SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Lens, Multifocal Intraocular

Device Trade Name: TECNIS® Multifocal 1-Piece Intraocular Lens, Models ZKB00 and ZLB00

Device Procode: MFK

Applicant's Name and Address: Abbott Medical Optics Inc.
1700 East Saint Andrew Place
Santa Ana, CA 92705

Premarket Approval Application (PMA) Number: P980040/S049

Date(s) of Panel Recommendation: None

Date of FDA Notice of Approval: December 17, 2014

The TECNIS® Multifocal 1-Piece Intraocular Lenses (IOLs), Models ZKB00 (+2.75 D) and ZLB00 (+3.25 D) are extensions of AMO's FDA-approved TECNIS® Multifocal 1-Piece IOL, Model ZMB00 (+4.00 D) (PMA P980040/S029), which was approved on January 22, 2010. The ZKB00 and ZLB00 IOLs share the same lens material and optic platform as the ZMB00 lenses, but with lower add powers of +2.75 D and +3.25 D, respectively. The TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00 combine the features of the two FDA-approved parent lenses: the SENSAR 1-Piece lens, Model AAB00 (monofocal mechanical parent), approved on October 10, 2007 under P980040/S015, and the Silicone TECNIS® Multifocal 3-Piece lens, Model ZM900 (multifocal optical parent) approved on January 16, 2009 under P080010. Like the multifocal optical parent, the ZKB00 and ZLB00 lenses are designed with the same optical features available with the ZM900 parent lens; which include an aspheric optic, diffractive multifocal posterior optic profile, and the dioptric power range of +5.0 D to +34.0 D in 0.5 D increments. Models ZM900 and ZMB00 are indicated for primary implantation for the visual correction of aphakia in adult patients with and without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire near, intermediate and distance vision with increased spectacular independence. Model AAB00 is indicated for visual correction of aphakia in adult patients whom a cataractous lens have been removed by extracapsular extraction. The SSED to support these indications are available on the CDRH website and is incorporated by reference here. The current supplement was submitted to include Models ZKB00 and ZLB00 for the TECNIS® Multifocal 1- Piece IOL.

II. INDICATIONS FOR USE

The TECNIS® Multifocal 1-Piece intraocular lenses, Models ZKB00 and ZLB00, are indicated for primary implantation for the visual correction of aphakia in adult patients with and without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire near, intermediate, and distance vision with increased spectacle independence. The intraocular lenses are 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® Multifocal 1-Piece IOL labeling.

V. DEVICE DESCRIPTION

The TECNIS® Multifocal 1-Piece Intraocular Lenses (IOLs), Models ZKB00 and ZLB00, are ultraviolet light-absorbing posterior chamber IOLs on a one-piece multifocal platform. The lenses are available in two add powers: Model ZKB00 has an add power of +2.75 D and Model ZLB00 has an add power of +3.25 D. All models of the TECNIS® Multifocal 1-Piece IOLs are available in the dioptric power range of +5.0 D to +34.0 D in 0.5 D increments.

A summary of the physical characteristics of the TECNIS® Multifocal 1-Piece IOLs is provided in Table 1.

Table 1:
Summary of Physical Characteristics

TECNIS® Multifocal 1-Piece IOL		
Model Numbers	ZKB00	ZLB00
Optic Type	Aspheric Anterior and Diffractive (Multifocal) Posterior Optic	
Optic/Haptic Material *Measured in Water	FDA-approved hydrophobic SENSAR® soft acrylic material with polyethylene glycol surface treatment UV cutoff at 10% Transmittance: 375nm* (5.0 diopter lens) 380nm* (34.0 diopter lens)	
IOL Power (Diopter)	+5.0 D to +34.0 D in +0.5 D increments	
Add Power at IOL Plane (Diopter)	+2.75 D	+3.25 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°	

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for providing this optical correction that is needed after cataract extraction, such as eye glasses, contact lenses, or intraocular lenses (IOLs) of different types. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00, are currently available in Australia, European Union, Hong Kong, India, Israel, New Zealand, Norway, Saudi Arabia, Serbia and Montenegro, Singapore, South Africa, Switzerland, Turkey, and Korea. The lenses have not been withdrawn 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 Intraocular Pressure (IOP) requiring treatment, and secondary surgical intervention.

Secondary surgical interventions include, but are not limited to, lens repositioning (due to decentration, subluxation, etc.), vitreous aspirations or iridectomy for pupillary block, wound leak repair, retinal detachment repair, corneal transplant, lens replacement due to refractive error, and unacceptable optical/visual symptoms or severe inflammation.
Multifocal IOLs in some patients can cause perception of halos around lights, glare, and other visual disturbances including reduced contrast sensitivity.

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

IX. SUMMARY OF PRECLINICAL STUDIES

The preclinical studies performed support the safety and effectiveness of the TECNIS® Multifocal 1-Piece IOLs. The results of these studies are summarized below.

A. Laboratory Studies

1. Physicochemical and Biocompatibility Testing

   All physicochemical and biocompatibility testing are incorporated by reference to P980040/S015 and P980040/S029. No additional testing was needed to support the current submission.

2. Dimensional, Optical, and Mechanical Testing

   Prior to design verification testing, a risk assessment was conducted to determine the appropriate dimensional, optical, mechanical and cosmetic tests required to mitigate any new risks identified for the TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00. The ZKB00 and ZLB00 lenses have identical mechanical and similar optical properties as the sibling lens, the TECNIS® Multifocal 1-Piece, Model ZMB00 (P980040/S029). Therefore, the dimensional and mechanical testing conducted in accordance with the requirements of ISO 11979-3:2006, *Part 3: Mechanical properties and test methods*, 11979-9:2006 for this lens model are incorporated by reference to P980040/S029 and P980040/S015.

   Required dimensional, optical, and mechanical testing was performed on finished, sterilized TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00 to verify the design's conformance to the American National Standards Institute (ANSI) Standard for Multifocal IOLs, ANSI Z80.12: 2007, *ANSI Standard for Ophthalmics – Multifocal Intraocular Lenses* as well ISO 11979-2:1999 *Part 2: Optical properties and test methods*, ISO 11979-3:2006, *Part 3: Mechanical properties and test methods*, 11979-9:2006, Part 9: *Multifocal Intraocular Lenses*, and internal specifications. Folding and insertion testing was also performed to verify recovery of lens properties, such as dioptric power, cosmetic and image quality, following simulated insertion. The ZKB00 and ZLB00 lenses passed all required tests established in the ANSI Z80.12 and ISO 11979-2:1999, 11979-3:2006, and 11979-9:2006 and met product specifications. A summary of the results of the dimensional, optical and mechanical testing performed are summarized in Table 2.

Table 2:
Dimensional, Optical and Mechanical Test Requirements Summary

Test	Purpose	Acceptance Criteria	Results
Optical Requirements			
Dioptric Power	To determine the base dioptric power of the lenses	Dioptric Power P ≤ 15.0 D ±0.3D tolerance 15.0 D < P ≤ 25.0 D ±0.4D tolerance 25.0 D <P ≤ 30.0 D ±0.5D tolerance >30.0 D ±1.0D tolerance	Pass
Image Quality	To evaluate the quality of the image produced by the lenses	ISO eye model Per ISO 11979-9: Mean MTF value minus two standard deviations	Pass
Recovery of Properties Following Simulated Surgical Manipulation			
Dioptric Power	To determine the base dioptric power of the lenses	Dioptric Power P ≤ 15.0 D ±0.3D tolerance 15.0 D <P ≤ 25.0 D ±0.4D tolerance 25.0 D <P ≤ 30.0 D ±0.5D tolerance >30.0 D ±1.0D tolerance	Pass
Image Quality	To evaluate the quality of the image produced by the lenses	ISO eye model Per ISO 11979-9: Mean MTF value minus two standard deviations	Pass
Surface and Bulk Homogeneity	To determine if the lenses are essentially free from defects	Essentially free from defects and deviations from intended features of design	Pass

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

The TECNIS® Multifocal 1-Piece IOLs (Models ZKB00 and ZLB00) are packaged in a polypropylene lens insert that is placed into a polycarbonate "daisy wheel" lens case, and sealed in double Tyvek/Mylar pouches. Pouched lenses are sterilized using ethylene oxide (EO). The EO process was validated using the "overkill" method to demonstrate that the process achieves a sterility assurance level (SAL) of 10^{-6}. In addition, the shelf life and transport stability studies demonstrate that the packaging configuration maintains its sterile barrier and protects the lens during transport. Testing was 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*
- USP 34/ Chapter 29 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 3.

Table 3:
Sterilization, Packaging, Shelf Life and Transport Stability Test Results

Test	Purpose	Acceptance Criteria	Results
EO Validation	Evaluate sterility	No positive biological indicators	Pass
Ethylene Oxide Residuals	Evaluate toxicity	≤1.25 µg/IOL	Pass
Ethylene Chlorohydrin Residuals	Evaluate toxicity	≤5.0 µg/IOL	Pass
Bioburden	Evaluate sterility	<100 cfu/IOL	Pass
Bacterial endotoxin	Evaluate sterility	<0.1 EU/IOL	Pass
Package Evaluation – Outer Pouch Burst strength	Evaluate seal integrity	Burst strength ≥ 24" in water	Pass
Package Evaluation – Inner Pouch Burst strength	Evaluate Package Seal Integrity	Burst strength ≥ 28" in water	Pass
Package Evaluation – Microbial Barrier Testing (Aerosol Challenge Test)	Evaluate Whole Package Integrity	No growth of challenge organism	Pass
Transport Stability	Evaluate package integrity and device stability	Manufacturing specification met after exposing samples to simulated transport conditions.	Pass
Exhaustive Extraction	To evaluate potential for toxic extractable components during shelf life	Conforms to SENSAR acrylic historical norms	Conforms

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of cataract surgery and intraocular lens implantation with the TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00 for primary implantation for the visual correction of aphakia in adult patients. The TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, are made of the same materials and geometry as the currently marketed TECNIS® Multifocal IOL, Model ZMB00; however, with lower IOL add powers (ZKB00 +2.75 D, ZLB00 +3.25 D, and ZMB00 +4.00 D). The study was conducted in the U.S. and the U.K. under G120091. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The study began on 11/6/2012 and all 6-month visits were complete as of 10/21/2013. The database for this PMA supplement was locked for analysis on 10/28/2013 and included 445 implanted subjects. (The study was a 1-year study and the applicant provided an update on safety in Amendment 1.) There were 19 investigative sites.

The study was a prospective, multicenter, bilateral, open-label, evaluator-masked, modified-parallel group, 3-armed, 1-year clinical investigation designed to evaluate approximately 150 bilateral ZKB00 subjects, 150 bilateral ZLB00 subjects and 150 bilateral TECNIS® monofocal ZCB00 control subjects (a legally marketed alternative with similar indications for use). Subjects, in consultation with their surgeon/investigators, chose the IOL model to be implanted.

Statistical analysis was based on frequentist and descriptive methods. The two TECNIS® Multifocal IOL models (ZKB00 and ZLB00) were compared to the monofocal control IOL (TECNIS® 1-Piece IOL Model ZCB00) for effectiveness endpoints and for the safety non-inferiority analysis of best corrected distance visual acuity (BCDVA) results. The primary analysis group consists of first-eye or binocular data as appropriate; second-eye data were considered supplementary. For monocular distance corrected near visual acuity (DCNVA) and binocular diopters of defocus (20/40 or better), mean values for each multifocal test lens group and the control lens group were compared using two-sample t-tests for superiority. For combined binocular distance and near visual acuity as well as spectacle independence, comparisons between lens groups were evaluated using logistic regression for imputed data or Fisher's Exact test for available binocular questionnaire data.

