significantly higher than the ISO SPE rate of 0.8% (**p=0.0030).** There were four lens-related, repositioning procedures performed in toric eyes to correct a rotated IOL; the rate for repositioning procedures (2.3%; 4/175) alone was not statistically significantly higher than the ISO SPE rate for surgical re-intervention. The lens repositioning procedures occurred in ZCT300 or ZCT400 first eyes only (7.3%; 4/55); no ZCT300 and ZCT400 second eyes underwent lens repositioning procedures, thereby yielding an overall rate of 4.7% (4/85) for all ZCT300 and ZCT400 eyes. The rate of non-lens-related re-interventions (two retinal repair procedures; 1.1%, 2/174) was not statistically significantly higher than the ISO SPE rate for surgical re-intervention.

Table 13:
Cumulative Adverse Events through Six Months
TECNIS® Toric ZCT First Eyes: ZCT150, ZCT225, ZCT300 and ZCT400

Cumulative Adverse Event	ZCT Eyes N=174		ISO SPE[a] Rate
	n	%	%
Cystoid macular edema	5	2.9	3.0
Hypopyon	0	0.0	0.3
Endophthalmitis	0	0.0	0.1
Lens dislocation	0	0.0	0.1
Pupillary block	0	0.0	0.1
Retinal detachment	1	0.6[b]	0.3
Surgical re-intervention	6	3.4[c]	
Lens-related: repositioning procedures	4	2.3[d]	0.8
Not lens-related: retinal repair procedures	2	1.1[e]	

%=n/Total Tested

[a] ISO 11979-7 Safety and Performance Endpoint (SPE).

[b] P=0.4071 compared to cumulative ISO SPE rate of 0.3%

[c] **P=0.0030** compared to cumulative ISO SPE rate of 0.8%

[d] P=0.0521 compared to cumulative ISO SPE rate of 0.8%

[e] P=0.4059 compared to cumulative ISO SPE rate of 0.8%

There were no persistent medical complications present at six months for Toric ZCT first eyes for comparison to the ISO SPE rates for persistent complications. In addition, no adverse events occurred in TECNIS® Toric ZCT second eyes (0%; 0/149) or for any ZCB00 control eyes.

IOL rotation was noted by investigators at one day postoperatively in four Toric first eyes; these were the four eyes (two ZCT300 and two ZCT400) that underwent IOL repositioning procedures in the study. IOL rotation at one day was estimated by the investigators to be 10^{o} in both ZCT300 eyes, 35^{o} in one ZCT400 eye, and 40^{o} in the other ZCT400 eye. The repositioning procedures were performed early in the postoperative period, between the 1-day and 1-month study visits. Photographic analyses showed good lens stability following the repositioning procedures with only 2^{o} to 5^{o} of calculated rotation at six months vs. following the repositioning procedures. At six months, only one of these eyes (ZCT400 eye with 40^{o} rotation) did not achieve uncorrected distance visual acuity (UCDVA) of 20/40 or better due to remaining residual refractive error.

Rotational Stability

A key safety endpoint of the clinical study was rotational stability of the TECNIS® Toric ZCT IOL. Lens axis alignment for toric IOLs was measured using a direct photographic method in which high-resolution, slit-lamp retroillumination, digital photographs were analyzed using a validated axis measurement software program to align and compare images (based on iris and/or scleral landmarks) to determine the degree of lens axis rotation between time points.

The TECNIS® Toric IOL was found to meet the ANSI Standard for Toric IOLs, Z80.30, requirement for rotational stability (>90% of eyes having ≤5° axis change between consecutive visits approximately three months apart) as ≥93% of Toric ZCT first eyes had a change in axis of ≤5° between stability visits approximately three months apart (**Table 14**).

Table 14:
Absolute Difference in Axis Alignment Between Visits
First Eyes - All Toric ZCT150, ZCT225, ZCT300, ZCT400 Pooled
Safety Population

Axis Shift (degrees)	Toric Eyes: Consistent Cases[a] 1 Month vs. 3 Months n	%	3 Months vs. 6 Months n	%	Toric Eyes with Data at Two or More Consecutive Visits[b] 1 Month vs. 3 Months n	%	3 Months vs. 6 Months n	%
>30	0	0.0	0	0.0	0	0.0	0	0.0
16-30	0	0.0	0	0.0	0	0.0	0	0.0
10-15	2	1.4	3	2.0	2	1.3	3	2.0
(<10)	146	98.6	145	98.0	154	98.7	149	98.0
6-9	9	6.1	6	4.1	9	5.8	6	3.9
0-5	**137**	**92.6**	**139**	**93.9**	**145**	**92.9**	**143**	**94.1**
Total	**148**	**100.0**	**148**	**100.0**	**156**	**100.0**	**152**	**100.0**

%=n/Total Tested
[a] Eyes with photographic axis data at all visits through six months
[b] Eyes with photographic axis data at two or more consecutive visits but not necessarily all visits

Axis change between baseline (1 day) and six months was also measured (**Table 15**). Of toric first eyes, 97% had <10° of axis change between baseline and six months and only two toric first eyes (1%) had axis change >30° (calculated rotation of 40° and 45°); these were two of the four toric eyes that underwent lens repositioning procedures during the study (the two ZCT400 eyes with estimated rotation of 35° and 40°).

Table 15:
Absolute Difference in Axis Alignment Between One Day and Six Months
First Eyes - All Toric ZCT150, ZCT225, ZCT300, ZCT400 Pooled
Safety Population

Axis Shift (degrees)	Toric Eyes: Consistent Cases[a] 1 Day vs. 6 Months n	%	Toric Eyes with Data at One Day and Six Months 1 Day vs. 6 Months n	%
>30	2[b]	1.4	2[b]	1.3
20-30	2[c,d]	1.4	2[c,d]	1.3
(<20)	144	97.3	152	97.4
16-19	1[e]	0.7	1[e]	0.6
10-15	0	0.0	0	0.0
(<10)	**143**	**96.6**	**151**	**96.8**
6-9	4	2.7	4	2.6
0-5	139	93.9	147	94.2
Total	**148**	**100.0**	**156**	**100.0**

%=n/Total Tested
[a] Eyes with photographic axis data at all visits through six months
[b] Two ZCT400 eyes with calculated rotation of 40° and 45° underwent repositioning procedures.
[c] One ZCT300 eye with calculated rotation of 21° underwent a repositioning procedure.

[d] One ZCT150 eye with calculated lens rotation of 24° was not repositioned.
[e] One ZCT300 eye with calculated rotation of 18° underwent a repositioning procedure.

Mean axial rotation was also assessed between stability time points (one to three months and three to six months) as well as overall (baseline to six months) as shown in **Table 16**. Mean axial rotation was minimal (<3°) whether taking direction of axis shift into account or regardless of direction (absolute value).

Table 16:
Mean Change in Axis
Difference Taking Direction into Account (+/- Sign Included)
and Degree Shift Regardless of Direction (Absolute Value)
First Eyes - All Toric ZCT150, ZCT225, ZCT300, ZCT400 Pooled
Safety Population

	Toric Eyes: Consistent Cases[a]			Toric Eyes with Data at Two or More Visits[b]		
Change in Axis Between Visits	N	MEAN (degrees)	STD. DEV.	N	MEAN (degrees)	STD. DEV.
1 Mon. vs. 3 Mon.	148	0.24	2.82	156	0.25	2.77
3 Mon. vs. 6 Mon.	148	-0.06	2.94	152	-0.09	2.96
Baseline (1 Day) vs. 6 Mon.	148	-1.35	6.13	156	-1.33	5.99
Abs. Value-1 Mon. vs 3 Mon.	148	1.82	2.17	156	1.79	2.12
Abs. Value-3 Mon. vs 6 Mon.	148	1.85	2.28	152	1.89	2.27
Abs. Value-Baseline (1 Day) vs. 6 Mon.	148	2.74	5.65	156	2.70	5.51

[a] Eyes with photographic axis data at all visits through six months
[b] Eyes with photographic axis data at two or more visits but not necessarily all visits

Visual Disturbances

The optical/visual profile of the toric lens was assessed during the study by both non-directed subject responses (to the open-ended question, “Are you having any difficulties with your eyes or vision?” as asked by investigators at each study visit) and directed responses (to specific questions regarding bother/trouble with visual symptoms from a questionnaire).

Table 17 presents the incidence of non-directed responses for optical/visual symptoms for first eyes in the RCA and OLA at six months postoperatively. The most reported visual symptom was generally “blurred vision” (mostly at near) for both toric and ZCB00 eyes with almost no reports of nighttime optical/visual disturbances such as halos or night glare for either toric or ZCB00 eyes.

Table 17:
Optical/Visual Symptoms Pertaining to Visual Disturbances and Image Quality at Six Months from Non-directed Responses
First Eyes - Randomized Control Arm and the Open Label Arm
Safety Population

Optical/Visual Symptoms	Randomized Control Arm		Open Label Arm		All Toric Eyes[b]
	ZCT150 N=101	ZCB00 Control N=93	ZCT225 N=17	ZCT300/ ZCT400[a] N=54	ZCT150, ZCT225, ZCT300, ZCT400 N=172
Visual Disturbances					
Day glare	1.0% (1)	0.0% (0)	5.9% (1)	1.9% (1)	1.7% (3)
Depth perception difficulty	0.0% (0)	1.1% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Dipliopia (binocular)	0.0% (0)	0.0% (0)	0.0% (0)	3.7% (2)	1.2% (2)
Flashes of light	1.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (1)
Floaters	1.0% (1)	2.2% (2)	5.9% (1)	1.9% (1)	1.7% (3)
Halos	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Night glare	1.0% (1)	0.0% (0)	5.9% (1)	0.0% (0)	1.2% (2)
Mild	1.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (1)
Moderate	0.0% (0)	0.0% (0)	5.9% (1)	0.0% (0)	0.6% (1)
Starburst	1.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (1)
Mild	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Moderate	1.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (1)
Restricted field of vision	1.0% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.6% (1)
Night vision difficulty	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Entoptic phenomena	3.0% (3[c])	0.0% (0)	0.0% (0)	0.0% (0)	1.7% (3)
Image Quality					
Blurred/difficulty with vision	17.8% (18)	18.3% (17)	5.9% (1)	16.7% (9)	16.3% (28)
Overall	3.0% (3)	3.2% (3)	0.0% (0)	3.7% (2)	2.9% (5)
Distance	3.0% (3)	7.5% (7)	0.0% (0)	0.0% (0)	1.7% (3)
Intermediate	3.0% (3)	0.0% (0)	0.0% (0)	3.7% (2)	2.9% (5)
Near	8.9% (9)	8.6% (8)	5.9% (1)	11.1% (6)	9.3% (16)
Cloudy/hazy/filmy/foggy vision	2.0% (2)	4.3% (4)	0.0% (0)	0.0% (0)	1.2% (2)
Decreased vision	0.0% (0)	3.2% (3)	0.0% (0)	0.0% (0)	0.0% (0)
Difficulty focusing	0.0% (0)	0.0% (0)	0.0% (0)	1.9% (1)	0.6% (1)
Fluctuation in acuity	0.0% (0)	2.2% (2)	5.9% (1)	3.7% (2)	1.7% (3)
Image distortion	0.0% (0)	2.2% (2)	0.0% (0)	0.0% (0)	0.0% (0)

[a] ZCT IOL models with >2 D of cylinder correction at corneal plane presented separately
[b] As control eyes had ≤1.5 D of preoperative Kcyl only, results for all toric eyes pooled are not to be compared to control values.
[c] Includes reports of arcs of light, dark arc/haze in vision

Table 18 presents the degree of bother/trouble for key ocular/visual symptoms at six months as collected from the study questionnaire, a modification of the Vitale RSVP questionnaire. Overall, most toric and ZCB00 control subjects reported “no trouble at all” for most items, including those that may be related to a toric IOL (things appearing distorted, judging distances when going up or down steps, objects appearing tilted, floors or flat surfaces appearing curved).

Table 18:
Degree of Bother/Trouble with Key Ocular/Visual Symptoms at Six Months from a Prompted-Choice Questionnaire
Bilateral Subjects[a] in the Randomized Control Arm and the Open Label Arm

During the past month, how bothered have you been by each of the following, using correction if needed?		Randomized Control Arm ZCT150 N=72	Randomized Control Arm ZCB00 N=78	Open Label Arm ZCT225 N=17	Open Label Arm ZCT300/ ZCT400[c] N=54	All Toric Subjects[b] ZCT150, ZCT225, ZCT300, ZCT400 N=172
Changes in your vision during the day	No trouble at all	93.1%	80.8%	94.1%	87.0%	90.9%
	A little trouble	5.6%	19.2%	5.9%	11.1%	7.7%
	Moderate trouble	1.4%	0.0%	0.0%	1.9%	1.4%
	Severe trouble	0.0%	0.0%	0.0%	0.0%	0.0%
Glare (reflections off shiny surfaces, snow)	No trouble at all	68.1%	50.0%	58.8%	51.9%	60.8%
	A little trouble	22.2%	33.3%	29.4%	27.8%	25.2%
	Moderate trouble	9.7%	14.1%	5.9%	20.4%	13.3%
	Severe trouble	0.0%	2.6%	5.9%	0.0%	0.7%
Things looking different out of one eye vs. the other	No trouble at all	84.7%	70.5%	100.0%	70.4%	81.1%
	A little trouble	12.5%	19.2%	0.0%	18.5%	13.3%
	Moderate trouble	2.8%	9.0%	0.0%	7.4%	4.2%
	Severe trouble	0.0%	1.3%	0.0%	3.7%	1.4%
Seeing in dim light	No trouble at all	84.7%	65.4%	70.6%	63.0%	74.8%
	A little trouble	15.3%	29.5%	23.5%	22.2%	18.9%
	Moderate trouble	0.0%	5.1%	5.9%	13.0%	5.6%
	Severe trouble	0.0%	0.0%	0.0%	1.9%	0.7%
Your depth perception	No trouble at all	98.6%	85.9%	82.4%	90.7%	93.7%
	A little trouble	1.4%	10.3%	17.6%	5.6%	4.9%
	Moderate trouble	0.0%	2.6%	0.0%	3.7%	1.4%
	Severe trouble	0.0%	1.3%	0.0%	0.0%	0.0%
Things appearing distorted	No trouble at all	97.2%	93.6%	94.1%	96.3%	96.5%
	A little trouble	1.4%	1.3%	0.0%	3.7%	2.1%
	Moderate trouble	1.4%	5.1%	5.9%	0.0%	1.4%
	Severe trouble	0.0%	0.0%	0.0%	0.0%	0.0%
Judging distance when going up or down steps (stairs, curbs)	No trouble at all	90.3%	87.2%	100.0%	88.9%	90.9%
	A little trouble	8.3%	9.0%	0.0%	9.3%	7.7%
	Moderate trouble	1.4%	2.6%	0.0%	1.9%	1.4%
	Severe trouble	0.0%	1.3%	0.0%	0.0%	0.0%
Objects appearing tilted	No trouble at all	100.0%	98.7%	100.0%	98.1%	99.3%
	A little trouble	0.0%	1.3%	0.0%	1.9%	0.7%
	Moderate trouble	0.0%	0.0%	0.0%	0.0%	0.0%
	Severe trouble	0.0%	0.0%	0.0%	0.0%	0.0%
Floors or flat surfaces appearing curved	No trouble at all	97.2%	100.0%	100.0%	98.1%	97.9%
	A little trouble	2.8%	0.0%	0.0%	1.9%	2.1%
	Moderate trouble	0.0%	0.0%	0.0%	0.0%	0.0%
	Severe trouble	0.0%	0.0%	0.0%	0.0%	0.0%

[a] Subjects bilaterally implanted with either toric or control lenses and with ≥0.75 D preoperative Kcyl in second eyes
[b] As control subjects had ≤1.5 D of preoperative Kcyl only, results for all toric subjects pooled are not be compared to control values.
[c] ZCT IOL models with >2 D of cylinder correction at corneal plane presented separately

Whether non-directed or directed (questionnaire), ocular symptoms for toric eyes with >2.00 D of cylinder correction at the corneal plane (ZCT300 and ZCT400) did not appear different from the lower cylinder models indicating no impact on the ocular/visual profile with higher cylinder correction.