Missing data were imputed using multiple imputation methods. Because the treatment assignment was not randomized, propensity analysis was performed. For monocular DCNVA and binocular diopters of defocus (20/40 or better), mean values for each multifocal test lens group and the control lens group were compared using two-sample t-tests. The Type-I error rate was set at 2.5% (one-sided). Hierarchical methods were used to adjust for multiple comparisons related to the primary effectiveness endpoint with the hypothesis for the higher-add ZLB00 IOL (+3.25 D)

tested first, followed by the lower-add ZKB00 IOL (+2.75 D). For combined binocular distance and near visual acuity as well as spectacle independence, comparisons between lens groups were evaluated using logistic regression for imputed data or Fisher's Exact test for available binocular questionnaire data. Complications and adverse events as well as the proportion of first eyes achieving 20/40 or better BCDVA were compared to ISO safety and performance endpoints (SPE) rates (ISO 11979-7:2006) for each multifocal test lens group using an Exact test based on the binomial distribution. Mean first-eye BCDVA for each multifocal test lens group were compared to the control lens group and analyzed using non-inferiority methods. Median binocular contrast sensitivity for each multifocal test lens group was compared to the control lens group.

Sample size was justified based on monocular, distance-corrected near visual acuity. There was over 90% power to detect a 0.7-line or greater difference in mean visual acuity between the test and control lens groups (assumes one-sided testing with an alpha of 0.025 and standard deviation of 1.6 lines) with 135 subjects in each lens group.

1. Clinical Inclusion and Exclusion Criteria

   All subjects were enrolled from the normal cataract surgical populations at the investigative sites. In general, subjects were to have healthy eyes with no pathology other than cataract in both eyes.

   Enrollment in the study was limited to patients who met the following key inclusion criteria:

   - Age 18 or greater
   - Bilateral cataracts 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 20/25 or better in each eye
   - Preoperative corneal astigmatism of 1.0 D or less

   Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

   - Requiring an intraocular lens power outside the available range of +16.0 to +28.0 D
   - 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, prior refractive or other 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 or any inability to focus, fixate or maintain binocular vision
  - Corneal abnormalities (including irregular astigmatism)
  - Pupil abnormalities
  - Capsule or zonule abnormalities
  - Glaucomatous changes
  - 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
- Desire for monovision correction

2. Follow-up Schedule

All patients in the study had regular examinations according to the schedule shown below, in Table 4.

Table 4:
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 month)	Both Eyes	30-60 days postop from 2nd eye surgery
9	Postop 4 (6 months)	Both Eyes	120-180 days postop from 2nd eye surgery
10	Postop 5 (1 year)	Both Eyes	330-420 days postop from 2nd eye surgery

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

Preoperatively, the evaluations that were performed in relation to the index procedure, and postoperatively, the objective and subjective parameters measured during the study, are portrayed in Table 5. Adverse events and complications were recorded at all visits.

The key timepoint for evaluation of the safety and effectiveness outcomes was at 6 months postoperatively.

Table 5: Summary of Examinations Required at Each Visit

Examination	Preop Both eyes	Op 1 1st eye	1 day 1st eye	1 wk 1st eye	Op 2 2nd eye	1 day 2nd eye	1 wk 2nd eye	1 mo Both eyes	6 mos Both eyes	1 year Both eyes
Ocular history, inclusion/exclusion criteria	X									
Informed consent	X									
Potential visual acuity	X									
Targeted refraction/IOL power calculation/axial length	X									
Lens power/serial number/operative procedures		X			X					
Manifest refraction (Snellen preop; ETDRS postop)	X			X			X	X	X	X
UCDVA-photopic, monocular (Snellen preop; ETDRS postop)	X			X			X	X	X	X
UCDVA-photopic, binocular (ETDRS)									X	X
BCDVA-photopic, monocular (Snellen preop; ETDRS postop)	X			X			X	X	X	X
BCDVA-photopic, binocular (ETDRS)									X	X
Binocular BCDVA defocus curve testing[a]									X	
UCNVA-photopic, monocular at 40 cm and best distance (ETDRS)								X	X	X
UCNVA-photopic, binocular at 40 cm and best distance (ETDRS)									X	X
DCNVA-photopic, monocular at 40 cm and best distance (ETDRS)								X	X	X
DCNVA-photopic, binocular at 40 cm and best distance (ETDRS)									X	X
DCNVA-mesopic, monocular at 40 cm and best distance (ETDRS)									X	
DCNVA-mesopic, binocular at 40 cm and best distance (ETDRS)									X	
BCNVA-photopic, threshold with **minimum** add binocular at 40 cm									X	
Binocular best-corrected distance contrast sensitivity testing[b]									X	
Pupil size, photopic	X							X	X	X
Pupil size, mesopic									X	
Keratometry	X[c]							X	X	X
Intraocular pressure	X		X	X		X	X	X	X	X
Biomicroscopic slit-lamp exam[d]	X		X	X		X	X	X	X	X
Dilated fundus exam	X								X[e]	X[e,f]
Adverse events		X	X	X	X	X	X	X	X	X
Ocular medications	X	X	X	X	X	X	X	X	X	X
Ocular symptoms	X		X	X		X	X	X	X	X
Subject questionnaire (by third party)									X	X

[a]Conducted on a subset of subjects
[b]Under mesopic conditions with and without glare, and photopic conditions with glare
[c]With corneal stability check for contact lens wearers
[d]Includes determination of medical and lens findings/complications, including lens decentration and tilt
[e]With fundus visualization
[f]If medically indicated

3. Clinical Endpoints

All clinical endpoints were evaluated at 6 months postoperatively. Because the lenses under study were modifications of approved IOLs, conclusions regarding device safety come primarily from the results from the study of the parent IOLs. See the SSED for the parent lenses for key safety results.

The key safety endpoints for this study were postoperative complication and adverse event rates vs. ISO SPE rates (ISO 11979-7:2006), binocular best corrected distance contrast sensitivity (mesopic with and without glare, and photopic with glare), mean monocular BCDVA compared to the monofocal control IOL, optical/visual symptoms, fundus visualization and lens stability.

The primary effectiveness endpoint was mean (LogMAR) DCNVA under photopic conditions at 40 cm. Secondary effectiveness endpoints were mean binocular best-corrected defocus range with 20/40 or better visual acuity (sub-study of ~60 subjects per arm), the proportion of subjects reporting that they "never" wear glasses, and the proportion of subjects achieving combined BCDVA of 20/25 or better and binocular DCNVA of 20/32 or better.

Other endpoints included the proportion of eyes achieving monocular BCDVA of 20/40 or better vs. ISO SPE rates, binocular BCDVA, monocular and binocular uncorrected distance visual acuity (UCDVA), monocular and binocular uncorrected near visual acuity (UCNVA) at 40 cm and best distance, monocular DCNVA at best distance, binocular DCNVA at 40 cm and best distance, monocular and binocular mesopic DCNVA at 40 cm and best distance, binocular threshold best-corrected near visual acuity (BCNVA) with minimum add at 40 cm, and subject satisfaction/other questionnaire items.

The primary and secondary study endpoints were analyzed for three population groups: safety (all implanted eyes), intent-to-treat (ITT) with data imputation for missing values (included all implanted eyes and all subjects not necessarily implanted), and per-protocol (subjects/eyes without any protocol deviations). Safety endpoints were primarily analyzed using only the safety population. Although the primary analysis population group for the primary and secondary study endpoints was the ITT population, results presented in this summary are predominantly presented for the safety population for consistency.

B. Accountability of PMA Cohort

A total of 445 subjects were enrolled and implanted in the clinical study across 19 clinical sites (18 in the US and 1 in the UK). Of these, 147 were in the ZKB00 IOL group, 150 in the ZLB00 IOL group and 148 in the monofocal control group. Only three subjects were not implanted bilaterally (2 ZKB00 and 1 ZCB00) for reasons unrelated to outcomes of the first-eye. At the time of database lock, of 445 subjects enrolled in the PMA study, 99% (441) primary eyes were available for analysis at time of endpoint evaluation, the 6-month postoperative visit.

Subject accountability through 6 months is presented in Table 6 to Table 9 for ZKB00, ZLB00 and ZCB00 first-eyes (subjects), respectively. At 6 months, the overall percent accountability was 99.1% (441/445). Only four subjects (0.9%; 4/445) were unavailable at 6 months; 3 of which (0.7%; 3/445) were lost-to-follow-up due to reasons unrelated to vision, well below the general guideline of 10%.

Table 6:
ZKB00 First Eye Accountability Through 6 Months
Safety Population (N=147)

	1 Day		1 Week		1 Month		6 Months	
Subject status	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Total Available for Analysis	**147**	**100**	**147**	**100**	**146**	**99.3**	**145**	**98.6**
--Out of Interval	0	0.0	3	2.0	1	0.7	0	0.0
--In Interval	147	100	144	98.0	145	98.6	145	98.6
Missing Subjects	0	0.0	0	0.0	1	0.7	2	1.4
--In interval or past interval (form not yet received)	0	0.0	0	0.0	0	0.0	0	0.0
--Active (not yet in visit interval)	0	0.0	0	0.0	0	0.0	0	0.0
--Missed visit	0	0.0	0	0.0	1[a]	0.7	1[b]	0.7
--Lost-to-follow-up	0	0.0	0	0.0	0	0.0	1[c,d]	0.7
--Discontinued	0	0.0	0	0.0	0	0.0	0	0.0

[a] Subject 1023 missed visit but was seen at 6 months.
[b] Subject 813 missed visit due to illness.
[c] Subject 501 exited the study due to illness.
[d] Note: an additional subject (#1115) exited the study after the 6-month exam (moved out of state).

Table 7:
ZLB00 First Eye Accountability Through 6 Months
Safety Population (N=150)

	1 Day		1 Week		1 Month		6 Months	
Subject status	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Total Available for Analysis	**150**	**100**	**150**	**100**	**149**	**99.3**	**150**	**100**
--Out of Interval	0	0.0	1	0.7	1	0.7	2	1.3
--In Interval	150	100	149	99.3	148	98.7	148	98.7
Missing Subjects	0	0.0	0	0.0	1	0.7	0	0.0
--In interval or past interval (form not yet received)	0	0.0	0	0.0	0	0.0	0	0.0
--Active (not yet in visit interval)	0	0.0	0	0.0	0	0.0	0	0.0
--Missed visit	0	0.0	0	0.0	1[a]	0.7	0	0.0
--Lost-to-follow-up	0	0.0	0	0.0	0	0.0	0	0.0
--Discontinued	0	0.0	0	0.0	0	0.0	0	0.0

[a] Subject 1017 missed visit but was seen at 6 months.

Table 8:
ZCB00 First Eye Accountability Through 6 Months
Safety Population (N =148)

Subject status	1 Day		1 Week		1 Month		6 Months	
	n	%	n	%	n	%	n	%
Total Available for Analysis	**148**	**100**	**148**	**100**	**146**	**98.6**	**146**	**98.6**
--Out of Interval	0	0.0	1	0.7	2	1.4	0	0.0
--In Interval	148	100	147	99.3	144	97.3	146	98.6
Missing Subjects	0	0.0	0	0.0	2	1.4	2	1.4
--In interval or past interval (form not yet received)	0	0.0	0	0.0	0	0.0	0	0.0
--Active (not yet in visit interval)	0	0.0	0	0.0	0	0.0	0	0.0
--Missed visit	0	0.0	0	0.0	0	0.0	0	0.0
--Lost-to-follow-up	0	0.0	0	0.0	2[a,b]	1.4	2[a,b]	1.4
--Discontinued	0	0.0	0	0.0	0	0.0	0	0.0

[a] Subject 1902 was uncooperative and refused further participation in the study.
[b] Subject 542 (unilateral subject) was uncooperative and refused further participation in the study prior to second-eye implantation.

Table 9 presents the questionnaire accountability at 6 months.

Table 9:
Questionnaire Accountability at 6 Months
Bilateral Subjects - ZKB00, ZLB00 and ZCB00 Control
Safety Population

Subject status	ZKB00 N	ZLB00 n	ZCB00 n
Available for Analysis	145	150	146
Unilateral Subjects (not analyzed)	2	0	0
Did Not Complete Questionnaire	1[a]	1[a]	1[b]
TOTAL	**142**	**149**	**145**

[a] Subjects were uncooperative when called for the questionnaire.
[b] Subject suffered a stroke following the 6-month visit and could not complete the questionnaire.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population were typical for an IOL study performed largely in the US. Subject demographics and preoperative baseline parameters were similar between the ZKB00 and ZLB00 lens groups vs. the ZCB00 control group. As this study was not randomized, age matching was performed during subject enrollment; analyses showed that mean ages between IOL groups were comparable with mean ages of approximately 68 in each lens group. Table 10 presents the demographic data for the ZKB00 and ZLB00 IOL groups vs. the ZCB00 control group. Table 11 and Table 12 present the key ocular baseline parameters.

Table 10:
Demographics for ZKB00, ZLB00 and ZCB00 Control Subjects
Safety Population

		ZKB00 N=147		ZLB00 N=150		ZCB00 N=148	
Age (years)	Mean	67.6		67.9		68.5	
	Std	6.9		6.8		6.8	
	Median	69		67		69	
	Min	48		49		49	
	Max	84		85		86	
	Not Reported	0		0		0	
	P-Value vs. ZCB00	0.2520[a]		0.4821[a]		N/A	
Age Group	<60	21	(14.3%)	18	(12.0%)	13	(8.8%)
	60-69	58	(39.5%)	68	(45.3%)	67	(45.3%)
	70-79	66	(44.9%)	59	(39.3%)	60	(40.5%)
	≥80	2	(1.4%)	5	(3.3%)	8	(5.4%)
	Not Reported	0	-	0	-	0	-
Sex	Male	73	(49.7%)	49	(32.7%)	63	(42.6%)
	Female	74	(50.3%)	101	(67.3%)	85	(57.4%)
	Not Reported	0	-	0	-	0	-
	P-Value vs. ZCB00	0.2437[b]		0.0940[b]		N/A	
Race	Asian	5	(3.4%)	4	(2.7%)	2	(1.4%)
	African American	5	(3.4%)	6	(4.0%)	4	(2.7%)
	Caucasian	137	(93.2%)	140	(93.3%)	142	(95.9%)
	Not Reported	0	-	0	(0.0%)	0	-
	P-Value vs. ZCB00	0.4196[b]		0.6725[b]		N/A	
Iris Color	Blue/Gray	59	(40.1%)	49	(32.7%)	58	(39.2%)
	Brown/Black	50	(34.0%)	68	(45.3%)	55	(37.2%)
	Green/Hazel	38	(25.9%)	33	(22.0%)	35	(23.6%)
	Not Reported	0	-	0	-	0	-
	P-value vs. ZCB00	0.8419[b]		0.3340[b]		N/A	

%=n/N(Total) excluding not reported
[a] P value from 2-sided 2-sample t-test
[b] P value from 2-sided Fisher's exact test

Table 11:
Mean Target Spherical Equivalent, Preop Keratometric Cylinder and IOL Power Implanted
First Eyes - ZKB00 and ZCB00 Control
Safety Population

Variable	IOL	N	Mean	Std. Dev.	Median	Min.	Max.	Lower 95% Conf. Limit	Upper 95% Conf. Limit	P Value[a]
Target Spherical Equivalent (D)	ZKB00	147	-0.050	0.106	-0.060	-0.28	0.22	-0.065	-0.036	-
	ZCB00	148	-0.070	0.126	-0.080	-0.49	0.40	-0.088	-0.053	-
	Difference	-	0.020	-	-	-	-	-0.002	0.042	0.1399
Keratometric Cylinder (D)	ZKB00	147	0.510	0.243	0.500	0.00	1.00	0.477	0.543	-
	ZCB00	148	0.543	0.266	0.570	0.00	1.09	0.507	0.579	-
	Difference	-	-0.033	-	-	-	-	-0.082	0.016	0.2652
IOL Power Implanted (D)	ZKB00	147	21.136	2.511	21.000	16.00	27.00	20.793	21.479	-
	ZCB00	148	21.044	1.992	21.000	16.00	28.00	20.773	21.315	-
	Difference	-	0.092	-	-	-	-	-0.344	0.528	0.7274

[a] P-Value from 2-sided 2-sample t-test

Table 12:
Mean Target Spherical Equivalent, Preop Keratometric Cylinder and IOL Power Implanted
First Eyes - ZLB00 and ZCB00 Control
Safety Population

Variable	IOL	N	Mean	Std. Dev.	Median	Min.	Max.	Lower 95% Conf. Limit	Upper 95% Conf. Limit	P Value[a]
Target Spherical Equivalent (D)	ZLB00	150	-0.052	0.117	-0.060	-0.26	0.42	-0.068	-0.036	-
	ZCB00	148	-0.070	0.126	-0.080	-0.49	0.40	-0.088	-0.053	-
	Difference	-	0.018	-	-	-	-	-0.005	0.042	0.1932
Keratometric Cylinder (D)	ZLB00	150	0.493	0.253	0.500	0.00	1.00	0.459	0.528	-
	ZCB00	148	0.543	0.266	0.570	0.00	1.09	0.507	0.579	-
	Difference	-	-0.050	-	-	-	-	-0.099	-0.000	0.0987
IOL Power Implanted (D)	ZLB00	150	21.550	2.475	22.000	16.00	26.00	21.215	21.885	-
	ZCB00	148	21.044	1.992	21.000	16.00	28.00	20.773	21.315	-
	Difference	-	0.506	-	-	-	-	0.077	0.935	0.0527

[a] P-Value from 2-sided 2-sample t-test

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the safety cohort of 297 subjects (147 ZKB00 model, 150 ZLB00 model) implanted with the investigational lenses, and the 441 subjects (145 ZKB00 model, 150 ZLB00 model, 146 ZCB00 control model) available for the 6-month evaluation. The key safety outcomes for this study are presented below in Table 13 to Table 26. Adverse effects are reported in Table 13 and Table 14.

ADVERSE EFFECTS THAT OCCURRED IN THE PMA CLINICAL STUDY:

Overall, 3.6% (16/445) of subjects experienced adverse events during the study to date; however, only 0.7% (3/445) of subjects (1 ZKB00, 1 ZLB00 and 1 ZCB00) experienced lens-related events, and only one of which was related to the optical/visual properties of the lens (1 ZLB00 lens was removed due to halos; 0.7%, 1/150). A slightly higher incidence of ZLB00 subjects (5.3%; 8/150) experienced adverse events compared to ZKB00 subjects (3.4%; 5/147) or ZCB00 subjects (2.0%; 3/148); however, the events were not lens-related and were generally a result of secondary surgical interventions (SSIs) to treat primary events (endophthalmitis, etc.).

The incidence rates of cumulative adverse events for the ZKB00 and ZLB00 first eyes compared to the ISO SPE rates are presented in Table 13. The incidence rates for the ZKB00 and ZLB00 compared favorably to the specified ISO SPE rates. Only the rate of surgical re-interventions in the ZLB00 group were statistically higher than the FDA grid rate of 0.8% (**p=0.0075** for first and second eyes, respectively). Secondary surgical intervention events for ZKB00 and ZLB00 are specified in Table 14.

Table 13:
6-Month Cumulative Medical Complications/Adverse Events
vs. ISO 11979-7 SPE[a] Rates
Safety Population

Cumulative Medical Complications/ Adverse Events	ISO SPE[a] Rate	ZKB00 First Eyes N=147		ZKB00 Second Eyes N=145		ZLB00 First Eyes N=150		ZLB00 Second Eyes N=150	
	%	n	%	n	%	n	%	n	%
Cystoid macular edema[b]	3.0	2	1.4	1	0.7	0	0.0	0	0.0
Hypopyon	0.3	0	0.0	0	0.0	0	0.0	1	0.7[c]
Endophthalmitis	0.1	0	0.0	0	0.0	0	0.0	1	0.7[d]
Lens dislocated from posterior chamber	0.1	0	0.0	0	0.0	0	0.0	0	0.0
Pupillary block	0.1	0	0.0	0	0.0	0	0.0	0	0.0
Retinal detachment	0.3	0	0.0	0	0.0	0	0.0	1	0.7[c]
Eyes with secondary surgical intervention	0.8	0	0.0	3	2.1[e]	5[f]	3.3[g]	5[h]	3.3[g]
-Lens related		0	0.0	1	0.7	1	0.7	0	0.0
-Not lens related		0	0.0	2	1.4	4[f]	2.7	5[h]	3.3[g]

[a] Per ISO 11979-7 Ophthalmic Implants-Intraocular Lenses (Part 7): The SPE rate is the safety and performance endpoint.
[b] Includes all cases of CME, regardless of investigator opinion regarding AE status.
[c] Incidence rate is not statistically significantly different than ISO SPE rate (p=0.3628)
[d] Incidence rate is not statistically significantly different than ISO SPE rate (p=0.1394)
[e] Incidence rate is not statistically significantly different than ISO SPE rate (p=0.1112)
[f] One incident was reported after database lock.
[g] Incidence rate is statistically significantly different than ISO SPE rate (**p=0.0075**)
[h] One of these 5 eyes underwent 3 SSIs for a total of 7 SSI procedures in 5 eyes.

Table 14:
Secondary Surgical Interventions
Safety Population

	ZKB00				ZLB00			
	First Eyes N=147		Second Eyes N=145		First Eyes N=150		Second Eyes N=150	
Secondary Surgical Interventions	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Secondary Surgical Interventions:								
Lens-Related	**0**	**0.0**	**1**	**0.7**	**1**	**0.7**	**0**	**0.0**
IOL exchange (halos)	0	0.0	0	0.0	1	0.7	0	0.0
IOL repositioning (decentration)	0	0.0	1	0.7	0	0.0	0	0.0
Secondary Surgical Interventions:								
Not Lens-Related	**0**	**0.0**	**2**	**1.4**	**4**	**2.7**	**5**	**3.3**
Blepharoplasty	0	0.0	0	0.0	2	1.3	2	1.3
Retinal repair - Endophthalmitis	0	0.0	0	0.0	0	0.0	1[a]	0.7
-Retinal detachment	0	0.0	0	0.0	0	0.0	1	0.7
- Retinal tear	0	0.0	0	0.0	1	0.7	0	0.0
Removal of residual cortex	0	0.0	1	0.7	0	0.0	0	0.0
Ruptured globe repair & iridoplasty	0	0.0	0	0.0	0	0.0	1[b]	0.7
Treatment injections for medical complications:								
-Endophthalmitis (with vitreous tap)	0	0.0	0	0.0	0	0.0	2[a]	1.3
-Episcleritis	0	0.0	0	0.0	1	0.7	0	0.0
-Diabetic retinopathy	0	0.0	1	0.7	0	0.0	0	0.0
TOTAL Eyes	**0**	**0.0**	**3**	**2.1**	**5**	**3.3**	**5**	**3.3**

[a] Same eye.
[b] Orbital fracture due to fall.