2. Effectiveness Results

Reduction in Cylinder

The primary effectiveness endpoint in the study, mean percent reduction in cylinder at six months, per the ANSI Standard for Toric IOLs, Z80.30, was met. Percent reduction in cylinder was calculated as the ratio of achieved postoperative refractive cylinder to the target refractive cylinder, adjusted for preoperative Kcyl. Specifically, the difference between postoperative refractive cylinder and preoperative keratometric cylinder was divided by the difference between the target refractive cylinder and preoperative Kcyl to calculate the percent reduction in cylinder. The target refractive cylinder is a combination of preoperative Kcyl, surgically induced astigmatism (SIA) from the cataract incision and the toric IOL. The calculation was performed similarly for all eyes; in the RCA, the target refractive cylinder for ZCB00 eyes was calculated as if the control subjects were receiving a ZCT150 IOL.

As shown in **Table 19** for the safety population, there were no statistically significant differences in preoperative keratometric cylinder or target refractive cylinder between ZCT150 toric and ZCB00 control eyes in the RCA. However, there were statistically significant differences in mean refractive cylinder and the mean percent reduction in cylinder in favor of the ZCT150 lens group vs. the control group in the RCA at six months postoperative. In addition, the mean percent reduction in cylinder for OLA first eyes at six months was statistically significantly higher than the target value of 25%. For all toric first eyes in the RCA and OLA safety populations combined (N=171), the mean percent reduction in cylinder was 75.24 (standard deviation = 59.29).

The primary analysis population for analysis of the percent reduction in cylinder was the ITT population with data imputation for missing data; in this population there were also statistically significant differences between lens groups in the RCA with percent cylinder reduction of 30.3% for ZCB00 eyes vs. 74.6% for ZCT150 eyes (**p<0.0001** using the adjusted ANSI formula for outliers). In additon, in the OLA, there was still a statistically significant difference (**p<0.0001**) between the percent reduction for all OLA lens models pooled (ZCT225, ZCT300 and ZCT400) of 76.0% vs. the target value of 25%.

Study results (residual refractive cylinder, change in cylinder, and uncorrected acuity) stratified by preoperative keratometric cylinder did not show evidence of significant benefit in the

treatment of preoperative corneal astigmatism of less than one diopter. (See Tables 31, 32, and 33.)

Table 19:
Mean Cylinder and Achieved Cylinder Reduction as a Percentage of Intended Reduction (Percent Cylinder Reduction) at Six Months
First Eyes[a] - Randomized Control Arm and Open Label Arm
Safety Population

	Randomized Control Arm					Open Label Arm				
VARIABLE	Lens Model	N[a]	Mean	Std. Dev.	P-Value	Lens Model	N[a]	Mean	Std. Dev.	P-Value
Preoperative Keratometric Cylinder (Kcyl; D)	ZCB00	91	1.11	0.24	0.3436	Pooled	70	2.16	0.66	N/A
	ZCT150	101	1.08	0.28		ZCT225	17	1.58	0.28	
						ZCT300	24	1.91	0.46	
						ZCT400	29	2.70	0.55	
Target Refractive Cylinder (D)	ZCB00	91	0.26	0.18	0.6267	Pooled	70	0.26	0.30	N/A
	ZCT150	101	0.25	0.17		ZCT225	17	0.12	0.10	
						ZCT300	24	0.19	0.12	
						ZCT400	29	0.41	0.40	
Refractive Cylinder (D)	ZCB00	91	0.85	0.57	**<0.0001**	Pooled	70	0.67	0.47	N/A
	ZCT150	101	0.45	0.41		ZCT225	17	0.49	0.37	
						ZCT300	24	0.62	0.43	
						ZCT400	29	0.82	0.52	
Percent Cylinder Reduction[b]	ZCB00	91	31.61	78.73	**<0.0001**	Pooled	70	76.27	33.09	**<0.0001[c]**
	ZCT150	101	74.53	72.25		ZCT225	17	73.78	27.17	
						ZCT300	24	72.03	38.57	
						ZCT400	29	81.23	31.78	

[a] Eyes with both preoperative and postoperative data
[b] Percent Reduction ANSI Formula=(Postop Ref. Cyl. minus Preop K. Cyl.)/(Target Ref. Cyl. minus Preop K. Cyl.); ANSI formula used except for a few eyes in the RCA with very small denominators (within ±0.1); for these eyes the ANSI formula was used but without the target value.
[c] Versus OLA target of 25% reduction

The TECNIS® Toric Calculator utilizes preoperative keratometry and surgeon-estimated surgically induced astigmatism (SIA) to calculate the expected postoperative keratometry and provide options for toric IOL selection. An analysis of the errors in the calculation of postoperative keratometry was performed using vector arithmetic. Results showed that error in magnitude prediction was on average 0.32 D (with a median value of 0.25 D due to bias toward lower values) and error in meridian prediction was on average 16° (with a median value of 8°, again with bias toward lower values). It is important to note that measurement noise in keratometry readings (estimated from 0.20 D to 0.83 D for magnitude[Zadnick,Visser] and up to 20° for axis[Visser]) and any potential errors in surgeon-estimated SIA are contributing factors to prediction errors of postoperative keratometry.

The absolute difference between refractive cylinder at six months vs. target for first eyes is presented in **Table 20**. In the RCA, 72.3% (73/101) of ZCT150 eyes compared to 49.5% (45/91) of ZCB00 eyes were within 0.50 D of target refractive cylinder. In addition, 94.1% (95/101) of ZCT150 eyes compared to 70.3% (64/91) of ZCB00 eyes were within 1.00 D of target refractive cylinder. In the OLA, 52.9% (37/70) were within 0.50 D and 84.3% (59/70) were within 1.00 D of target refractive cylinder.

Table 20:
Absolute Difference Between Refractive Cylinder at Six Months vs. Target
First Eyes - Randomized Control Arm and Open Label Arm
Safety Population

Diopter Group	Randomized Control Arm ZCT150 N=101		Randomized Control Arm ZCB00 N=93		Open Label Arm ZCT225, ZCT300, ZCT400 N=71		All Toric Eyes[a] ZCT150, ZCT225, ZCT300, ZCT400 N=172	
	n	%	n	%	n	%	n	%
>2.0	0	0.0	0	0.0	0	0.0	0	0.0
1.51-2.00	1	1.0	6	6.6	2	2.9	3	1.8
1.01-1.50	5	5.0	21	23.1	9	12.9	14	8.2
(≤1.00)	**95**	**94.1**[a]	**64**	**70.3**[a]	**59**	**84.3**	**154**	**90.0**
0.51-1.00	22	21.8	19	20.9	22	31.4	44	25.7
(≤0.50)	**73**	**72.3**[b]	**45**	**49.5**[b]	**37**	**52.9**	**110**	**64.3**
Total Tested	101	100.0	91	100.0	70	100.0	171	100.0
Not Reported	0		2		1		1	

%=n/Total Tested
[a] As control eyes had ≤1.5 D of preoperative Kcyl only, results for all toric eyes pooled are not to be compared to control values.

The mean change in absolute refractive cylinder between one to three months and three to six months was negligible with <0.10 D of mean change for any lens model (ZCT150, ZCT225, ZCT300, ZCT400 and ZCB00 control) indicating refractive stability over time.

Mean manifest refraction spherical equivalent (MRSE) at six months was within emmetropia (defined as ±0.25 D) for all first eyes (all toric ZCT models and control ZCB00). In addition, at least 70% of all first eyes (all toric ZCT models and control ZCB00) achieved MRSE within 0.50 D of intended and 95% achieved within 1.00 D of intended at six months.

Distance Visual Acuity

Both uncorrected distance visual acuity (UCDVA) and best corrected distance visual acuity (BCDVA) were measured under photopic lighting conditions (85 cd/m^2) using 100% LogMAR ETDRS charts at a distance of 4.0 meters.

Uncorrected Distance Visual Acuity (UCDVA)

Key effectiveness endpoints of the study were mean UCDVA and the proportion of eyes achieving UCDVA of 20/20 or better. In the RCA, a statistically significant improvement in mean UCVDA was found at six months in favor of ZCT150 eyes vs. ZCB00 control eyes (**Table 21**) with a 0.6 line improvement for ZCT150 eyes compared to ZCB00 control eyes. The primary analysis population for the RCA for this endpoint was the ITT population with data imputation for missing values; in this population there was also a statistically significant difference (**p=0.0008** as compared to an alpha level adjusted for multiplicity of 0.0125) with a 0.7 line difference between lens models in favor of ZCT150 eyes (LogMAR 0.10; Snellen 20/25) compared to ZCB00 control eyes (LogMAR 0.17; Snellen 20/30). Results for best-case eyes were similar to the overall safety population as only one ZCT300 first eye was not best-case due to the presence of macular degeneration postoperatively. For all toric eyes in the RCA and OLA safety populations combined (N=172), the mean UCDVA LogMAR score was 0.10 (standard deviation = 0.13), Snellen equivalent of 20/25.

Table 21:
Mean Monocular Uncorrected Distance Visual Acuity at Six Months
Reported in LogMAR Values with Snellen Equivalent
First Eyes - Randomized Control Arm[a] and Open Label Arm[b]
Safety Population

Randomized Control Arm						Open Label Arm				
Lens Model	N	UCDVA Mean	Snellen Equivalent 20/	Std. Dev.	P-Value	Lens Model	N	UCDVA Mean	Snellen Equivalent 20/	Std. Dev.
ZCB00	93	0.16	29	0.16	**0.0009**	Pooled	71	0.11	26	0.12
ZCT150	101	0.10	25	0.14		ZCT225	17	0.07	23	0.10
						ZCT300	25[b]	0.11[b]	26	0.11
						ZCT400	29	0.12	27	0.14

[a] All RCA first eyes were best case; therefore, the RCA safety population is the same as a best-case population.

[b] Only one ZCT300 eye was not best-case; best-case mean and SD for ZCT300 eyes (N=24) was 0.12 LogMAR (±0.11) (Snellen 20/26); the best-case mean and standard deviation for all pooled OLA results were the same as the safety population.

The distribution of monocular UCDVA results at six months is presented in **Table 22**. There were statistically significant differences between lens groups in the RCA with a higher proportion of ZCT150 eyes vs. ZCB00 eyes achieving 20/20 or better and 20/40 or better. In addition,

there was a statically significant difference between the proportion of OLA pooled eyes achieving 20/20 or better vs. the target value of 6%. The primary analysis population for the OLA for this endpoint was the ITT population with data imputation for missing values; in this population, there was also a statistically significantly (**p=0.0001** as compared to an alpha level adjusted for multiplicity of 0.0063) higher proportion of OLA first eyes achieving 20/20 or better (37.5%; 27/72) than the target value of 6%.

Table 22:
Distribution of Monocular Uncorrected Distance Visual Acuity at Six Months
First Eyes - Randomized Control Arm and Open Label Arm
Safety Population

Uncorrected Distance Visual Acuity	Randomized Control Arm			Open Label Arm		All Toric Eyes[a]
	ZCT150 N=101	ZCB00 N=93	P-Value	ZCT225, ZCT300, ZCT400 Pooled N=71	P-Value	ZCT150, ZCT225, ZCT300, ZCT400 N=172
20/20 or better	**43.6%**	**23.7%**	**0.0026**	**38.0%**	**<0.0001[b]**	**41.3%**
20/25 or better	71.3%	54.8%		69.0%		70.3%
20/32 or better	89.1%	74.2%		90.1%		89.5%
20/40 or better	**97.0%**	**87.1%**	**0.0092**	**97.2%**	**N/A**	**97.1%**
20/50 – 20/80	3.0%	12.9%		2.8%		2.9%
20/100 or worse	0.0%	0.0%		0.0%		0.0%

[a] As control eyes had ≤1.5 D of preoperative Kcyl only, results for all toric eyes pooled are not to be compared to control values.
[b] Versus target value of 6%

Best Corrected Distance Visual Acuity (BCDVA)

For the analysis of BCDVA, data from all first-eye toric lenses (ZCT150, ZCT225, ZCT300 and ZCT400) were pooled and compared to ISO SPE rates (**Table 23**). At six months, 100% of all toric eyes and 100% of toric best-case eyes achieved BCDVA of 20/40 or better exceeding the ISO SPE rates for posterior chamber IOLs.

Table 23:
Monocular Best Corrected Distance Visual Acuity at Six Months
Proportion Achieving 20/40 or Better vs. ISO SPE[a] Rates
First Eyes – All Toric ZCT150, ZCT225, ZCT300 and ZCT400 Pooled
Safety Population

Toric First Eyes	ISO SPE[a] %	ZCT150, ZCT225, ZCT300, ZCT400 Pooled	
		n	%
All	92.5	172/172	100.0
Best-case	96.7	171/171	100.0

%=n/Total Tested
[a] ISO 11979-7 Safety and Performance Endpoint (SPE).

The distribution of monocular BCDVA at six months is presented for eyes in each study arm and for all toric eyes pooled in **Table 24**.

Table 24:
Distribution of Monocular Best Corrected Distance Visual Acuity at Six Months
First Eyes - All Toric Eyes Pooled, Randomized Control Arm and Open Label Arm
Safety Population

Best Corrected Visual Acuity	Randomized Control Arm		Open Label Arm	All Toric Eyes
	ZCT150 N=101	ZCB00 N=93	ZCT225, ZCT300, ZCT400 N=71	ZCT150, ZCT225, ZCT300, ZCT400 N=172
20/20 or better	**87.1%**	**77.4%**	**90.1%**	**88.4%**
20/25 or better	98.0%	97.8%	95.8%	97.1%
20/32 or better	99.0%	100.0%	98.6%	98.8%
20/40 or better	**100.0%**	**100.0%**	**100.0%**	**100.0%**
20/50 – 20/80	0.0%	0.0%	0.0%	0.0%
20/100 or worse	0.0%	0.0%	0.0%	0.0%

No effects of age, sex, race, best-case status, or site differences on BCDVA outcomes for toric eyes were found. There was a statistically significant effect (**p=0.0042**) on BCDVA outcomes with eyes having better preoperative BCDVA more likely to achieve better postoperative BCDVA.

Spectacle Independence and Subject Satisfaction

Spectacle independence and subject satisfaction were evaluated at six months based on directed subject responses from a bilateral questionnaire, a modification of the Vitale RSVP questionnaire. Results are reported for only those subjects bilaterally implanted with toric lenses or control lenses and with ≥0.75 D in the second eye.

Spectacle Independence

Spectacle independence was a key effectiveness study endpoint and was based on subject answers to the question “How much of the time do you wear glasses for seeing objects at distance?” The answer “None of the time” was considered to be spectacle independent. This question originated from the Modified Cataract TyPE Spec.

The difference between the proportion of spectacle independent subjects in the two arms of the RCA (ZCT150 implanted vs control ZCB00 implanted) was not statistically significant. In the OLA, the proportions of spectacle independent OLA subjects were statistically significantly higher than the target value of 15% (**p<0.0001**) for all analysis populations (**Table 25**).

For all toric subjects in the RCA and OLA safety populations combined (N=143), 80.4% (115/143) were considered spectacle independent, as they reported wearing glasses “none of the time” for far.