There were no persistent medical complications (0%) present at 6 months for TECNIS® Multifocal IOLs, Models ZKB00 or ZLB00 first or second eyes; therefore, the persistent event rates for the ZKB00 and ZLB00 lens models are below the ISO SPE persistent rates (for corneal edema 0.3%; cystoid macular edema 0.5%; iritis 0.3%; and raised IOP requiring treatment 0.4%).

The safety of the device for multifocal correction of aphakia was not based on this sample alone, but rather on all available data for the device (and the parent IOLs) to date. The safety data from this study were for confirmatory purposes.

Adverse events and complications and their observed rates were generally similar to those seen from studies of similar types of IOLs.

Distance Visual Acuity

Distance visual acuities were tested using 100% Early Treatment Diabetic Retinopathy Study (ETDRS) charts at 4.0 meters under photopic conditions (85 cd/m^2). Table 15 presents monocular distance visual acuity results for ZKB00, ZLB00 and ZCB00 control first-eyes at 6 months. The proportions of first eyes achieving monocular BCDVA of 20/40 or better for the ZKB00 lens group (99.3%) and the ZLB00 lens group (100%) were above the ISO SPE criterion for percent of

eyes with best-corrected distance visual acuity achieving 20/40 or better (92.5%). In addition, the proportions of best-case (Table 16**)** first eyes achieving monocular BCDVA of 20/40 or better also exceeded the best-case ISO SPE rate (96.87%) for both the ZKB00 group (99.3%) and the ZLB00 group (100%). The distribution of binocular distance visual acuity results for ZKB00, ZLB00 and ZCB00 subjects at 6 months are presented in Table 17.

Table 15:
Monocular Distance Visual Acuity at 6 Months
Safety Population

Visual Acuity		ZKB00 (+2.75) N=145				ZLB00 (+3.25) N=150				ZCB00 N=146			
		Uncorrected		Best Corrected		Uncorrected		Best Corrected		Uncorrected		Best Corrected	
LogMAR	(Snellen)	n	%	n	%	N	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	60	41.4	123	84.8	60	40.0	124	82.7	71	48.6	128	87.7
0.1	**(20/25 or Better)**	102	70.3	141	97.2	101	67.3	141	94.0	118	80.8	143	97.9
0.2	**(20/32 or Better)**	125	86.2	144	99.3	127	84.7	150	100.0	131	89.7	145	99.3
0.3	**(20/40 or Better)**	**135**	**93.1**	**144**	**99.3**	**144**	**96.0**	**150**	**100.0**	**139**	**95.2**	**146**	**100.0**
0.4-0.6	**(20/50-20/80)**	10	6.9	1	0.7	6	4.0	0	0.0	7	4.8	0	0.0
0.7	**(20/100) or worse**	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

%=n/Total Tested

Table 16:
Monocular Best Corrected Distance Visual Acuity at 6 Months
Best-Case Safety Population

Visual Acuity		ZKB00 (+2.75) N=144		ZLB00 (+3.75) N=149		ZCB00 N=144	
LogMAR	(Snellen)	n	%	n	%	n	%
0.0	**(20/20 or Better)**	123	85.4	124	83.2	127	88.2
0.1	**(20/25 or Better)**	140	97.2	141	94.6	141	97.9
0.2	**(20/32 or Better)**	143	99.3	149	100.0	143	99.3
0.3	**(20/40 or Better)**	**143**	**99.3**	**149**	**100.0**	**144**	**100.0**
0.4-0.6	**(20/50-20/80)**	1	0.7	0	0.0	0	0.0
0.7	**(20/100) or worse**	0	0.0	0	0.0	0	0.0

%=n/Total Tested

Table 17:
Binocular Distance Visual Acuity at 6 Months
Safety Population

Visual Acuity		ZKB00 (+2.75) N=145				ZLB00 (+3.25) N=150				ZCB00 N=146			
		Uncorrected		Best Corrected		Uncorrected		Best Corrected		Uncorrected		Best Corrected	
LogMAR (Snellen)		n	%	n	%	N	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	105	73.4	135	94.4	108	72.0	141	94.0	110	75.3	140	95.9
0.1	**(20/25 or Better)**	133	93.0	142	99.3	138	92.0	150	100.0	133	91.1	146	100.0
0.2	**(20/32 or Better)**	140	97.9	143	100.0	148	98.7	150	100.0	141	96.6	146	100.0
0.3	**(20/40 or Better)**	**142**	**99.3**	**143**	**100.0**	**149**	**99.3**	**150**	**100.0**	**145**	**99.3**	**146**	**100.0**
0.4-0.6	**(20/50-20/80)**	1	0.7	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0
0.7	**(20/100) or worse**	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

%=n/Total Tested

Table 18 presents mean monocular distance visual acuities at 6 months for ZKB00, ZLB00 and ZCB00 first eyes. Comparison of mean monocular BCDVA to the control lens was one of the key safety endpoints. Non-inferiority testing showed that the upper limit of the 90% confidence intervals of the mean difference in BCDVA between each of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, and the ZCB00 control group to be less than 1.0 line in both cases (LogMAR 0.030, 0.3 lines, for the ZKB00 group vs. the ZCB00 group; and, LogMAR 0.041, 0.4 lines, for the ZLB00 group vs. the ZCB00 group). These results indicate that both the ZKB00 and ZLB00 IOLs are non-inferior to the monofocal control lens in providing distance visual acuity. Table 19 presents mean binocular distance visual acuities at 6 months for ZKB00, ZLB00 and ZCB00 subjects.

Table 18:
Mean Monocular Distance Visual Acuity at 6 Months
First Eyes - ZKB00 and ZLB00 vs. ZCB00 Control
Safety Population

	IOL	N	Mean LogMAR	Snellen Line Equivalent	Std. Dev.	Lower 90% Conf. Limit	Upper 90% Conf. Limit
Uncorrected	**ZKB00**	145	0.102	20/25	0.136	0.083	0.121
	ZCB00	146	0.078	20/25	0.134	0.060	0.097
	Difference	-	0.024	0.2 lines	-	-0.002	0.050
	ZLB00	150	0.112	20/25	0.131	0.094	0.130
	ZCB00	146	0.078	20/25	0.134	0.060	0.097
	Difference	-	0.034	0.3 lines	-	0.008	0.059
Best Corrected	**ZKB00**	145	-0.022	20/20	0.087	-0.034	-0.011
	ZCB00	146	-0.036	20/20	0.087	-0.048	-0.024
	Difference	-	0.013	0.1 lines	-	-0.003	0.030[a]
	ZLB00	150	-0.012	20/20	0.085	-0.023	-0.000
	ZCB00	146	-0.036	20/20	0.087	-0.048	-0.024
	Difference	-	0.024	0.2 lines	-	0.008	0.041[a]

[a] The upper 90% CI is used for non-inferiority comparison due to the mean difference of test minus control with negative LogMAR values.

Table 19:
Mean Binocular Distance Visual Acuity at 6 Months
First Eyes - ZKB00 and ZLB00 vs. ZCB00 Control
Safety Population

	IOL	N	Mean LogMAR	Snellen Line Equivalent	Std. Dev.	Lower 90% Conf. Limit	Upper 90% Conf. Limit
Uncorrected	**ZKB00**	143	0.008	20/20	0.101	-0.006	0.022
	ZCB00	146	-0.005	20/20	0.112	-0.020	0.011
	Difference	-	0.013	0.1 lines	-	-0.008	0.034
	ZLB00	150	0.016	20/20	0.100	0.003	0.030
	ZCB00	146	-0.005	20/20	0.112	-0.020	0.011
	Difference	-	0.021	0.2 lines	-	0.000	0.041
Best Corrected	**ZKB00**	143	-0.073	20/16	0.079	-0.084	-0.062
	ZCB00	146	-0.085	20/16	0.076	-0.095	-0.075
	Difference	-	0.012	0.1 lines	-	-0.003	0.028
	ZLB00	150	-0.062	20/16	0.075	-0.072	-0.052
	ZCB00	146	-0.085	20/16	0.076	-0.095	-0.075
	Difference	-	0.023	0.2 lines	-	0.008	0.037

Contrast Sensitivity

Binocular best corrected distance contrast sensitivity testing was performed using the Vector Vision ETDRS light box and contrast sensitivity charts under three lighting conditions: mesopic without glare (Table 20), mesopic with glare (Table 21), and photopic with glare (Table 22). As expected with multifocality, median contrast scores for both the ZKB00 and ZLB00 multifocal subject groups were somewhat reduced compared to the monofocal control group under each lighting condition and spatial frequency (Table 20 - Table 22). The most challenging condition was mesopic lighting with glare as median scores were slightly lower for all IOL groups and median differences between IOL groups were the most prominent. However, with the exception of the mesopic 12 cpd conditions, median differences between IOL groups were generally within -0.15 log units. The largest median differences were between the ZKB00 (+2.75 add) multifocal lens and the ZCB00 monofocal control lens (-0.250 and -0.255 for the 12 cpd mesopic without glare and mesopic with glare conditions, respectively). Assignment of reference patch scores to unmeasurable values would bias the mean values higher and parametric variability estimates lower. The medians (50^{th} percentile values) in Table 20 - Table 22 are unbiased, because less than 25% of the values were unmeasurable (i.e., subjects not seeing the reference pattern) for any condition. The 25^{th} and 75^{th} percentiles are also reported to give unbiased estimates of the variability of the results. In addition, no appreciable pupil-size effects were seen when results were analyzed by pupil size; this was expected due to the optic design of the TECNIS® Multifocal IOLs.

Table 20:
Contrast Sensitivity[a] at 6 Months Mesopic Without Glare

Spatial Frequency	Lens Model	N	Mesopic Without Glare				
			25th percentile	Median[b] 50th percentile	75th percentile	Subjects who did not see the reference pattern[a]	
						n	%
1.5 cpd	ZKB00 (+2.75)	143	1.445	1.595	1.745	0	0.0
	ZLB00 (+3.25)	150	1.370	1.595	1.745	0	0.0
	ZCB00	146	1.520	1.670	1.745	0	0.0
3.0 cpd	ZKB00 (+2.75)	143	1.415	1.635	1.780	0	0
	ZLB00 (+3.25)	150	1.485	1.705	1.855	0	0.0
	ZCB00	146	1.415	1.630	1.780	1	0.7
6.0 cpd	ZKB00 (+2.75)	143	1.380	1.625	1.700	5	3.5
	ZLB00 (+3.25)	150	1.380	1.550	1.770	3	2.0
	ZCB00	146	1.465	1.700	1.770	3	2.1
12.0 cpd	ZKB00 (+2.75)	143	0.610	0.995	1.250	17	11.9
	ZLB00 (+3.25)	150	0.760	1.080	1.395	17	11.3
	ZCB00	146	0.995	1.245	1.470	13	8.9

[a] All subjects analyzed; Note: reference scores assigned for subjects who did not see the reference pattern for a spatial frequency.
[b] $Log_{10}(Contrast^{-1})$.