Table 25:
Spectacle Independence at Distance at Six Months
Bilateral Subjects in the Randomized Control Arm and Open Label Arm
Safety, ITT[a] and Per-Protocol Populations

Analysis Population	How much time do you wear glasses for seeing objects at distance	Randomized Control Arm ZCT150	Randomized Control Arm ZCB00	Randomized Control Arm P-Value[b]	Open Label Arm ZCT225, ZCT300, ZCT400 Pooled	Open Label Arm ZCT225, ZCT300, ZCT400 P-Value[b]
Safety		**N=72**	**N=78**		**N=71**	
	None of the time	**83.3%**	**70.5%**	0.0476[c]	**77.5%**	**<0.0001[d]**
	Some, Half, Most or All of the time	16.7%	29.5%		22.5%	
ITT[a]		**N=73**	**N=80**		**N=72**	
	None of the time	**83.6%**	**70.8%**	0.0333[c]	**76.4%**	**<0.0001[d]**
	Some, Half, Most or All of the time	16.4%	29.2%		23.6%	
Per-Protocol		**N=58**	**N=66**		**N=68**	
	None of the time	**86.2%**	**68.2%**	N/A	**79.4%**	**<0.0001[d]**
	Some, Half, Most or All of the time	13.8 %	31.8%		20.6%	

[a] Modified Intent-to-Treat (ITT) population (bilateral subjects) with data imputation for missing data
[b] P-values from one-sided testing compared to a significance (alpha) level of 0.025 comparing none vs not-none (some, half, most, and all of the time)
[c] P-values are not statistically significant (comparison to an alpha level of 0.025).
[d] Versus target value of 15%

Figures 1 and 2 graphically present the frequency of spectacle wear for seeing objects at distance for bilateral subjects in the safety and per-protocol populations.

Figure 1:
Frequency of Spectacle Wear for Distance Vision at Six Months
Bilateral Subjects in the Randomized Control Arm and the Open Label Arm
Safety Population

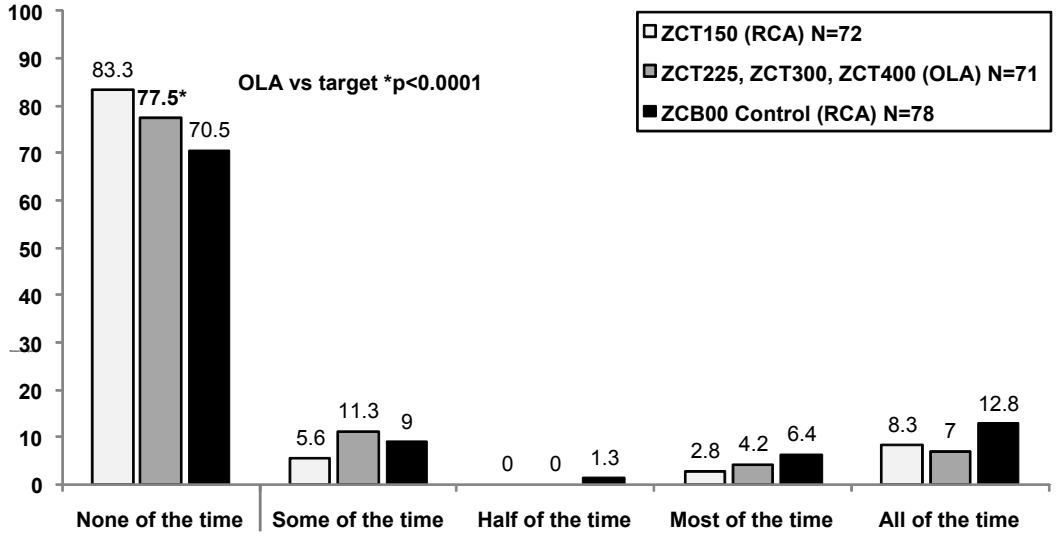
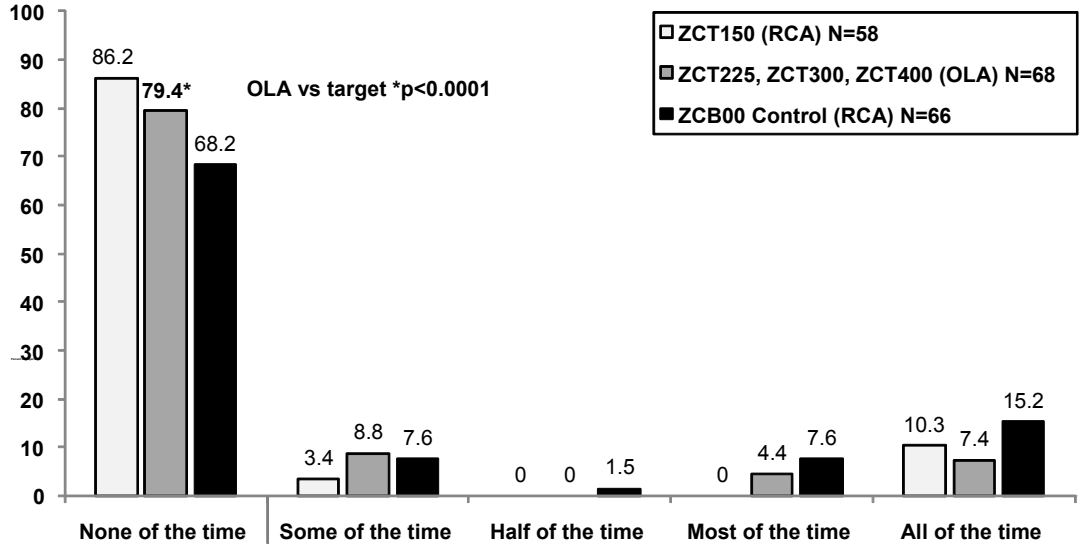


Figure 2:
Frequency of Spectacle Wear for Distance Vision at Six Months
Bilateral Subjects in the Randomized Control Arm and the Open Label Arm
Per-Protocol Population



Difficulty performing various activities without glasses was also assessed at six months. With the exception of near tasks, the majority of subjects reported no difficulty performing various activities without glasses. **Table 26** presents the difficulty reported by subjects when performing certain activities without glasses such as watching TV or movies, driving at night in general, driving in the rain, and driving with glare from oncoming headlights.

Table 26:
Difficulty with Certain Activities without Glasses at Six Months
Bilateral Subjects in the Randomized Control Arm and the Open Label Arm
Safety Population

Question		Randomized Control Arm ZCT150 N=72 n	%	ZCB00 N=78 n	%	Open Label Arm ZCT225, ZCT300, ZCT400 N=71 n	%	All Toric Eyes[a] ZCT150, ZCT225, ZCT300, ZCT400 N=143 n	%
Watching TV or movies	No difficulty at all	63	91.3	60	78.9	57	87.7	120	89.6
	A little difficulty	4	5.8	8	10.5	6	9.2	10	7.5
	Moderate difficulty	2	2.9	6	7.9	2	3.1	4	3.0
	Severe difficulty	0	0.0	1	1.3	0	0.0	0	0.0
	So much difficulty that I did not do the activity without glasses	0	0.0	1	1.3	0	0.0	0	0.0
	Never did the activity for other reasons (not related to vision)	*0*	-	*0*	-	*0*	-	*0*	-
	Not applicable	*3*	-	*2*	-	*6*	-	*9*	-
Driving at night	No difficulty at all	57	91.9	49	73.1	35	63.6	92	78.6
	A little difficulty	1	1.6	9	13.4	14	25.5	15	12.8
	Moderate difficulty	4	6.5	7	10.4	2	3.6	6	5.1
	Severe difficulty	0	0.0	1	1.5	3	5.5	3	2.6
	So much difficulty that I did not do the activity without glasses	0	0.0	1	1.5	1	1.8	1	0.9
	Never did the activity for other reasons (not related to vision)	*5*	-	*4*	-	*6*	-	*11*	-
	Not applicable	*5*	-	*7*	-	*10*	-	*15*	-
Driving when it is raining	No difficulty at all	59	92.2	48	71.6	42	70.0	101	81.5
	A little difficulty	3	4.7	10	14.9	12	20.0	15	12.1
	Moderate difficulty	2	3.1	6	9.0	2	3.3	4	3.2
	Severe difficulty	0	0.0	2	3.0	3	5.0	3	2.4
	So much difficulty that I did not do the activity without glasses	0	0.0	1	1.5	1	1.7	1	0.8
	Never did the activity for other reasons (not related to vision)	*4*	-	*3*	-	*3*	-	*7*	-
	Not applicable	*4*	-	*8*	-	*8*	-	*12*	-
Driving when there is a glare from oncoming headlights	No difficulty at all	47	74.6	38	55.9	35	59.3	82	67.2
	A little difficulty	8	12.7	19	27.9	18	30.5	26	21.3
	Moderate difficulty	8	12.7	8	11.8	2	3.4	10	8.2
	Severe difficulty	0	0.0	2	2.9	3	5.1	3	2.5
	So much difficulty that I did not do the activity without glasses	0	0.0	1	1.5	1	1.7	1	0.8
	Never did the activity for other reasons (not related to vision)	*5*	-	*3*	-	*4*	-	*9*	-
	Not applicable	*4*	-	*7*	-	*8*	-	*12*	-

%=n/Total Tested
Note: Percentages do not include subject reports of "Not applicable" or "Never did the activities for other reasons". The denominator for percentage calculations was based on "N" minus reports of "Not applicable" and "Never did this activity for other reasons".
[a] As control eyes had ≤1.5 D of preoperative Kcyl only, results for all toric eyes pooled are not to be compared to control values.
[b] "Not applicable" or "Never did the activities for other reasons" were excluded from p-value calculations

Subject Satisfaction

Subject satisfaction was also assessed in the questionnaire. At six months, almost all toric and ZCB00 subjects indicated they would elect to have the same IOL implanted again; 94.4% of RCA ZCT150 subjects, 93.6% of RCA ZCB00 subjects and 98.6% of OLA ZCT subjects (**Table 27**). The primary reasons subjects would not elect the IOL again were varied including the desire for a multifocal IOL (both toric and control subjects) as well as dissatisfaction with optical quality (control subjects only).

Table 27:
Desire to Elect IOL Again
Directed Response to a Prompted Choice Questionnaire
Bilateral Subjects in the Randomized Control Arm and the Open Label Arm
Safety Population

Elect IOL Again	Randomized Control Arm ZCT150 N=72		Randomized Control Arm ZCB00 N=78		Open Label Arm ZCT225, ZCT300, ZCT400 N=71		All Toric Subjects[a] ZCT150, ZCT225, ZCT300, ZCT400 N=143	
	n	%	n	%	n	%	n	%
Yes	68	94.4	73	93.6	70	98.6	138	96.5
No	4[b]	5.6	5[b,c]	6.4	1[b]	1.4	5	3.5

%=n/Total Tested
[a] As control subjects had ≤1.5 D of preoperative Kcyl only, results for all toric subjects pooled are not be compared to control values.
[b] Miscellaneous reasons: frequent visits/long wait times, unsure, prefer a multifocal/reading IOL
[c] Dissatisfaction with optical quality (n=3)

Table 28 presents the degree of satisfaction of current vision without glasses. Although a large proportion of both toric and ZCB00 subjects were satisfied with their current vision without glasses, approximately 23% more ZCT150 subjects were “very satisfied” than ZCB00 control subjects (62.5% of ZCT150 subjects were “very satisfied” vs. 39.7% of ZCB00 control subjects).

Mean ratings of distance vision (on a scale of 0-10 with 10 being best) with and without glasses were high for both toric and ZCB00 subjects (**Table 29**). In the RCA, mean ratings of vision without glasses were 9.2 for ZCT150 subjects and 8.5 for ZCB00 subjects; in the OLA, the mean rating of vision without glasses was 9.0.

Table 28:
Satisfaction with Vision Without Glasses at Six Months
Bilateral Subjects in the Randomized Control Arm and the Open Label Arm
Safety Population

Satisfaction of current vision without glasses	Randomized Control Arm ZCT150 N=72		Randomized Control Arm ZCB00 N=78		Open Label Arm ZCT225, ZCT300, ZCT400 N=71		All Toric Subjects[a] ZCT150, ZCT225, ZCT300, ZCT400 N=143	
	n	%	n	%	n	%	n	%
Very dissatisfied	1	1.4	3	3.8	2	2.8	3	2.1
Dissatisfied	2	2.8	4	5.1	1	1.4	3	2.1
Neither[b]	5	6.9	6	7.7	5	7.0	10	7.0
Satisfied	19	26.4	34	43.6	18	25.4	37	25.9
Very Satisfied	45	62.5	31	39.7	45	63.4	90	62.9

%=n/Total Tested
[a] As control subjects had ≤1.5 D of preoperative Kcyl only, results for all toric subjects pooled are not be compared to control values.
[b] Neither satisfied nor dissatisfied

Table 29:
Rating of Distance Vision[a] at Six Months
Bilateral subjects in the Randomized Control Arm and Open Label Arm
Safety Population

Rating of Distance Vision		Randomized Control Arm ZCT150 N=72	Randomized Control Arm ZCB00 N=78	Open Label Arm ZCT225, ZCT300, ZCT400 N=71	All Toric Subjects[b] ZCT150, ZCT225, ZCT300, ZCT400 N=143
Rating of distance vision without glasses	N	71	78	70	141
	Mean	**9.2**	**8.5**	**9.0**	**9.1**
	SD	1.13	1.78	1.35	1.24
Rating of distance vision with glasses	N[c]	15	23	18	33
	Mean	**9.5**	**8.5**	**9.3**	**9.4**
	SD	0.74	1.27	0.83	0.78

[a] On a scale from 0 to 10, where 0 means "completely blind" and 10 means "perfect vision".
[b] As control subjects had ≤1.5 D of preoperative Kcyl only, results for all toric subjects pooled are not be compared to control values.
[c] Number of subjects who have worn glasses for distance vision in the past month

3. Subgroup Analyses

Stratifications of the effectiveness endpoints of percent reduction in cylinder, UCDVA, spectacle independence (at distance) and postoperative refractive cylinder at six months by the preoperative variables of age, gender, race and preoperative BCDVA were performed. No effects on percent reduction in cylinder or postoperative refractive cylinder due to age, gender, race or preoperative BCDVA were apparent. No effects on UCDVA outcomes due to age, gender or race were apparent; however, as seen for BCDVA (see Distance Visual Acuity section), eyes with better preoperative BCDVA tended to have better postoperative UCDVA. No effects on spectacle independence outcomes due to age, gender or race were apparent. (Note:

Spectacle independence was unable to be analyzed by preoperative BCDVA, as this is a monocular variable which may be different for each eye; whereas, spectacle independence is a binocular outcome.)

Results in the RCA were also stratified by preoperative Kcyl alone and by predicted Kcyl [i.e., vector sum of preoperative Kcyl (magnitude and axis) SIA, and incision axis] in 0.25 D increments as shown in **Tables 30**, **31**, **32 and 33**. When results from the clinical study were stratified by preoperative Kcyl alone, the results for eyes with preoperative Kcyl less than 1.00 D did not show evidence of effectiveness. However, when results were stratified by predicted Kcyl (preoperative Kcyl combined with the expected effect of SIA), results were consistent with those in the overall RCA.

Table30:
Achieved Cylinder Reduction as a Percentage of Intended Reduction (Percent Reduction in Cylinder ANSI formula[a]) at 6 Months Stratified by Keratometric Cylinder
First Eyes Randomized Control Arm ZCT150 and ZCB00
Safety Population

Model	Preoperative Keratometric Cylinder (D)	N	Percent Reduction in Cylinder (ANSI)[a] Mean	Std Dev	Predicted Keratometric Cylinder (D)[b] (Preop Kcyl + SIA)	N	Percent Reduction in Cylinder (ANSI)[a] Mean	Std Dev
ZCB00	<0.75	4	-45.26	80.51	<0.75	13	-1.28	136.54
ZCT150		5	-79.77	51.59		16	78.20	122.83
ZCB00	0.75-0.99	22	32.32	111.09	0.75-0.99	23	7.39	48.81
ZCT150		30	69.20	87.53		21	55.38	58.57
ZCB00	1.00-1.24	34	41.06	68.41	1.00-1.24	31	43.44	59.77
ZCT150		38	94.88	52.09		36	61.88	49.80
ZCB00	1.25-1.49	27	32.31	60.95	1.25-1.49	20	45.09	73.00
ZCT150		22	74.82	45.78		26	100.27	63.21
ZCB00	≥1.50	4	19.43	17.23	≥1.50	4	118.57	50.01
ZCT150		6	99.88	32.32		2	139.43	31.58
ZCB00	**All**	91	31.61	78.73	**All**	91	31.61	78.73
ZCT150		101	74.53	72.25		101	74.53	72.25

[a] Percent Cylinder Reduction (ANSI Formula)=(Postop Ref. Cyl. minus Preop Kcyl)/(Target Ref. Cyl. minus Preop Kcyl); Percent cylinder reduction (ANSI formula) adjusted for eyes (3) with small denominators (±0.10) where target value was not used.