Table 21:
Contrast Sensitivity[a] at 6 Months Mesopic With Glare

Spatial Frequency	Lens Model	N	Mesopic With Glare				
			25th percentile	Median[b] 50th percentile	75th percentile	Subjects who did not see the reference pattern[a]	
						n	%
1.5 cpd	ZKB00 (+2.75)	143	1.370	1.595	1.745	1	0.7
	ZLB00 (+3.25)	150	1.370	1.595	1.820	0	0.0
	ZCB00	146	1.445	1.670	1.745	0	0.0
3.0 cpd	ZKB00 (+2.75)	143	1.415	1.560	1.780	1	0.7
	ZLB00 (+3.25)	150	1.490	1.705	1.855	1	0.7
	ZCB00	146	1.490	1.630	1.780	0	0.0
6.0 cpd	ZKB00 (+2.75)	143	1.380	1.550	1.700	9	6.3
	ZLB00 (+3.25)	150	1.380	1.625	1.700	6	4.0
	ZCB00	146	1.465	1.700	1.840	3	2.1
12.0 cpd	ZKB00 (+2.75)	143	0.610	0.995	1.325	26	18.2
	ZLB00 (+3.25)	150	0.610	1.080	1.375	22	14.7
	ZCB00	146	0.910	1.250	1.540	13	8.9

[a] All subjects analyzed; Note: reference scores assigned for subjects who did not see the reference pattern for a spatial frequency.
[b] $Log_{10}(Contrast^{-1})$.

Table 22:
Contrast Sensitivity[a] at 6 Months Photopic With Glare

Spatial Frequency	Lens Model	N	Photopic With Glare				
			25th percentile	Median[b] 50th percentile	75th percentile	Subjects who did not see the reference pattern[a] n	%
3.0 cpd	ZKB00 (+2.75)	143	1.485	1.705	1.780	1	0.7
	ZLB00 (+3.25)	150	1.490	1.705	1.855	1	0.7
	ZCB00	146	1.630	1.743	1.855	0	0.0
6.0 cpd	ZKB00 (+2.75)	143	1.625	1.770	1.915	4	2.8
	ZLB00 (+3.25)	150	1.625	1.770	1.990	5	3.3
	ZCB00	146	1.770	1.915	2.065	2	1.4
12.0 cpd	ZKB00 (+2.75)	143	1.165	1.400	1.615	7	4.9
	ZLB00 (+3.25)	150	1.250	1.470	1.690	9	6.0
	ZCB00	146	1.325	1.540	1.690	8	5.5
18.0 cpd	ZKB00 (+2.75)	143	0.640	0.960	1.180	9	6.3
	ZLB00 (+3.25)	150	0.725	0.995	1.175	14	9.3
	ZCB00	146	0.885	1.100	1.250	9	6.2

[a] All subjects analyzed; Note: reference scores assigned for subjects who did not see the reference pattern for a spatial frequency.
[b] $Log_{10}(Contrast^{-1})$.

General Medical and Lens Findings

Medical and lens findings in this study were typical and within expected ranges for the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, as well as the TECNIS® ZCB00 monofocal control IOL. The most reported finding at 6 months was posterior capsule opacification (PCO) for all three lens types (29%-37%) with the majority of reports noted as "trace". General medical and lens findings for the TECNIS® Multifocal IOLs were comparable to the monofocal control IOL, indicating that the difference in optical surface design for the TECNIS® Multifocal IOLs does not impact the safety of the lens with respect to general medical outcomes.

Fundus Visualization

At the 6-month study visit, investigators evaluated the ability to visualize the fundus during the dilated fundus exams. In all cases (100%; 145/145 ZKB00 (+2.75), 150/150 ZLB00 (+3.25) multifocal first eyes and 146/146 ZCB00 monofocal first eyes), fundus visualization was deemed "adequate." During the study, no difficulties were reported in evaluating or treating retinal complications in multifocal eyes; however, only three multifocal eyes underwent a surgical retinal procedure in this study.

Optical/Visual Symptoms

Table 23 provides a summary of patient questionnaire results (directed reports) concerning difficulties with visual problems. The most reported symptom/difficulty was for halos for the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00 compared to the TECNIS® 1-Piece monofocal control IOL, Model ZCB00, as might be expected. Optical/visual symptoms spontaneously reported by subjects (non-directed reports) are presented in Table 24. These non-directed reports are typically noted with lower incidences than when subjects are specifically asked about difficulties with visual problems via the questionnaire.

Table 25 presents the trouble with glare reported when driving toward the sun or oncoming headlights. Higher incidence/difficulty was noted for ZLB00 subjects compared to ZKB00 subjects, in line with the higher amount of add power in each multifocal IOL (+2.75 D for the ZKB00 IOL vs. +3.25 D for the ZLB00 IOL). Nevertheless, directed reports of severe difficulty with halos for either the ZKB00 IOL (5.6%) or the ZLB00 IOL (10.7%) at 6 months are within that of the original TECNIS® Multifocal IOL, Model ZM900, at 1 year (18.3%). Similarly, non-directed responses of severe halos for ZKB00 first eyes (0.7%) and ZLB00 first eyes (4.0%) at 6 months are also within that of the original TECNIS® Multifocal IOL, Model ZM900, at 1 year (5.4%).

Table 23:
Degree of Difficulty with Night Vision, Glare/Flare and Halos at 6 Months
(Directed Reports from a Questionnaire; Scale of 1-7)
(With Glasses if You Need Them)
Safety Population

	ZKB00 N=142		ZLB00 N=149		ZCB00 N=145	
	n	%	n	%	n	%
Night Vision						
No difficulty (1, 2)	129	90.8	125	83.9	125	86.2
Moderate difficulty (3, 4, 5)	12	8.5	20	13.4	14	9.7
Severe difficulty (6, 7)	1	0.7	4	2.7	6	4.1
Glare/Flare						
No difficulty (1, 2)	109	76.8	103	69.1	117	80.7
Moderate difficulty (3, 4, 5)	31	21.8	38	25.5	18	12.4
Severe difficulty (6, 7)	2	1.4	8	5.4	10	6.9
Halos						
No difficulty (1, 2)	98	69.0	85	57.0	122	84.1
Moderate difficulty (3, 4, 5)	36	25.4	48	32.2	20	13.8
Severe difficulty (6, 7)	8	5.6	16	10.7	3	2.1

%=n/N

Table 24:
Non-Directed Reports of Ocular Symptoms (First Eyes) at 6 Months
Safety Population

Ocular Symptoms	ZKB00 N=145		ZLB00 N=150		ZCB00 N=146	
	n	%	n	%	n	%
Image Quality						
Blurred vision	28	19.3	25	16.7	38	26.0
- Overall	4	2.8	7	4.7	2	1.4
- Distance	5	3.4	2	1.3	3	2.1
- Intermediate	3	2.1	3	2.0	2	1.4
- Near	18	12.4	14	9.3	33	22.6
Optical/Visual						
Halos	29	20.0	37	24.7	6	4.1
- Mild	20	13.8	20	13.3	4	2.7
- Moderate	8	5.5	11	7.3	2	1.4
- Severe	1	0.7	6	4.0	0	0.0
Night Glare	7	4.8	8	5.3	2	1.4
- Mild	5	3.4	2	1.3	1	0.7
- Moderate	2	1.4	3	2.0	1	0.7
-Severe	0	0.0	3	2.0	0	0.0
Starbursts	3	2.1	6	4.0	0	0.0
- Mild	1	0.7	3	2.0	0	0.0
- Moderate	2	1.4	1	0.7	0	0.0
-Severe	0	0.0	2	1.3	0	0.0
Night vision difficulty (overall)	0	0.0	4	2.7	2	1.4
Sensation						
Irritated/itchy/scratchy/burning/gritty	7	4.8	20	13.3	13	8.9
Dryness	16	11.0	22	14.7	18	12.3

Note: Includes reports of symptoms common to multifocal IOLs (halos, night glare, starbursts, and night vision difficulties) as well as any findings reported with an incidence of 10% or more at 6 months.

%=n/N

Table 25:
Degree[a] of Trouble with Glare at 6 Months
(Without Glasses)

	ZKB00 N=142		ZLB00 N=149		ZCB00 N=145	
	n	**%**	**n**	**%**	**n**	**%**
Driving towards the sun						
No trouble at all (0)	84	60.0	94	65.3	87	61.7
A little bit of trouble (1)	24	17.1	16	11.1	23	16.3
Moderate trouble (2)	20	14.3	18	12.5	17	12.1
Considerable trouble (3)	10	7.1	12	8.3	11	7.8
Major or overwhelming trouble (4)	2	1.4	4	2.8	3	2.1
I do not perform this activity for reasons unrelated to my vision (5)	2	-	5	-	3	-
Not reported	0	-	0	-	1	-
Driving toward oncoming headlights						
No trouble at all (0)	70	51.9	66	48.5	84	64.1
A little bit of trouble (1)	30	22.2	30	22.1	22	16.8
Moderate trouble (2)	19	14.1	23	16.9	13	9.9
Considerable trouble (3)	13	9.6	13	9.6	8	6.1
Major or overwhelming trouble (4)	3	2.2	4	2.9	4	3.1
I do not perform this activity for reasons unrelated to my vision (5)	7	-	13	-	13	-
Not reported	0	-	0	-	1	-

%=n/N excluding Not reported and Do Not Perform this activity.
[a] On a scale of 0-4 (5 = I do not perform this activity for reasons unrelated to my vision)

Table 26 presents the rating of the quality of near and far vision while indoors. Over 90% of subjects reported good vision indoors overall; however, fewer multifocal subjects reported good vision while indoors under dim lighting.

The questionnaire administered was not validated according to FDA's guidance document entitled "Patient-reported outcome measures: use in medical product development to support labeling claims", dated December 2009.

Table 26:
Rating of the Quality[a] (Sharpness, Clarity) of Near and Far Vision at 6 Months (With Glasses if Needed)

	Near Vision						Far Vision					
	ZKB00 N=142		ZLB00 N=149		ZCB00 N=145		ZKB00 N=142		ZLB00 N=149		ZCB00 N=145	
	n	%	%	%	n	%	n	%	n	%	n	%
Indoors												
Poor Vision (1,2)	0	0.0	1	0.7	2	1.4	0	0.0	0	0.0	0	0.0
Fair Vision (3,4,5)	12	8.5	9	6.0	9	6.2	8	5.6	8	5.4	8	5.5
Good Vision (6,7)	130	91.5	139	93.3	134	92.4	134	94.4	140	94.6	137	94.5
Not Reported	0	-	0	-	0	-	0	-	1	-	0	-
Indoors with dim lighting												
Poor Vision (1,2)	3	2.1	2	1.3	2	1.4	0	0.0	1	0.7	0	0.0
Fair Vision (3,4,5)	48	33.8	53	35.6	35	24.1	27	19.0	29	19.7	20	13.8
Good Vision (6,7)	91	64.1	94	63.1	108	74.5	115	81.0	117	79.6	125	86.2
Not Reported	0	-	0	-	0	-	0	-	2	-	0	-

%=n/N excluding Not Reported
[a] On a scale of 1-7

2. Effectiveness Results

The analysis of effectiveness was based primarily on the acuity data evaluable at the 6 month time point. Key effectiveness outcomes are presented in Table 27 to Table 35 and Figure 1 to Figure 4.