[b] Predicted keratometric cylinder is the vector combination of preoperative keratometric cylinder (magnitude and axis), estimated SIA and incision axis.

Table 31:
Residual Refractive Cylinder at 6 Months Stratified by Keratometric Cylinder
First Eyes Randomized Control Arm ZCT150 and ZCB00
Safety Population

Model	Preoperative Keratometric Cylinder (D)	N	Residual Refractive Cylinder (D) Mean	Std Dev	Predicted Keratometric Cylinder (D)[a] (Preop Kcyl + SIA)	N	Residual Refractive Cylinder (D) Mean	Std Dev
ZCB00	<0.75	5	0.85	0.42	<0.75	14	0.77	0.49
ZCT150		5	0.91	0.14		16	0.55	0.43
ZCB00	0.75-0.99	22	0.56	0.50	0.75-0.99	23	1.03	0.51
ZCT150		30	0.50	0.40		21	0.43	0.33
ZCB00	1.00-1.24	34	0.80	0.55	1.00-1.24	31	0.84	0.68
ZCT150		38	0.36	0.36		36	0.48	0.45
ZCB00	1.25-1.49	27	1.09	0.59	1.25-1.49	21	0.84	0.52
ZCT150		22	0.48	0.49		26	0.39	0.43
ZCB00	≥1.50	5	1.35	0.28	≥1.50	4	0.43	0.42
ZCT150		6	0.34	0.44		2	0.38	0.18
ZCB00	**All**	93	0.86	0.57	**All**	93	0.86	0.57
ZCT150		101	0.45	0.41		101	0.45	0.41

[a] Predicted keratometric cylinder is the vector combination of preoperative keratometric cylinder (magnitude and axis), estimated SIA and incision axis.

Table 32:
Mean Uncorrected Distance Visual Acuity at Six Months Stratified by Keratometric Cylinder
Reported in LogMAR Values with Snellen Equivalent
First Eyes Randomized Control Arm ZCT150 and ZCB00
Safety Population

Model	Preoperative Keratometric Cylinder (D)	UCDVA N	UCDVA LogMAR Mean	UCDVA Snellen Equiv.	UCDVA Std Dev	Predicted Keratometric Cylinder (D)[a] (Preop Kcyl + SIA)	UCDVA N	UCDVA LogMAR Mean	UCDVA Snellen Equiv.	UCDVA Std Dev
ZCB00	<0.75	5	0.04	22	0.19	<0.75	14	0.08	24	0.14
ZCT150		5	0.17	30	0.14		16	0.06	23	0.13
ZCB00	0.75-0.99	22	0.09	25	0.11	0.75-0.99	23	0.22	33	0.15
ZCT150		30	0.08	24	0.11		21	0.15	28	0.17
ZCB00	1.00-1.24	34	0.18	30	0.16	1.00-1.24	31	0.17	30	0.17
ZCT150		38	0.08	24	0.16		36	0.09	25	0.12
ZCB00	1.25-1.49	27	0.20	32	0.16	1.25-1.49	21	0.16	29	0.14
ZCT150		22	0.10	25	0.12		26	0.09	25	0.12
ZCB00	≥1.50	5	0.26	36	0.13	≥1.50	4	0.08	24	0.13
ZCT150		6	0.18	30	0.12		2	0.13	27	0.18
ZCB00	**All**	93	0.16	29	0.16	**All**	93	0.16	29	0.16
ZCT150		101	0.10	25	0.14		101	0.10	25	0.14

[a] Predicted keratometric cylinder is the vector combination of preoperative keratometric cylinder (magnitude and axis), estimated SIA and incision axis.

Table 33:
Change in Absolute Cylinder[a] at Six Months Stratified by Keratometric Cylinder
First Eyes Randomized Control Arm ZCT150 and ZCB00
Safety Population

			Absolute Cylinder Reduction >0.50 D		Change ≤ +/-0.50 D[b]		Increase >0.50 D				Absolute Cylinder Reduction >0.50 D		Change ≤ +/-0.50 D[d]		Increase >0.50 D	
Model	**Preoperative Keratometric Cylinder**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**Predicted Keratometric Cylinder (D)[c] (Preop Kcyl + SIA)**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
ZCB00	<0.75	5	0	0.00	4	80.00	1	20.0	<0.75	14	2	14.29	10	71.43	2	14.29
ZCT150		5	0	0.00	4	80.00	1	20.0		16	5	31.25	9	56.25	2	12.50
ZCB00	0.75-0.99	22	7	31.82	13	59.09	2	9.09	0.75-0.99	23	2	8.70	18	78.26	3	13.04
ZCT150		30	10	33.33	19	63.33	1	3.33		21	15	71.43	6	28.57	0	0.00
ZCB00	1.00-1.24	34	12	35.29	19	55.88	3	8.82	1.00-1.24	31	12	38.71	17	54.84	2	6.45
ZCT150		38	29	76.32	9	23.68	0	0.00		36	22	61.11	14	38.89	0	0.00
ZCB00	1.25-1.49	27	9	33.33	16	59.26	2	7.41	1.25-1.49	21	10	47.62	10	47.62	1	4.76
ZCT150		22	18	81.82	4	18.18	0	0.00		26	19	73.08	7	26.92	0	0.00
ZCB00	≥1.50	5	1	20.00	4	80.00	0	0.00	≥1.50	4	3	75.00	1	25.00	0	0.00
ZCT150		6	6	100.0	0	0.00	0	0.00		2	2	100.0	0	0.00	0	0.00
ZCB00	**All**	93	29	31.18	56	60.22	8	8.60	**All**	93	29	31.18	56	60.22	8	8.60
ZCT150		101	63	62.38	36	35.64	2	1.98		101	63	62.38	36	35.64	2	1.98

%=n/Total Tested

[a] Change in Absolute Cylinder=Postop Ref. Cyl minus Preop Kcyl

[b] Not all eyes were targeted for a reduction in absolute cylinder greater than 0.50 D; therefore, some eyes that achieved the intended cylinder change will be included in the ± 0.50 D column.

[c] Predicted keratometric cylinder is the vector combination of preoperative keratometric cylinder (magnitude and axis), estimated SIA and incision axis.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The TECNIS® Toric ZCT IOL has been marketed in Europe since January 2011 and a European registry database collects clinical data of the TECNIS® Toric IOL.

European registry results from a prospective, observational study conducted at four European hospital eye clinics were presented at Winter ESCRS 2012 (Prague) and have also been compiled into a manuscript for publication. The study included 67 astigmatic eyes of 60 subjects undergoing cataract surgery with implantation of the TECNIS® Toric IOL. At 4-8 weeks postoperatively, UCDVA was 0.15 (±0.17) LogMAR and 20/40 or better in 88% of eyes. Mean refractive cylinder decreased significantly following surgery, from -1.91 (±1.07) to -0.67 (±0.54) diopters. Mean IOL rotation was 3.36 (±3.30) degrees (range 0-12 degrees). Good UCDVA achieved resulted in high levels of patient satisfaction. .