Near Visual Acuities

Near visual acuities were tested using 100% ETDRS near charts at the fixed test distance of 40 cm and at the subjects' best test distance, with and without distance correction under photopic (85 cd/m^2) lighting conditions and with distance correction under mesopic (3 cd/m^2) lighting conditions.

The primary effectiveness endpoint of improved mean, monocular, photopic distance-corrected near visual acuity (DCNVA) at 40 cm was achieved for both TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, with statistically significant improvements ($p<0.0001$) in mean DCNVA at 6 months vs. the control IOL. Model ZKB00 (+2.75 D add power) was found to have a statistically significant improvement ($p<0.0001$) of 3.3 lines of monocular DCNVA over the control IOL (Table 27) while Model ZLB00 (+3.25 D add power) was found to have a statistically significant improvement ($p<0.0001$) of 4.0 lines of monocular DCNVA over the control IOL (Table 27) when tested at 40 cm. For the primary analysis group of the ITT population, results were also statistically significant ($p<0.0001$) with similar improvements in favor of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00.

Table 27:
Mean Monocular Distance Corrected Near Visual Acuity at 40 cm at 6 Months
First Eyes - ZKB00 and ZLB00 vs. ZCB00 Control
Safety Population

IOL	N	Mean LogMAR	Snellen Line Equivalent	Std. Dev.	Lower 95% Conf. Limit	Upper 95% Conf. Limit	P Value[a]
ZKB00	145	0.252	20/40	0.143	0.229	0.276	
ZCB00	146	0.582	20/80	0.166	0.555	0.609	
Difference		**-0.329**	**-3.3 lines**	-	-0.365	-0.294	**<0.0001**
ZLB00	150	0.179	20/32	0.129	0.158	0.200	
ZCB00	146	0.582	20/80	0.166	0.555	0.609	
Difference		**-0.403**	**-4.0 lines**	-	-0.437	-0.369	**<0.0001**

[a] P value from 1-sided 2-sample t-test

Mean outcomes for all monocular and binocular near visual acuities tested at 6 months for the ZKB00, ZLB00 and ZCB00 lens groups are presented in Table 28**.** In all cases, mean visual acuity outcomes at 6 months were improved for the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, by 3 to 4 lines compared to the control IOL, similar to outcomes for the primary study endpoint of DCNVA at 40 cm. Overall, the various near visual acuity results demonstrate the effectiveness of the TECNIS® Multifocal IOL, Models ZKB00 (+2.75) and ZLB00 (+3.25) in providing substantial near vision compared to the monofocal control lens.

Table 28:
Mean Near Visual Acuity at 6 Months
Safety Population

			Monocular				Binocular			
Near Visual Acuity	**Test Distance**	**Lens Group**	**N**	**Mean LogMAR**	**Snellen Line Equiv.**	**Line Gain vs. ZCB00**	**N**	**Mean LogMAR**	**Snellen Line Equiv.**	**Line Gain vs. ZCB00**
Uncorrected (Photopic)	40 cm	ZKB00 (+2.75)	145	0.238	20/32	3.3	143	0.135	20/25	3.1
		ZLB00 (+3.25)	150	0.185	20/32	3.8	150	0.097	20/25	3.5
		ZCB00	146	0.568	20/80		146	0.443	20/50	
	Best[a]	ZKB00 (+2.75)	145	0.148	20/25	3.3	143	0.079	20/25	2.7
		ZLB00 (+3.25)	150	0.141	20/25	3.3	150	0.068	20/25	2.8
		ZCB00	146	0.476	20/63		146	0.346	20/40	
Distance Corrected[b] (Photopic)	40 cm	ZKB00 (+2.75)	145	0.252[b]	20/40	3.3	143	0.170	20/32	3.2
		ZLB00 (+3.25)	150	0.179[b]	20/32	4.0	150	0.106	20/25	3.8
		ZCB00	146	0.582	20/80		146	0.488	20/63	
	Best[a]	ZKB00 (+2.75)	145	0.154	20/32	3.5	143	0.093	20/25	3.2
		ZLB00 (+3.25)	150	0.141	20/25	3.6	150	0.077	20/25	3.3
		ZCB00	146	0.503	20/63		146	0.408	20/50	
Distance Corrected Mesopic	40 cm	ZKB00 (+2.75)	145	0.447	20/50	3.3	143	0.362	20/50	3.4
		ZLB00 (+3.25)	150	0.375	20/50	4.0	150	0.282	20/40	4.2
		ZCB00	146	0.773	20/126		146	0.698	20/100	
	Best[a]	ZKB00 (+2.75)	145	0.367	20/50	3.2	143	0.292	20/40	3.3
		ZLB00 (+3.25)	150	0.330	20/40	3.6	150	0.259	20/40	3.6
		ZCB00	146	0.692	20/100		146	0.624	20/80	

[a] Best test distance is the distance at which the subject can read the smallest letters with the most ease.
[b] The primary study endpoint was photopic distance corrected near VA for first eyes. ZKB00 & ZLB00 showed statistically significantly better VA compared to ZCB00 with **p <0.0001** (from one sided two sample t-test).

Table 29**,** Table 30**,** and Table 31 present the distributions of monocular UCNVA, DCNVA and mesopic DCNVA at 6 months for ZKB00, ZLB00 and ZCB00 first eyes. Table 32, Table 33, and Table 34 present the distributions of binocular UCNVA, DCNVA and mesopic DCNVA at 6 months for ZKB00, ZLB00 and ZCB00 subjects.

Table 29:
Monocular Uncorrected Near Visual Acuity at 6 Months
First Eyes - ZKB00, ZLB00 and ZCB00 Control
Safety Population

Visual Acuity		ZKB00 (+2.75)				ZLB00 (+3.25)				ZCB00			
		40 cm N=145		Best N=145		40 cm N=150		Best N=150		40 cm N=146		Best N=146	
LogMAR (Snellen)		n	%	n	%	n	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	11	7.6	25	17.2	21	14.0	30	20.0	0	0.0	0	0.0
0.1	**(20/25 or Better)**	44	30.3	76	52.4	74	49.3	123	82.0	1	0.7	6	4.1
0.2	**(20/32 or Better)**	89	61.4	119	82.1	109	72.7	127	84.7	5	3.4	19	13.0
0.3	**(20/40 or Better)**	**112**	**77.2**	**135**	**93.1**	**132**	**88.0**	**140**	**93.3**	**26**	**17.8**	**44**	**30.1**
0.4-0.6	**(20/50-20/80)**	31	21.4	10	6.9	17	11.3	10	6.7	67	45.9	72	49.3
0.7	**(20/100) or worse**	2	1.4	0	0.0	1	0.7	0	0.0	53	36.3	30	20.5

%=n/Total Tested

Table 30:
Monocular Distance Corrected Near Visual Acuity at 6 Months
First Eyes - ZKB00, ZLB00 and ZCB00 Control
Safety Population

Visual Acuity		ZKB00 (+2.75)				ZLB00 (+3.25)				ZCB00			
		40 cm N=145		Best N=145		40 cm N=150		Best N=150		40 cm N=146		Best N=146	
LogMAR (Snellen)		n	%	n	%	n	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	10	6.9	31	21.4	19	12.7	39	26.0	0	0.0	0	0.0
0.1	**(20/25 or Better)**	38	26.2	73	50.3	77	51.3	87	58.0	1	0.7	3	2.1
0.2	**(20/32 or Better)**	74	51.0	110	75.9	113	75.3	123	82.0	6	4.1	11	7.5
0.3	**(20/40 or Better)**	**116**	**80.0**	**136**	**93.8**	**136**	**90.7**	**136**	**90.7**	**16**	**11.0**	**25**	**17.1**
0.4-0.6	**(20/50-20/80)**	27	18.6	9	6.2	14	9.3	14	9.3	83	56.8	95	65.1
0.7	**(20/100) or worse**	2	1.4	0	0.0	0	0.0	0	0.0	47	32.2	26	17.8

%=n/Total Tested

Table 31:

Monocular Mesopic Distance Corrected Near Visual Acuity at 6 Months
First Eyes - ZKB00, ZLB00 and ZCB00 Control
Safety Population

Visual Acuity		ZKB00 (+2.75)				ZLB00 (+3.25)				ZCB00			
		40 cm N=145		Best N=145		40 cm N=150		Best N=150		40 cm N=146		Best N=146	
LogMAR (Snellen)		n	%	n	%	n	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	0	0.0	1	0.7	2	1.3	3	2.0	0	0.0	0	0.0
0.1	**(20/25 or Better)**	3	2.1	12	8.3	17	11.3	28	18.7	0	0.0	0	0.0
0.2	**(20/32 or Better)**	15	10.3	40	27.6	39	26.0	62	41.3	0	0.0	0	0.0
0.3	**(20/40 or Better)**	**46**	**31.7**	**74**	**51.0**	**74**	**49.3**	**90**	**60.0**	**0**	**0.0**	**1**	**0.7**
0.4-0.6	**(20/50-20/80)**	88	60.7	63	43.4	62	41.3	46	30.7	34	23.3	58	39.7
0.7	**(20/100) or worse**	11	7.6	8	5.5	14	9.3	14	9.3	112	76.7	87	59.6

%=n/Total Tested

Table 32:
Binocular Uncorrected Near Visual Acuity at 6 Months
ZKB00, ZLB00 and ZCB00 Control
Safety Population

Visual Acuity		ZKB00 (+2.75)				ZLB00 (+3.25)				ZCB00			
		40 cm N=143		Best N=143		40 cm N=150		Best N=150		40 cm N=146		Best N=146	
LogMAR (Snellen)		n	%	n	%	n	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	35	24.5	57	39.9	52	34.7	64	42.7	0	0.0	6	4.1
0.1	**(20/25 or Better)**	91	63.6	107	74.8	118	78.7	123	82.0	6	4.1	16	11.0
0.2	**(20/32 or Better)**	120	83.9	133	93.0	142	94.7	145	96.7	23	15.8	48	32.9
0.3	**(20/40 or Better)**	**136**	**95.1**	**141**	**98.6**	**148**	**98.7**	**149**	**99.3**	**49**	**33.6**	**74**	**50.7**
0.4-0.6	**(20/50-20/80)**	7	4.9	2	1.4	2	1.3	1	0.7	83	56.8	66	45.2
0.7	**(20/100) or worse**	0	0.0	0	0.0	0	0.0	0	0.0	14	9.6	6	4.1

%=n/Total Tested

Table 33:
Binocular Distance Corrected Near Visual Acuity at 6 Months
ZKB00, ZLB00 and ZCB00 Control
Safety Population

Visual Acuity		ZKB00 (+2.75)				ZLB00 (+3.25)				ZCB00			
		40 cm N=143		Best N=143		40 cm N=150		Best N=150		40 cm N=146		Best N=146	
LogMAR (Snellen)		n	%	n	%	n	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	16	11.2	43	30.1	47	31.3	56	37.3	0	0.0	2	1.4
0.1	**(20/25 or Better)**	72	50.3	108	75.5	111	74.0	120	80.0	2	1.4	6	4.1
0.2	**(20/32 or Better)**	109	76.2	133	93.0	136	90.7	135	90.0	10	6.8	18	12.3
0.3	**(20/40 or Better)**	**139**	**97.2**	**142**	**99.3**	**146**	**97.3**	**148**	**98.7**	**34**	**23.3**	**55**	**37.7**
0.4-0.6	**(20/50-20/80)**	4	2.8	1	0.7	4	2.7	2	1.3	88	60.3	77	52.7
0.7	**(20/100) or worse**	0	0.0	0	0.0	0	0.0	0	0.0	24	16.4	14	9.6

%=n/Total Tested

Table 34:
Binocular Mesopic Distance Corrected Near Visual Acuity at 6 Months
ZKB00, ZLB00 and ZCB00 Control
Safety Population

Visual Acuity		ZKB00 (+2.75)				ZLB00 (+3.25)				ZCB00			
		40 cm N=143		Best N=143		40 cm N=150		Best N=150		40 cm N=146		Best N=146	
LogMAR (Snellen)		n	%	n	%	n	%	n	%	n	%	n	%
0.0	**(20/20 or Better)**	1	0.7	3	2.1	11	7.3	19	12.7	0	0.0	1	0.7
0.1	**(20/25 or Better)**	9	6.3	24	16.8	40	26.7	47	31.3	0	0.0	1	0.7
0.2	**(20/32 or Better)**	34	23.8	65	45.5	77	51.3	89	59.3	1	0.7	1	0.7
0.3	**(20/40 or Better)**	**73**	**51.0**	**103**	**72.0**	**104**	**69.3**	**113**	**75.3**	**2**	**1.4**	**12**	**8.2**
0.4-0.6	**(20/50-20/80)**	64	44.7	34	23.8	37	24.7	29	19.3	61	41.8	70	47.9
0.7	**(20/100) or worse**	6	4.2	6	4.2	9	6.0	8	5.3	83	56.8	64	43.8

%=n/Total Tested

Defocus Testing

Defocus curve testing was performed on a subset of approximately 60 subjects from each lens group at the 6-month study exam to evaluate binocular best corrected distance visual acuity defocus curves, and any effects of pupil size. The substudy was a non-randomized, modified parallel-group comparison of the binocular best corrected visual acuity depth of focus. Results were also analyzed for three pupil size ranges: ≤2.5 mm; >2.5 mm and <4.0 mm; and ≥4.0 mm.

Figure 1 presents the defocus curves for all three lens groups combined; results were adjusted for cases with residual refractive error following manifest refraction. Prominent near peaks are shown in Figure 1 at approximately -2.0 D for the ZKB00 (+2.75) IOL and -2.5 D for the ZLB00 (+3.25) IOL. Both ZKB00 (+2.75) and ZLB00 (+3.25) multifocal subjects were found to have a statistically significantly increased ($p<0.0001$) range of defocus with visual acuity of 20/40 or better compared to monofocal subjects (Figure 1 and Table 35), achieving the secondary study endpoint of increased range of defocus with visual acuity of 20/40 or better compared to the monofocal control group. For the ITT population, results were also statistically significant ($p<0.0001$) with similar improvements in favor of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00.

Figure 1:
Binocular Defocus Curves at 6 Months
Bilateral Subjects- ZKB00, ZLB00, and ZCB00
Substudy Safety Population

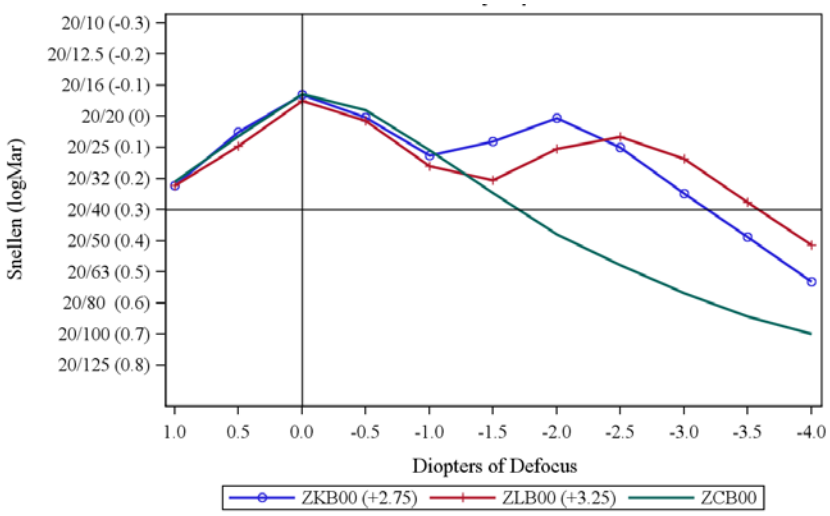


Table 35:
Mean of Diopter Range With Binocular Visual Acuity of 20/40 or Better at 6 Months Defocus Testing[a] Using Range of 0 to -4 Diopters
Substudy Safety Population

IOL	N	Mean (D)	Std Dev.	P-value[b]
ZKB00 (+2.75)	59	3.16	0.50	
ZCB00	61	1.75	0.70	
Difference		1.42		**<0.0001**
ZLB00 (+3.25)	63	3.30	0.69	
ZCB00	61	1.75	0.70	
Difference		1.56		**<0.0001**

[a] Adjusted for cases with residual refractive error following manifest refraction
[b] P-value is from one-sided two-sample t-test

The defocus results of the ZKB00 (+2.75) and ZLB00 (+3.25) multifocal IOLs strongly illustrate the multifocality of the optic design at any pupil size for both the ZKB00 IOL (Figure 2) and the ZLB00 IOL (Figure 3). Minimal pupil size effect was observed.

Figure 2:
Binocular Defocus Curve by Average Pupil Size at 6 Months
Bilateral Subjects—ZKB00

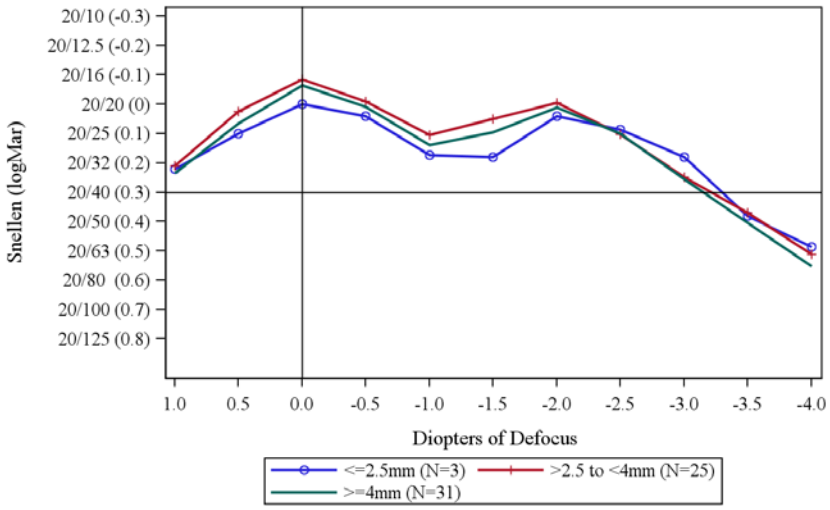
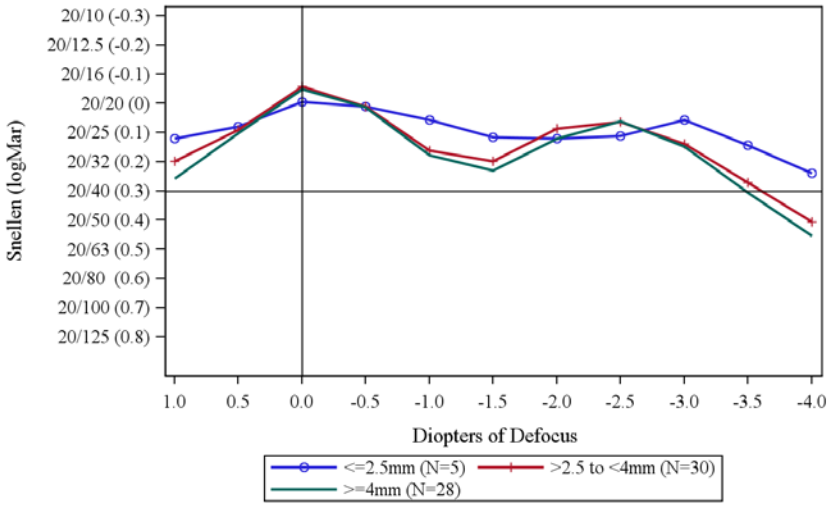


Figure 3:
Binocular Defocus Curve by Average Pupil Size at 6 Months
Bilateral Subjects—ZLB00



Spectacle Independence

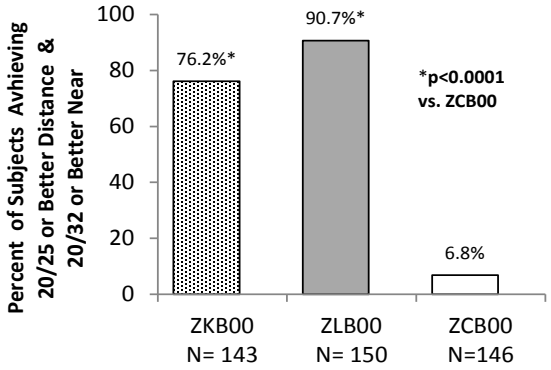
The Modified TyPE Specification for Cataracts (Jonathan Javitt,, M.D., M.P.H.) questionnaire was used to collect information on spectacle usage, visual quality, optical/visual symptoms and other items. The study questionnaires were administered by telephone by third-party, trained interviewers following the completion of the 6-month study exams. Interviewers were masked regarding subject lens type (multifocal or monofocal). The spectacle independence study endpoint was based on a single question from the questionnaire: "How often do you wear glasses?" with the response options of "always," "sometimes" or "never;" only the response "never" was considered spectacle independent. This item was not determined to be a psychometrically valid assessment of the concept of spectacle independence. Both TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, achieved the secondary endpoint of the overall rates of "never using spectacles" for the ZKB00 (+2.75) and ZLB00 (+3.25) lens groups were statistically significantly higher than the monofocal control group (61.3%(87/142), 75.0%(3/145) and 2.1%(3/145), $p<0.001$). For the ITT population, results were also statistically significant ($p<0.0001$) with similar improvements in favor of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00.

Combined Visual Acuities

Combination visual acuities represent the proportion of subjects that simultaneously achieved both binocular best corrected distance visual acuity (BCDVA) of 20/25 or better and binocular distance corrected near visual acuity (DCNVA) of 20/32 or better at the same visit. Figure 4 presents the proportions of subjects that achieved 20/25 or better binocular BCDVA and 20/32 or better binocular DCNVA at 6 months for all three lens groups. The secondary study endpoint of combination distance and near acuities was met for both TECNIS®

Multifocal IOLs, Models ZKB00 and ZLB00, as statistically significantly ($p<0.0001$) more ZKB00 and ZLB00 multifocal subjects achieved the specified combined visual acuities compared to monofocal subjects. With distance correction in place eliminating any effect from residual refractive error, 76.2% of ZKB00 (+2.75 D) subjects and 90.7% of ZLB00 (+3.25 D) subjects achieved 20/25 or better binocular distance and 20/32 or better binocular near visual acuity compared to only 6.8% of monofocal subjects. For the ITT population, results were also statistically significant ($p<0.0001$) with similar improvements in favor of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00.