Several other European registry study results from individual physicians were presented at ESCRS 2011 (Vienna). In these presentations, there were limited numbers of patients implanted with the TECNIS® Toric 1-Piece IOL (<20). There were no negative outcomes.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

None

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The TECNIS® Toric 1-Piece IOL is made of the same FDA-approved SENSAR soft acrylic material (P980040/S015), which has a long history of safe clinical use. The results of prior preclinical laboratory testing and animal studies on the surface-treated SENSAR acrylic material and the one-piece lens design support preclinical safety of this lens model. The results of dimensional, optical and mechanical testing of the TECNIS® Toric 1-Piece IOLs demonstrate conformance to applicable ISO standards for intraocular lenses, as well as the ANSI Standard for Toric IOLs, Z80.30, and requirements for cylindrical power correction and optical surface qualities, as well as fold and recovery properties.

The IDE clinical investigation of the TECNIS® Toric 1-Piece IOL provides reasonable assurance of the safety of the TECNIS® Toric 1-Piece IOLs, Models ZCT150, ZCT225, ZCT300 and ZCT400. The primary safety endpoint of the study, best corrected distance visual acuity (BCDVA) vs. ISO 11979-7 SPE (Safety and Performance Endpoint) rates, was achieved at six months as all TECNIS® Toric ZCT first eyes (100%) achieved BCDVA of 20/40 or better, exceeding the ISO SPE rates for posterior chamber IOLs. In addition, the TECNIS® Toric ZCT IOL was found to meet the ANSI Standard for Toric IOLs, Z80.30, requirement for rotational stability (>90% of eyes having ≤ 5^o axis change between consecutive visits approximately three months apart) as ≥ 93% of Toric ZCT first eyes had a change in axis of ≤5^o between stability visits approximately three months apart. Four toric first eyes (2.3%; 4/174) underwent lens repositioning procedures early in the postoperative period due to lens rotation noted one day postoperatively. In all four cases, the lenses were stable following the repositioning procedures. The rate of lens repositioning procedures in this study was not statistically above the ISO SPE rate for secondary-surgical intervention (0.8%). The lens repositioning procedures occurred in ZCT300 and ZCT400 first eyes only (7.3%; 4/55); no ZCT300 or ZCT400 second eyes underwent lens repositioning procedures, thereby yielding an overall rate of 4.7% (4/85) for all ZCT300 and ZCT400 eyes. (Note that repositioning is an elective procedure as subjects can wear glasses to correct residual astigmatism.) Other complications reported were typical and within the remaining ISO SPE rates. Optical/visual symptoms were assessed during the study and no impact from the toric surface was found as results were comparable or improved for toric vs. control eyes and also comparable between low cylinder and higher cylinder (>2.00 D at the corneal plane) toric correction.

In addition, the safety of the one-piece platform as well as the TECNIS® aspheric surface for the reduction of spherical aberration was previously established with the FDA-approved TECNIS® 1-Piece IOL, Model ZCB00 (P980040/S015).

B. Effectiveness Conclusions

The overall effectiveness of the TECNIS® Toric 1-Piece IOLs, Models ZCT150, ZCT225, ZCT300 and ZCT400 was demonstrated in the USA clinical study. The primary effectiveness endpoint, mean percent reduction in cylinder, was met with statistically significant improvements in the mean percent reduction in cylinder at six months for ZCT150 toric eyes vs. ZCB00 control eyes as well as for ZCT225, ZCT300 and ZCT400 (vs. target). Other refractive outcomes were also in favor of toric eyes vs. control eyes. In addition, improvements in uncorrected distance visual acuity (UCDVA) outcomes were also found with the TECNIS® Toric 1-Piece IOL. Subgroup analysis of refractive and acuity results provided evidence to support device effectiveness at all levels of preoperative keratometric cylinder studied, except for cylinder < 1.00 diopter. Therefore, the indicated range of preoperative corneal astigmatism is limited to greater than or equal to 1.00 diopter. Spectacle independence (at distance) was also improved with the toric IOL for subjects implanted with the ZCT225, ZCT300 and ZCT400 IOLs.

C. Overall Conclusions

The results of both preclinical and clinical evaluations provide reasonable assurance of the safety and effectiveness of the TECNIS® Toric 1-Piece IOLs, Models ZCT150, ZCT225, ZCT300 and ZCT400, for use in the indicated population. Preclinical testing results support the safety of the lens material and the design and packaging configuration for the TECNIS® Toric 1-Piece lenses. The results of the USA clinical investigation provide reasonable assurance of the safety and effectiveness of the TECNIS® Toric 1-Piece IOL for the visual correction of aphakia and pre-existing corneal astigmatism of one diopter or greater in adult patients in whom a cataractous lens has been removed by phacoemulsification.

XIV. CDRH DECISION

CDRH issued an approval order on April 15, 2013. The final conditions of approval cited in the approval order are described below.

As a condition of approval, the applicant must conduct the following post-approval study (PAS):

The New Enrollment Post-Approval Study: This study will evaluate the visual distortions for the TECNIS® Toric IOLs with ≥2.0 D of cylinder correction at the corneal plane (Models ZCT300 and ZCT400). This study will be in a larger population, in clinical practice, compared to a control and is meant to ensure the continued safety of the approved devices. This study will be conducted in two phases:

a. Validation Phase: Before beginning patient enrollment in the PAS phase, the applicant will conduct a validation study of the patient reported outcomes (PRO) instrument, including qualitative and quantitative validation, as outlined in the file "PRO INSTRUMENT VALIDATION FOR THE POST-APPROVAL STUDY OF THE TECNIS TORIC LENS MODELS, ZCT300 AND ZCT400, PROTOCOL NUMBER: TIOL-201-VPAS." Results of the complete validation of the PRO instrument will be provided within 9 months. The PRO instrument will need to be approved by FDA before it can be used in the PAS phase.

b. PAS Phase: This phase will consist of a prospective, multicenter (up to 80 sites), bilateral, non-randomized, open-label comparative clinical study of TECNIS® Toric patients implanted with ZCT300 and/or ZCT400 IOLs compared to monofocal patients with the same level of preoperative corneal astigmatism.

   The primary endpoint consists of the rates of severe complications related to visual distortions at 6 months for the following items: 1) things appearing distorted; 2) objects appearing tilted; 3) floors or flat surfaces appearing curved; and 4) queasiness related to vision. Rates of severe complications related to visual distortions for the TECNIS® Toric IOL group will be no greater than 10 percentage points above those for the monofocal control group.

A total of 385 patients will be enrolled: 220 TECNIS® Toric ZCT300 and ZCT400 patients and 165 control patients, assuming a 10% drop-out rate, a minimum of 200 Toric and 150 control patients will be available for evaluation at 6 months.

The complete adverse event (AE) data will also be reported. This includes the comparative incidence and severity of AEs by treatment group, comparison of device-related events and comparison of unanticipated AEs.

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling. *(See General hints)*

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

ANSI/AAMI/ISO 11135-1, *Sterilization of Healthcare Products – Ethylene Oxide – Part 1: Requirements for Development, Validation, and Routine Control of a Sterilization Process*

ANSI Z80.30 *Ophthalmics – Toric Intraocular Lenses*

ISO 10993, *Biological Evaluation of Medical Devices*

ISO 11979-2, *Ophthalmic Implants – Intraocular Lenses – Part 2: Optical properties and test methods*

ISO 11979-3, *Ophthalmic Implants – Intraocular Lenses – Part 3: Mechanical properties and test methods*

ISO 11979-5, *Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility*

ISO 11979-6, *Ophthalmic Implants – Intraocular Lenses – Part 6: Shelf-life and transport stability*

ISO 11979-7, *Ophthalmic Implants – Intraocular lenses – Part 7: Clinical Investigations*

34/29 USP 2011, *Bacterial Endotoxin Testing*

Zadnik, K, Mutti, D, Adams A. The repeatability of measurement of the ocular components. Invest Ophthalmol Vis Sci. 1992 Jun; 33(7): 2325-33

Visser N, Berendschot T, Verbakel F, de Brabander J, Nuijts R. Comparability and repeatability of corneal astigmatism measurements using different measurement technologies. J. Cataract Refract Surg. 2012 Oct; 38(1): 1764-70