Figure 4:
Combined 20/25 or Better Binocular Best Corrected Distance and 20/32 or Better Binocular Distance-Corrected Near Visual Acuity at 6 Months Safety Population



3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: site, gender, age, race, and preoperative BCDVA.

POOLING OF DATA ACROSS SITES:

For the primary effectiveness endpoint of mean DCNVA at 40 cm, at all investigational sites, the difference in mean DCNVA between the ZKB00 or ZLB00 IOLs and the ZCB00 control IOL favored the ZKB00 or ZLB00 IOLs. Based on an analysis of variance (ANOVA) model to test for treatment differences between the treatment and control groups while controlling for study site, there were no significant site-by-treatment interactions for either the ZLB00 vs. ZCB00 comparison ($p=0.373$) or the ZKB00 vs. ZCB00 comparison ($p=0.7222$). Thus, results for the primary effectiveness endpoint were consistent across investigative sites.

EFFECTS OF AGE, GENDER, RACE AND PREOPERATIVE BCDVA:

The primary and secondary effectiveness endpoints were calculated separately by subgroups defined by age decade, gender, race and preoperative BCDVA. These analyses were descriptive in nature. For the primary endpoint of mean DCNVA at 40 cm, the difference in mean DCNVA between the ZKB00 or ZLB00 IOLs and the ZCB00 control IOL was 2.0 lines or more favoring the investigational IOLs for all groups within each subgroup for age, gender and preoperative visual acuity. All racial groups, with the exception of Asian (includes Indian), showed a 2-line improvement in mean DCNVA favoring the ZKB00 and ZLB00 IOLs. The mean improvement for Asian subjects receiving the ZKB00 IOL over the control was 1.7 lines (n<10). Thus, for the primary effectiveness endpoint, there was a consistent benefit favoring ZKB00 and ZLB00 IOLs over the ZCB00 control for all subgroup variables.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 19 of which none were full-time or part-time employees of the sponsor and 6 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 6
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00 were CE marked in October 2012 and have been marketed in Europe as of October, 2013. One prior clinical investigation of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, was conducted in Europe. Additionally, a European registry collects clinical data of the marketed lenses, Models ZKB00 and ZLB00.

A. Market Assessment Study of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00

A prospective, multi-center, bilateral, open-label, 3-month market assessment of the TECNIS® Multifocal 1-piece acrylic IOLs, Models ZKB00 and ZLB00, was conducted at six sites in three EU countries. A total of 30 subjects were enrolled; 15 were bilaterally implanted with Model ZKB00 and 15 were bilaterally implanted with Model ZLB00.

Results at the 3 months demonstrated acceptable clinical outcomes of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00. Monocular uncorrected distance visual acuity (UCDVA) of ≤0.3 LogMAR (20/40 Snellen equivalent or better) and monocular best corrected distance visual acuity (BCDVA) of ≤0.1 LogMAR (20/25 Snellen equivalent or better) was achieved for all implanted first eyes. Monocular uncorrected near visual acuity (UCNVA) of ≤0.3 LogMAR (20/40 Snellen equivalent or better) was achieved by 80.0% (12/15) of ZKB00 first eyes and 93.3% (14/15) of ZLB00 first eyes when tested at 40 cm. Monocular distance corrected near visual acuity (DCNVA) of ≤0.3 LogMAR (20/40 Snellen equivalent or better) was achieved by 86.7% (13/15) of ZKB00 first eyes and 100.0% (15/15) of ZLB00 first eyes when tested at 40 cm. However, 100% (15/15) of both ZKB00 and ZLB00 first eyes achieved DCNVA of ≤0.3 LogMAR (20/40 Snellen equivalent or better) at best distance (best score at either 40 cm or the subject's best distance). Both the ZKB00 and ZLB00 multifocal IOLs were found to provide acceptable combination distance and near visual acuities with 93.3% (14/15) of ZKB00 subjects and 100% (15/15) of ZLB00 subjects achieving binocular BCDVA of 20/25 or better and binocular DCNVA of 20/32 or better simultaneously. Binocular defocus results for both lens models demonstrated the typical bimodal multifocal curves with a distance and near peak. The defocus positions of the near peaks were consistent with the add powers of each TECNIS® Multifocal IOL with peaks at approximately -2.0 D of defocus (corresponding to 50 cm) for the ZKB00 IOL (+2.75 D add power), -2.5 D (corresponding to 40 cm) for the ZLB00 IOL (+3.25 D add power). In addition, 80.0% (12/15) of ZKB00 subjects and 93.3% (14/15) of ZLB00 subjects reported never wearing glasses at 3 months. Medical and lens findings reported during the study were minimal and typical of cataract surgery and no lens-related or unanticipated adverse events occurred. Rates of optical/visual symptoms for the ZKB00 and ZLB00 IOLs were consistent with that of the historical, multifocal parent Model ZM900, with the highest rates and most difficulty reported for halos.

Overall, this market assessment study demonstrated that the TECNIS® Multifocal 1-Piece IOL Models ZKB00 and ZLB00 have acceptable clinical outcomes with good distance and near visual acuity and rates of optical/visual symptoms, complications and adverse events, consistent with those of the parent TECNIS Multifocal IOL and typically observed for multifocal IOLs.

XII. PANEL RECOMMENDATIONS

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices

Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The overall effectiveness of the TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00, was demonstrated based on the 6-month results of the IDE clinical investigation. All primary and secondary effectiveness endpoints were achieved by both TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00.

The primary effectiveness endpoint, an improvement in mean monocular DCNVA at 40 cm compared to control, was achieved by both of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, with statistically significant improvements (**p<0.0001**) of 3.3 lines for the ZKB00 IOL group and 4.0 lines for the ZLB00 IOL group compared to the ZCB00 monofocal IOL group. Near visual acuities were also tested uncorrected, at best distance, binocularly, and under mesopic conditions as well. In all cases, mean visual acuity results were approximately 3-4 lines better for the ZKB00 and ZLB00 IOLs compared to the ZCB00 IOL and the proportions of eyes/subjects achieving 20/40 or better near acuity for the ZKB00 and ZLB00 groups were substantially greater than the control group as well.

The effectiveness of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, was also demonstrated by achievement of the secondary study endpoints. The mean range of defocus with visual acuity of 20/40 or better was statistically significantly greater (**p<0.0001**) for the ZKB00 group (3.16 D) and ZLB00 group (3.30 D) compared to the control group (1.75 D). In addition, statistically significantly (**p<0.0001**) greater proportions of ZKB00 subjects (76.2%(109/143)) and ZLB00 subjects (90.7%(136/150)) achieved simultaneous, combined binocular BCDVA of 20/25 or better and DCNVA of 20/32 or better compared to control subjects (6.8%(10/146)), demonstrating the hallmark of multifocality.

Overall, the effectiveness of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, was demonstrated in the clinical IDE investigation with the ability of the IOLs to provide near vision, an expanded range of vision at least 20/40 or better, decreased spectacle use, and good simultaneous distance and near vision.

B. Safety Conclusions

The TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00 are 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® Multifocal 1-Piece IOLs, Models ZMB00, ZKB00 and ZLB00 demonstrate conformance to applicable ISO standards

for IOLs, as well as the ANSI Standard for Multifocal IOLs, Z80.12, requirements for optical surface qualities, and fold and recovery properties.

The 6-month results of the IDE clinical investigation of the TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00 provide reasonable assurance of the safety of the TECNIS® Multifocal 1-Piece IOLs, Models ZKB00 and ZLB00. BCDVA results at 6 months for the ZKB00 and ZLB00 IOLs were clinically comparable and statistically non-inferior to those for the ZCB00 monofocal control group. Furthermore, the proportion of first eyes achieving BCDVA of 20/40 or better for the ZKB00 IOL (99.3% overall and best-case) and the ZLB00 IOL (100% overall and best-case) exceeded the ISO SPE rates of 92.5% for overall BCDVA and 96.7% for best-case BCDVA for posterior chamber IOLs. As might be expected, the most reported optical symptom/difficulty was noted for halos for the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, compared to the TECNIS® ZCB00 Monofocal control IOL. The optical/visual profiles of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00 were as expected and within that of the parent TECNIS® Multifocal IOL, Model ZM900. The incidence of adverse events in the study was low (3.6% (16/445) with only 0.7% (3/445) of subjects (1 ZKB00, 1 ZLB00 and 1 ZCB00) experienced lens-related events, and only one of which was related to the optical/visual properties of the lens (1 ZLB00 lens was removed due to halos; 0.7%, 1/150). The observed complication/adverse event rates for the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, were not statistically higher than the specified ISO SPE rates with the exception of the rate for SSIs for the ZLB00 lens model which was statistically significantly above the ISO SPE rate (0.8%). These results are comparable to the parent TECNIS® Multifocal IOL, Model ZM900.

Overall, the safety of the TECNIS® Multifocal IOLs, Models ZKB00 and ZLB00, was demonstrated in the clinical IDE investigation by non-inferior distance visual acuity outcomes, acceptable contrast sensitivity outcomes, typical optical/visual profiles (consistent with the add power in each IOL), and typical rates of adverse events for both IOL models. In addition, the safety of the one-piece platform was previously established with the FDA-approved TECNIS® 1-Piece IOL, Model ZCB00 (P980040/S015).

C. Benefit-Risk Conclusions

The probable benefits of the devices are based on data collected in clinical studies conducted to support PMA approval as described above. Subjects experienced a mean improvement of approximately 3 – 4 lines in distance-corrected near vision, compared to the monofocal control IOL. With distance correction in place eliminating any effect from residual refractive error, 76.2% of ZKB00 (+2.75 D) subjects and 90.7% of ZLB00 (+3.25 D) subjects achieved 20/25 or better binocular distance and 20/32 or better binocular near visual acuity compared to only 6.8% of monofocal subjects. Since the devices are permanent implants, the benefits are long-lasting.

Additional factors to be considered in determining probable risks and benefits for the TECNIS® Multifocal 1-Piece Intraocular Lenses, Models ZKB00 and ZLB00, devices included the following factors. While the study was non-randomized, demographics

of arms were comparable, internal results were consistent on various outcome measures, including patient-reported outcomes, and results were consistent with prior findings from the parent lenses. Whether a given patient should have one of these lenses implanted depends upon individual tolerance for visual disturbances and reduced contrast sensitivity associated with multifocal lenses versus the perceived benefit of improved clarity of near vision with reduced use of reading glasses.

In conclusion, given the available information above, the data support that, for the primary implantation for the visual correction of aphakia in adult patients, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of these devices when used in accordance with the indications for use.

XIII. CDRH DECISION

CDRH issued an approval order on December 17, 2014.
The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.
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.

XV. REFERENCES

Javitt JC, et al. Cataract extraction with multifocal intraocular lens implantation: Clinical, functional, and quality-of-life outcomes. J Cataract and Refract Surg. September 2000; 26: 1356-1366

Javitt JC, Steinert RF. Cataract Extraction with Multifocal Intraocular Lens Implantation: A Multinational Clinical Trial Evaluating Clinical, Functional, and Quality-of-life-Outcomes. Opthalmology November 2000; 107: 2040-2048